National Institute for Health and Care Excellence

Draft for consultation

Pancreatitis

Pancreatitis: diagnosis and management

NICE guideline <number>

Appendices A – Q

January 2018

Draft for consultation

Developed by the National Guideline Centre, hosted by the Royal College of Physicians

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Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and, where appropriate, their carer or guardian.

Local commissioners and providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

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Appendices

Appendix A: Scope

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Guideline scope

Pancreatitis: diagnosis and management

Topic

The Department of Health in England has asked NICE to develop a clinical guideline on the diagnosis and management of pancreatitis.

This guideline will also be used to develop the NICE quality standard for pancreatitis (including acute pancreatitis).

The guideline will be developed using the methods and processes outlined in Developing NICE guidelines: the manual.

For more information about why this guideline is being developed, and how the guideline will fit into current practice, see the context section.

Who the guideline is for

- People using services, families, carers and the public.
- Healthcare professionals.
- Clinical commissioning groups.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK provinces are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive.

Equality considerations

NICE has carried out an equality impact assessment during scoping. The assessment identified no equality issues relevant to the scope.

NICE guideline: Pancreatitis: diagnosis and management final scope 1 of 12

1 What the guideline is about

1.1 Who is the focus?

Groups that will be covered

- Children, young people and adults with acute or chronic pancreatitis.

Groups that will not be covered

- Children, young people and adults with pancreatic cancer.

1.2 Settings

Settings that will be covered

- All settings in which NHS-commissioned care is provided.

1.3 Activities, services or aspects of care

We will look at evidence on the areas listed below when developing the guideline, but it may not be possible to make recommendations on all the areas.

Key areas that will be covered

1. Fluid resuscitation for people with acute pancreatitis.
2. Using antibiotics to prevent infection in people with acute pancreatitis (including who should be offered antibiotics and which type of antibiotic they should be offered).
3. Referring people with acute pancreatitis to specialist centres.
4. Managing necrosis in people with acute pancreatitis.
5. Managing nutrition in acute pancreatitis.
6. Assessing aetiology of acute pancreatitis.
7. Diagnosing chronic pancreatitis.
8. Assessing aetiology of chronic pancreatitis.
9. Managing pain in people with chronic pancreatitis.
10. Managing biliary obstruction in people with chronic pancreatitis.
11. Managing malabsorption or malnutrition in people with chronic pancreatitis.

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12 Follow-up for people with chronic pancreatitis.
13 Surveillance for pancreatic cancer in people with chronic pancreatitis.
14 Managing pancreatic ascites and pleural effusion secondary to acute or chronic pancreatitis.
15 Managing diabetes secondary to pancreatitis (type 3c diabetes).
16 Lifestyle interventions for people with acute or chronic pancreatitis.
17 Information and support for people with acute or chronic pancreatitis, their families and carers.

Areas that will not be covered

1 Diagnosing and managing pancreatic cancer.
2 Diagnosing acute pancreatitis.
3 Managing gallstones.
4 Duodenal obstruction.
5 Managing haemorrhage secondary to pancreatitis.

1.4 Economic aspects

We will take economic aspects into account when making recommendations. We will develop an economic plan that states for each review question (or key area in the scope) whether economic considerations are relevant, and if so whether this is an area that should be prioritised for economic modelling and analysis. We will review the economic evidence and carry out economic analyses, using an NHS and personal social services (PSS) perspective, as appropriate.

1.5 Key issues and questions

While writing this scope, we have identified the following key issues and draft review questions related to them:

1 Fluid resuscitation for people with acute pancreatitis
1.1 What is the most clinically and cost-effective type of intravenous fluid for resuscitation in people with acute pancreatitis?
1.2 What is the most clinically and cost-effective speed of administration of intravenous fluid for resuscitation in people with acute pancreatitis?

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2 Using antibiotics to prevent infection in acute pancreatitis (including who should be offered antibiotics and which type of antibiotic they should be offered)

2.1 What is the clinical and cost effectiveness of prophylactic antibiotics to prevent infection in people with acute pancreatitis?

3 Referring people with acute pancreatitis to specialist centres

3.1 What are the indications for referring people with acute pancreatitis for specialist input or to a specialist centre?

4 Managing necrosis in people with acute pancreatitis

4.1 What is the most clinically and cost-effective method for managing necrosis in people with acute pancreatitis?

5 Managing nutrition in acute pancreatitis

5.1 What is the most clinically and cost-effective route of feeding for people with acute pancreatitis?

6 Assessing aetiology of acute pancreatitis

6.1 What is the clinical and cost effectiveness of assessing the aetiology of acute pancreatitis to prevent recurrent attacks?

7 Diagnosing chronic pancreatitis

7.1 What is the most clinically and cost-effective method for diagnosing chronic pancreatitis?

8 Assessing aetiology of chronic pancreatitis

8.1 What is the most clinically and cost-effective investigative pathway (including testing for genetic markers and auto-antibodies) for identifying the aetiology of chronic pancreatitis?

9 Managing pain in people with chronic pancreatitis

9.1 What is the most clinically and cost-effective strategy for managing pain in people with chronic pancreatitis secondary to pancreatic duct obstruction, with or without an inflammatory mass?

9.2 What is the most clinically and cost-effective strategy for managing pain in people with chronic pancreatitis secondary to pseudocysts?

9.3 What is the most clinically and cost-effective strategy for managing pain in people with chronic pancreatitis secondary to small-duct disease?

10 Managing biliary obstruction in people with chronic pancreatitis

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10.1 What is the most clinically and cost-effective intervention for treating biliary obstruction in people with chronic pancreatitis?

11 Managing malabsorption or malnutrition in people with chronic pancreatitis

11.1 What is the most clinically and cost-effective intervention (including dietary advice) for managing malabsorption or malnutrition in people with chronic pancreatitis?

12 Follow-up for people with chronic pancreatitis

12.1 What investigations should be conducted during follow-up for people with chronic pancreatitis?

12.2 Where should follow-up for people with chronic pancreatitis take place – primary, secondary or tertiary care?

13 Surveillance for pancreatic cancer in people with chronic pancreatitis

13.1 What is the best assessment for surveillance for pancreatic cancer in people with chronic pancreatitis?

13.2 What is the clinical and cost effectiveness of routine surveillance for pancreatic cancer in people with chronic pancreatitis?

14 Managing pancreatic ascites and pleural effusion secondary to acute or chronic pancreatitis

14.1 What are the most clinically and cost-effective interventions for treating pancreatic ascites and pleural effusion secondary to acute or chronic pancreatitis?

15 Managing diabetes secondary to pancreatitis (type 3c diabetes)

15.1 What are the most clinically and cost-effective management strategies specifically for diabetes secondary to pancreatitis (type 3c diabetes) that is difficult to control?

16 Lifestyle interventions for people with pancreatitis

16.1 What is the effectiveness of stopping or reducing alcohol consumption in reducing recurrent episodes of acute pancreatitis and improving quality of life in people with both chronic and acute pancreatitis?

17 Information and support for people with acute or chronic pancreatitis, their families and carers

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17.1 What information and support should people with acute or chronic pancreatitis, their family and carers receive after diagnosis?

1.6 *Main outcomes*

The main outcomes that will be considered when searching for and assessing the evidence are:

1 Health-related quality of life.
2 Mortality.
3 Pain.

2 Links with other NICE guidance, NICE quality standards, and NICE Pathways

2.1 *NICE guidance*

NICE has produced the following guidance on the experience of people using the NHS. This guideline will not include additional recommendations on these topics unless there are specific issues related to the diagnosis and management of pancreatitis.

- Patient experience in adult NHS services (2012) NICE guideline CG138
- Medicines adherence (2009) NICE guideline CG76
- Medicines optimisation (2015) NICE guideline NG5
- Antimicrobial stewardship (2015) NICE guideline NG15

NICE guidance that is closely related to this guideline

Published

NICE has published the following guidance that is closely related to this guideline:

- Intravenous fluid therapy in children and young people in hospital (2015) NICE guideline NG29
- Gallstone disease: diagnosis and initial management (2014) NICE guideline CG188

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- Intravenous fluid therapy in adults in hospital (2013) NICE guideline CG174
- Alcohol-use disorders: diagnosis, assessment and management of harmful drinking and alcohol dependence (2011) NICE guideline CG115
- Alcohol-use disorders: diagnosis and management of physical complications (2010) NICE guideline CG100
- Alcohol-use disorders: prevention (2010) NICE guideline PH24
- Nutrition support for adults: oral nutrition support, enteral tube feeding and parenteral nutrition (2006) NICE guideline CG32
- Endoscopic transluminal pancreatic necrosectomy (2011) NICE interventional procedure guidance IPG411
- Percutaneous retroperitoneal endoscopic necrosectomy (2011) NICE interventional procedure guidance IPG384 https://guidance.nice.org.uk/IPG384
- Autologous pancreatic islet cell transplantation for improved glycaemic control after pancreatectomy (2008) NICE interventional procedure guidance
- Laparoscopic distal pancreatectomy (2007) NICE interventional procedure guidance IPG204

In development

NICE is currently developing the following guidance that is closely related to this guideline:

- Pancreatic cancer NICE guideline. Publication expected January 2018
- Endoscopic transluminal pancreatic necrosectomy NICE interventional procedure. Publication expected November 2016

2.2 *NICE quality standards*

NICE quality standards that may use this guideline as an evidence source when they are being developed

Pancreatitis (including acute pancreatitis) NICE quality standard. Publication date to be confirmed.

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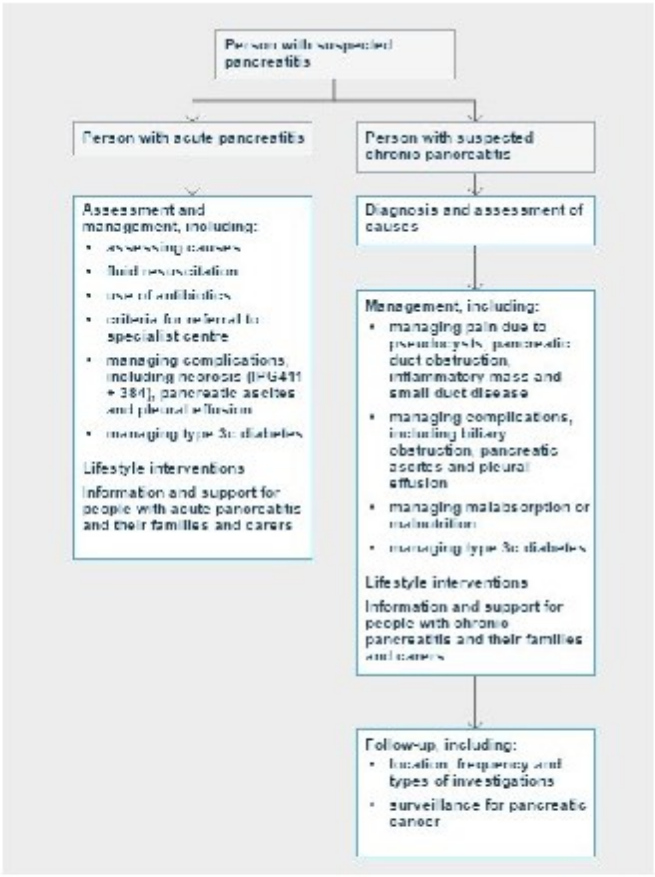
2.3 NICE Pathways

NICE Pathways bring together all NICE guidance and associated products on a topic in an interactive flow chart.

When this guideline is published, the recommendations will be incorporated into a new pathway on pancreatitis.

An outline of the new pathway, based on the scope, is included below. It will be adapted and more detail added as the recommendations are written during guideline development.



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3 Context

3.1 Key facts and figures

Acute pancreatitis

Acute pancreatitis is acute inflammation of the pancreas and a common cause of acute abdominal pain. The incidence in the UK is approximately 56 cases per 100,000 people per year. In the UK approximately 50% of cases are caused by gallstones, 25% by alcohol and 25% by other factors. In 25% of cases acute pancreatitis is severe and associated with complications such as respiratory or kidney failure, or the development of abdominal fluid collections. In these more severe cases people often need intensive care and a prolonged hospital stay, and the mortality rate is 25%, giving an overall mortality rate in acute pancreatitis of approximately 5%.

A small proportion of people with severe acute pancreatitis will develop pancreatic necrosis, and some of these people will need treatment for infected necrosis. Treatment may be by surgery, endoscopy or interventional radiology. Acute pancreatitis is a self-limiting condition and the majority of people who recover will return to normal activities. They will then need treatment, often cholecystectomy, to eradicate the cause of the pancreatitis. If the cause can be found then appropriate treatment can prevent recurrent attacks.

Chronic pancreatitis

Chronic pancreatitis is a continuous prolonged inflammatory process of the pancreas that results in fibrosis, cyst formation and stricturing of the pancreatic duct. It usually presents with chronic abdominal pain but may be painless. The clinical course is variable but most people with chronic pancreatitis have had one or more attacks of acute pancreatitis that has resulted in inflammatory change and fibrosis. In some people, however, chronic pancreatitis has a more insidious onset. The intensity of pain can range from mild to severe, even in people with little evidence of pancreatic disease on imaging.

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The annual incidence of chronic pancreatitis in western Europe is about 5 new cases per 100,000 people, although this is probably an underestimate. The male to female ratio is 7:1 and the average age of onset is between 36 and 55 years. Alcohol is responsible for 70–80% of cases of chronic pancreatitis. Although cigarette smoking is not thought to be a primary cause in itself, it is strongly associated with chronic pancreatitis and is thought to exacerbate the condition. Chronic pancreatitis may be idiopathic or, in about 5% of cases, caused by hereditary factors (in these cases there is usually a positive family history). Other causes include hypercalcaemia, hyperlipidaemia or autoimmune disease.

Chronic pancreatitis causes a significant reduction in pancreatic function and the majority of people have reduced exocrine (digestive) function and reduced endocrine function (diabetes). They usually need expert dietary advice and medication. Chronic pancreatitis can also give rise to specific complications including painful inflammatory mass and obstructed pancreatic duct, biliary or duodenal obstruction, haemorrhage, or accumulation of fluid in the abdomen (ascites) or chest (pleural effusion). Managing these complications may be difficult because of ongoing comorbidities and social problems such as alcohol or opiate dependence. Chronic pancreatitis significantly increases the risk of pancreatic cancer. This risk is much higher in people with hereditary pancreatitis.

3.2 Current practice

People with acute pancreatitis usually present to their local hospital as an emergency with acute abdominal pain. If organ failure (usually respiratory or kidney failure) occurs, then admission to intensive care is necessary. About 75% of people recover quickly; the remainder develop severe acute pancreatitis that is associated with organ failure, or with intra-abdominal fluid collections or pancreatic necrosis. The amount and type of fluid resuscitation varies. The use of prophylactic antibiotics also varies.

Interventions such as drainage of necrotic collections are offered locally or by referral to a pancreatic centre. There is uncertainty about where these interventions are best offered. Techniques used to treat infected necrosis

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vary. Open surgery is the conventional technique but percutaneous (radiological) and endoscopic techniques have been developed and are in widespread use. These less invasive techniques are not used in all hospitals managing acute pancreatitis because of limited availability of expertise.

Variation also exists in the care of people with chronic pancreatitis. Newer techniques for the diagnosis and assessment of chronic pancreatitis are available but are not in widespread use. There is uncertainty about using tests for hereditary pancreatitis and autoimmune pancreatitis. This is of particular concern in children with pancreatitis.

The indications for referral to specialist centres vary significantly in chronic pancreatitis. Surgical and endoscopic management of complications is very well developed in some specialist centres and less so in others. Use of enzyme replacement therapy and specialist advice also varies.

There are many interventional treatments available for pain caused by pancreatic duct obstruction associated with chronic calcific pancreatitis. These include surgery, endoscopy and extracorporeal shockwave lithotripsy for pancreatic stone destruction. Availability of these treatments varies from hospital to hospital and region to region. For people whose only treatment option is total pancreatectomy, islet auto-transplant is available.

Support for people with pancreatitis, their families and carers also varies widely. In some regions there are specific pancreatitis nurse specialists and patient support groups.

3.3 Policy, legislation, regulation and commissioning

Policy

Service specifications for adults are set out in the NHS England 2013/14 standard contract for hepatobiliary and pancreas (adult). The Association of Upper Gastrointestinal Surgeons' provision of services document) also provides guidance on service configuration.

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Legislation, regulation and guidance

The British Society of Gastroenterology's UK guidelines for the management of acute pancreatitis (2005) have been used extensively but are now out of date. The American College of Gastroenterology published a comprehensive guideline on the management of acute pancreatitis in 2013. However, this guideline is mainly written by and for US physicians, whereas the majority of people with pancreatitis in the UK are cared for by gastrointestinal surgeons.

Guidelines on chronic pancreatitis sponsored by United European Gastroenterology are in preparation, with publication expected in late 2016 or early 2017.

Commissioning

Services for pancreatitis are commissioned by clinical commissioning groups unless tertiary care is provided by pancreatic centres, in which case specialised commissioning is responsible.

4 Further information

This is the final scope, incorporating comments from registered stakeholders during consultation.

The guideline is expected to be published in September 2018.

You can follow progress of the guideline.

Our website has information about how NICE guidelines are developed.

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Appendix B: Declarations of interest

B.1 Richard Charnley (chair)

Meeting	Declaration	Classification	Action taken
Initial application	None	-	-
GC 01	None	-	-
GC 02	None	-	-
GC 03	None	-	-
GC 04	None	-	-
GC 05	None	-	-
GC 06	None	-	-
GC 07	None	-	-
GC 08	None	-	-
GC 09	None	-	-
GC 10	None	-	-
GC 11	None	-	-
GC 12	None	-	-

B.2 Alex Horton (radiologist)

Meeting	Declaration	Classification	Action taken
Initial application	Local radiologist for the following trials: • Epock and STOP HCC, both commercial trials funded by BTG UK. • TACE2 trial: Closed prior to recruitment at local site. • Sillajen (PHOCUS) study: Funded by Sillajen, San Franscisco, USA	Non-specific non-personal non-financial	Declare and participate
GC 01	None	-	-
GC 02	HCC Round table meeting in London 22/3/16. Paid honorarium by Bayer. Not related to pancreatitis	Non-specific Personal Financial	Withdraw from the nutritional intervention protocol discussions because it was initially thought to be Specific personal financial classification. Bayer previously involved in enzyme replacement therapy. However,

Meeting	Declaration	Classification	Action taken
			have not been involved with this for some time. a
	BTG Rep training event DC Beads in TACE 5/3/15. Paid attendance. (entry left in register as in GC minutes on NICE website)	Non-specific Personal Financial (item over 1 year old)	Declare and Participate
GC 03	None	-	-
GC 04	None	-	-
GC 05	None	-	-
GC 06	HCC round table meeting in London, April 2017. Paid honorarium by Bayer. Not related to pancreatitis	Non-specific Personal Financial	Withdraw from the nutritional intervention protocol discussions because it was initially thought to be Specific personal financial classification. Bayer previously involved in enzyme replacement therapy. However, have not been involved with this for some time. b
GC 07	None	-	-
GC 08	None	-	-
GC 09	None	-	-
GC 10	None	-	-
GC 11	None	-	-
GC 12	None	-	-

B.3 Amy Lucas (lay member)

Meeting	Declaration	Classification	Action taken

[a] Later found to not be a conflict.
[b] Later found to not be a conflict.

Meeting	Declaration	Classification	Action taken
Initial application	None	-	-
GC 01	None	-	-
GC 02	None	-	-
GC 03	None	-	-
GC 04	Liverpool patient group member for pancreatitis, delivered talk on NICE guideline experience. February 2016.	Specific personal non-financial	Declare and participate
GC 05	None	-	-
GC 06	Will be doing a talk about the scope of this guideline at the Liverpool National Pancreatic Patients Forum – 5 May 2017. Will only mention what is available online.	Specific personal non-financial	Declare and participate
GC 07	None	-	-
GC 08	None	-	-
GC 09	None	-	-
GC 10	None	-	-
GC 11	None	-	-
GC 12	None	-	-

B.4 Ashraf Rasheed (upper GI surgeon)

Meeting	Declaration	Classification	Action taken
Initial application	None	-	-
GC 01	None	-	-
GC 02	None	-	-
GC 03	None	-	-
GC 04	None	-	-
GC 05	None	-	-
GC 06	None	-	-
GC 07	None	-	-
GC 08	None	-	-
GC 09	None	-	-
GC 10	None	-	-

Meeting	Declaration	Classification	Action taken
GC 11	None	-	-
GC 12	None	-	-

B.5 Ganesan Baranidharan (pain specialist)

Meeting	Declaration	Classification	Action taken
Initial application	My special interest is in Neuromodulation for Pain Management. I am considered an International Key Opinion Leader in this field.	Non-specific personal non-financial	Declare and participate
	Have been on the Advisory Board of various Neuromodulation Companies.	Non-specific personal financial	
	In 2016 I attended a Neuromodulation training weekend with Boston Scientific in Budapest at their cost.	Non-specific personal financial	
	21st April 2015 Lecturing at a GP education meeting sponsored by Grunenthal specifically educating regarding Palexia: fee for the event was £200. Other drugs produced by Grunenthal are Arcoxia(R) Tramacet (R) Versatis (R) Zydol (R) In 2014 I attended 2 Neuromodulation training weekends paid completely by Medtronic both in Europe. On 27th June 2015 I attended a Neuromodulation training weekend with NEVRO Corp in Budapest at their cost.	Specific personal financial – over one year ago	
	International Advisory Board for St Jude Medical and Nevro Corporation. Advisory Board member of a new start-up company Nalu Medical (paid for number of hours' advice). (develop neurostimulation for chronic pain management, not an intervention considered in guideline).	Non-specific personal financial	Declare and participate
	Un Restricted Educational Grant Nevro Corporation – Currently running a study on managing Low back pain using neurostimulation (NHS portfolio study)	Non-specific Non-personal financial	
	St Jude Medical – Have been offered an Educational Grant to do a Pilot RCT on use of Dorsal Root Ganglion Stimulation for managing Pain secondary to Pancreatitis (develop neurostimulation for chronic pain management, not an intervention considered in guideline).	Non-specific Non-Personal financial	
	St Jude Medical and Nevro – Grant for a Research Nurse organised by the Trust (develop neurostimulation for chronic pain management, not an intervention considered in guideline).	Non-specific Non-personal Financial	

Meeting	Declaration	Classification	Action taken
	Secretary, Neuromodulation Society of the UK and Ireland	Non-specific personal Non-financial	
GC 01	None	-	-
GC 02	None	-	-
GC 03	Dec 2016 - Cadaver Workshop in Barcelona organised by ECMT (http://ecmt-training.com/) Attended as an invited Faculty with Honorarium	Non-specific personal financial	Declare and participate
	Dec 2016 – European Advisory Board for Boston Scientific as a Consultant (Paid Personal)	Non-specific personal financial	Declare and participate
	Nov 2016 – Represented Nevro Corporation as a Clinical Expert (paid Personal) for a Court Hearing on Patent	Non-specific personal non-financial	Declare and participate
GC 04	Had an advisory board meeting on 20th January 2017 at North American Neuromodulation Society Meeting, Las Vegas. This is for advice on their development of the neuromodulation device and plans for their clinical study looking at back pain.	Specific personal non-financial	Declare and participate
GC 05	Two day International Executive Advisory Board meeting Abbott (previous St Jude Medical). Financial as per previous declarations – ongoing consultancy agreement. Invited article on abdominal pain by Mundipharma.	Non-Specific personal financial	Declare and participate
GC 06	Conducted a course on Neuromodulation aimed at advanced pain trainees, sponsored by Industry and approved by Royal College of Anaesthetists in March 2017.	Non-specific personal financial	Declare and participate
GC 07	Attended International Neuromodulation Society Meeting in Edinburgh as a Faculty. This waived my registration fee and my stay. Attended International Advisory Board on Peripheral Nerve Stimulation for treating Chronic Pain. This meeting was to advice on development of a new product (30/05/2017). Paid role, not related to Pancreatitis.	Non-specific personal non-financial Non-specific personal financial	Declare and participate
GC 08	None	-	-
GC 09	None	-	-
GC 10	None	-	-
GC 11	None	-	-
GC 12	None	-	-

B.6 James Shaw (diabetes specialist) – co-opted member

Meeting	Declaration	Classification	Action taken
Initial application	Member of the Medtronic UK Scientific Advisory Board	Non-specific personal financial	Declare and participate
	Received travel support from Novo Nordisk to attend and present data at the American Diabetes Association Annual Scientific Sessions, New Orleans, June 2016	Non-specific personal non-financial	
GC 01	None	-	-
GC 02	None	-	-
GC 03	None	-	-
GC 04	None	-	-
GC 05	None	-	-
GC 06	None	-	-
GC 07	None	-	-
GC 08	None	-	-
GC 09	None	-	-
GC 10	None	-	-
GC 11	None	-	-
GC 12	None	-	-

B.7 Jonathan Booth (non-specialist gastroenterologist)

Meeting	Declaration	Classification	Action taken
Initial application	Annual meeting sponsored by Mylan - they make creon, does not get paid but the company helps to organise the event. Creon is an enzyme replacement therapy	Specific personal non-financial	Declare and participate
	I also own a few shares in Advanced Medical Solutions [advanced wound care, surgical and wound closure] - personal investment choice	Non-specific personal financial	
GC 01	None	-	-
GC 02	None	-	-
GC 03	None	-	-
GC 04	None	-	-
GC 05	None	-	-

Meeting	Declaration	Classification	Action taken
GC 06	None	-	-
GC 07	None	-	-
GC 08	None	-	-
GC 09	None	-	-
GC 10	None	-	-
GC 11	None	-	-
GC 12	None	-	-

B.8 Louise Carr (lay member)

Meeting	Declaration	Classification	Action taken
Initial application	None	-	-
GC 01	None	-	-
GC 02	None	-	-
GC 03	None	-	-
GC 04	None	-	-
GC 05	None	-	-
GC 06	None	-	-
GC 07	None	-	-
GC 08	None	-	-
GC 09	None	-	-
GC 10	None	-	-
GC 11	None	-	-
GC 12	None	-	-
GC 13		-	-

B.9 Manu Nayar (specialist gastroenterologist)

Meeting	Declaration	Classification	Action taken
Initial application	European Group for Endoscopic Ultrasonography meeting; Edinburgh, October 2015 - 300 euros by Medtronic U.K.	Non-specific Personal financial	Declare and participate

Meeting	Declaration	Classification	Action taken
	LEEDS Endoscopic retrograde cholangio-pancreatography (ERCP) MASTERCALSS – JULY 2016 - £1500/- by Olympus U.K. Paid speaking arrangement.	Specific Personal Financial	Declare and withdraw for discussions on Diagnosing Chronic Pancreatitis
GC 01	None	-	-
GC 02	None	-	-
GC 03	Declared during initial interviews: Leeds: ERCP Master class, July 2016, £1500 – by Olympus UK.	Specific personal financial	Declare and withdraw for discussions on Diagnosing Chronic Pancreatitis
GC 04	None	-	-
GC 05	None	-	-
GC 06	None	-	-
GC 07	I was invited faculty for the International ERCP symposium in Stoke on Trent on 28/04/2017. Aquilant UK paid for my travel and accommodation expenses. No personal honorariums received.	Personal non-financial non-specific	Declare and participate
GC 08	None	-	-
GC 09	None	-	-
GC 10	None	-	-
GC 11	None	-	-
GC 12	None	-	-

B.10 Mary Phillips (dietitian)

Meeting	Declaration	Classification	Action taken
Initial application	The course I ran in September in Guildford was the same PEI course mentioned below (on pancreatic enzyme replacement therapy). Delivered to a group of 20 Dietitians, as previously there was no attendance by industry, and they have no input into the content of the course. It is funded by an unconditional educational grant that includes an honorarium for the trainer.	Specific Personal Financial	Declare and withdraw for reviews including enzyme replacement therapy
	Mylan Pharmaceuticals I have received honoria and travel expenses for speaking at educational meetings:	Specific Personal	Declare and withdraw for reviews

Meeting	Declaration	Classification	Action taken
	The Nutrition Interest Group of the Pancreatic Society of Great Britain and Ireland (NIGPS) run a course for Dietitians on the identification and management of pancreatic exocrine insufficiency; this is funded by an unconditional education grant from Mylan. Mylan have not had any input to the content of the course, and we do not encourage trade-stands at the meetings. For each course I run I submit a budget request to Mylan, and this is paid to NIGPS to allow us to run the course. This includes a honoria for the speakers. I have run 13 courses to date, and have a financial commitment from Mylan to continue running them over the next 2 years. Mylan produce an enzyme replacement therapy product.	Financial	including enzyme replacement therapy
	I have spoken at various nutrition and dietetic department journal clubs on nutritional management of patients with pancreatic exocrine insufficiency, and received honoraria from Mylan for doing so, Mylan have had no input to the content of my presentation. Mylan produce an enzyme replacement therapy product.	Specific Personal Financial	Declare and withdraw for reviews including enzyme replacement therapy
	Conference attendance sponsorship (registration and accommodation only) for Pancreatic Society Meetings 2015 and 2016 and HPBSurg 2016 (registration, travel and accommodation).	Specific Personal Non financial	Declare and participate
	Site PI on a European commercial trial September 2015-June 2016. This was a non-intervention validation of a patient questionnaire with the aim of developing and validating a screening tool for chronic pancreatitis patients with pancreatic exocrine insufficiency, this trial is completed. My Trust received a payment for each patient recruited (n=10); this was part of a bank contract I hold with the trust, and I did not receive any payment other than my usual hourly rate for the time taken to complete the patient questionnaire.	Non-specific Non-Personal Financial	Declare and participate
	Nutricia Clinical Care Site PI on a commercial multicentre clinical trial on the efficacy of an enteral feed – due to commence October 2016. This is a trial to evaluate a new peptide enteral feeding product licensed for use in patients with intractable malabsorption, with the aim of assessing tolerance of a product compared to other commercially available products. The sample group will be patients already receiving peptide based enteral feeds. We have been asked to recruit 6 patients. The contracts are not yet finalised for this trial, and I am prepared to withdraw if this is deemed a conflict of interest by NICE. Comparison of enteral feeds not an intervention in guideline. Nutricia makes oral feeds too. There is a question comparing oral to enteral feeding.	Specific Non-personal Financial	Declare and participate

Meeting	Declaration	Classification	Action taken
	Vitaflo International Honoria for speaking at an educational event: Vitaflo sponsored a British Dietetic association study day in January 2016 in Birmingham on the management of pancreatic and liver disease. I spoke on the nutritional management of pancreatic disease, and received travel and accommodation reimbursement and an honoraria. Vitaflo did not have any input to the content of my presentation, and I did not include any reference to their products within the presentation. Vitaflo make oral supplements that could be used for nutrition support in pancreatitis. Not comparing oral supplements in guideline.	Non-specific Personal Financial	Declare and participate
	MERCK I received honoria for speaking at an Enhanced Recovery Study day funded by MERCK in Guildford in June, and this is being repeated in September 2016. My session is part of a surgical and anaesthetic study day, and my presentation is on the implementation of an enhanced recovery programme in pancreatico-duodenectomy. MERCK have not had any input into the content of my presentation.	Non-specific Personal Financial	Declare and participate
GC 01	No change	-	-
GC 02	Pancreatic exocrine insufficiency (PEI) course taught in Guildford (Sept 2016): Honoria received. National Course (previously declared) sponsored by an unconditional educational grant from Mylan. Mylan had no input to the content of the course and were not in attendance. Mylan produce an enzyme replacement therapy product.	Specific personal financial	Declare and participate for this meeting. Withdraw for reviews including enzyme replacement therapy discussed at other meetings.
	CECOG (Central European Cooperative Oncology Group) conference in Vienna (12.11.16) – speaking on Pancreatic Cancer and Nutrition. Honoria, travel and accommodation paid for by conference organiser	Non specific Personal Financial	Declare and participate
GC 03	None	-	-
GC 04	None	-	-
GC 05	None	-	-
GC 06	None	-	-
GC 07	None	-	-

Meeting	Declaration	Classification	Action taken
GC 08	Honoria received from Northern Ireland Health Board for presentation at Dietitians education meeting on pancreatic exocrine insufficiency. Honoria received from Mylan for presenting at Diabetes Nurse Study day (TREND) on pancreatic exocrine insufficiency.	Non-specific personal financial Specific personal financial	Declare and participate Declare and participate for this meeting. Withdraw for reviews including enzyme replacement therapy discussed at other meetings.
GC 09	None		
GC 10	None	-	-
GC 11	None	-	-
GC 12	None	-	-

B.11 Peter Hampshire (critical care specialist) – co-opted member

Meeting	Declaration	Classification	Action taken
Initial application	None	-	-
GC 01	None	-	-
GC 02	None	-	-
GC 03	None	-	-
GC 04	None	-	-
GC 05	None	-	-
GC 06	None	-	-
GC 07	None	-	-
GC 08	None	-	-
GC 09	None	-	-
GC 10	None	-	-
GC 11	None	-	-
GC 12	None	-	-

B.12 Robert Sutton (pancreatic surgeon)

Meeting	Declaration	Classification	Action taken
Initial application	I have an over-riding, specific interest in the prevention, diagnosis and treatment of acute and chronic pancreatitis. Specifically I am interested in the research development of new and personalised approaches to the management of pancreatitis, to reduce death, to prolong survival and to alleviate human suffering from pancreatitis, over and above what can be achieved through the fullest implementation of optimal guidelines. This is my over-riding professional concern alongside making every endeavour to provide optimal care for all patients with pancreatic digestive diseases at a leading regional specialist unit in Liverpool. Institutional research grant income is essential to this objective, guided by the Nolan Principles of Public Life: selflessness, integrity, objectivity, accountability, openness, honesty and leadership. Importantly, there are no drugs available for the treatment of pancreatitis to modify the disease, and much of my research is directed at development of new and/or repositioned drugs to treat the disease. This is to achieve the aims of reducing death, prolonging survival and alleviating human suffering. [PUBLICLY HELD VIEW]	Specific personal non-financial	Declare and participate
	I have spent many years unravelling critical mechanisms and encouraging development of new drugs for acute pancreatitis, one of which is intended to enter phase I studies (CalciMedica's CM 4620, safety and pharmacokinetic studies; n.b. CalciMedica do not market any approved product for any disease) within six months, but which will have to go through years of development (phase IIa, then phase IIb and then phase III 'pivotal' regulatory trials) before it might be considered to be clinically applicable; many drugs fail these steps. [RESEARCH]	Non specific Personal Non financial	Declare and participate
	I am the principal investigator on an Efficacy and Mechanism Evaluation (MRC/NIHR) application to conduct a multicentre phase IIb (efficacy not effectiveness) randomised study of infliximab (from Merck/MSD who market this as Remicade®) in acute pancreatitis, that has reached 'intent to fund' status. Infliximab is not used in the treatment of acute pancreatitis, nor are there sufficient data and there is no regulatory approval for the use of infliximab in acute pancreatitis. There is no reason whatsoever for investigation of the potential effects of these drugs to influence the current management of acute pancreatitis, as all these compounds have no current role at all in the treatment of acute pancreatitis. There are no data within the evidence base from which the guidelines are to be compiled for the use of any of these drugs in the management of pancreatitis, and there is no reason to modify any guideline on pancreatitis as a result of the	Non specific Personal Non financial	Declare and participate

Meeting	Declaration	Classification	Action taken
	research that I am undertaking on drug discovery and development described above.		
	Other than occasional medicolegal expert witness (I have a current instruction relating to a bile duct injury and undertaken at the request of a senior physician but my last case was over 5 years ago)	Specific non-personal non financial:	Declare and participate
	[Additionally] a small number of holiday lettings on a privately owned property My sole source of income is paid by salary from the University of Liverpool, through my employment as a Professor of Surgery and Honorary Consultant Surgeon. I hold this honorary position at the Royal Liverpool and Broadgreen University Hospitals NHS Trust. I do not undertake private practice. [EMPLOYMENT/INCOME – NOT RELEVANT TO THE GUIDELINE'S WORK]		Declare and participate
	My principal non-personal financial interest is to secure and develop innovative programmes of research at the University of Liverpool and Royal Liverpool and Broadgreen University Hospitals NHS Trust, endeavouring to maintain the highest ethical standards to advance the management of pancreatitis. Much of this research is preclinical (funded by the Medical Research Council and members of the Association of Medical Research Charities) or early stage translational (proof of principle, funded by the National Institute for Health Research) and has unfortunately yet to achieve late stage translation that would enter the realm of the evidence base that will inform guidelines for the management of pancreatitis. The number and size of the grants are commensurate with what is necessary to have a significant likelihood of reducing death, prolonging survival and/or alleviating human suffering from pancreatitis through research, over and above what can be achieved through the fullest implementation of optimal guidelines from the current evidence base.	Non-specific Financial Non-Personal	Declare and participate
	I am chief/principal/co- investigator on the following research grants awarded to the University of Liverpool and/or Royal Liverpool and Broadgreen University Hospitals NHS Trust that are current or have expired within the last 12 months: The role of IP3 receptors and Orai channels in the physiology and pathophysiology of pancreatic acinar cells (CoI). Liverpool-RIKEN PhD Studentship for David Collier: 1 October 2011 to 30 September 2015: £75,000	Non-specific non-personal Financial	Declare and participate
	(2) Preclinical testing of agents for acute pancreatitis (PI). China Scholarship Council: Research Fellowship for Li Wen: 1 October 2011 to 30 September 2015; £100,000	Non-specific Non-personal Financial	Declare and participate

Meeting	Declaration	Classification	Action taken
	(3) Pancreatic Digestive Diseases Biomedical Research Unit (PI). NIHR: BRU Revenue Funding: 1 April 2012 to 31 March 2017: £6,500,000	Non-specific Non personal Financial	Declare and participate
	(4) Chemical synthesis of novel cyclophilin D inhibitors (CoI). EPSRC 50% PhD Studentship for Emma Shore: 1 October 2012 to 30 September 2016: £70,000	Non specific Non personal Financial	Declare and participate
	(5) Interaction of endocytic vacuoles with cellular organelles as a trigger for the cell damage in acute pancreatitis (CoI). MRC Research Grant: 1 April 2013 to 31 March 2016: £509,047	Non specific Non personal Financial	Declare and participate
	(6) Liverpool Imaging Partnership: Molecular physiology and drug response (CoI). MRC Infrastructure Award: 1 April 2013 to 31 March 2017: £1,025,736	Non specific Non personal Financial	Declare and participate
	(7) Liverpool Biomedical Research Centre in Personalised Health (CI). Liverpool Health Partners (non-NIHR): 1 October 2014 to 31 March 2017: £1,500,000 (2014-17)	Non specific Non personal Financial	Declare and participate
	(8) Preclinical drug testing for acute pancreatitis (PI). China Scholarship Council: Research Studentship for Stephanie Zhang: 1 October 2014 to 30 September 2018: £100,000	Non Specific Non personal Financial	Declare and participate
	(9) Preclinical development of cyclophilin inhibitors in acute pancreatitis (PI). Cypralis Research Grant: 1 January 2015 to 31 December 2016: £84,000	Non specific Non personal financial	Declare and participate
	(10) TNF alpha signaling in acute pancreatitis (PI): Mersey Deanery: Madel Research Fellowship for Ajay Sud: 1 April 2015 to 31 March 2017: £90,000	Non specific Non personal Financial	Declare and participate
	(11) Neutrophil-acinar cell interactions in acute pancreatitis (PI). Royal College of Surgeons of England: Research Fellowship for Peter Szatmary; 1 August 2015 to 31 July 2016: £50,000	Non specific Non personal Financial	Declare and participate
	(12) Chemical synthesis of novel inhibitors of cyclophilin D (Co-I). EPSRC 50% PhD Studentship for Michael Rogers: 1 October 2015 to 30 September 2019: £70,000	Non specific Non personal Financial	Declare and participate
	(13) The role of the mitochondrial Ca2+ uniporter in initiation and development of acute pancreatitis (Co-I). MRC: Research Grant: 1 April 2016 to 31 March 2019:	Non specific Non personal	Declare and participate

Meeting	Declaration	Classification	Action taken
	£403,000	Financial	
	(14) NIHR Senior Investigator (PI). NIHR: Investigator Award: 1 April 2016 to 31 March 2012: £450,000 (£375,000 to Research Capability Funding at RLBUHT)	Non specific Non personal Financial	Declare and participate
	(15) TNF alpha signaling in acute pancreatitis (PI). Royal College of Surgeons of England: Research Fellowship for Ajay Sud: 1 April 2017 to 31 March 2018: £50,000	Non specific Non personal financial	Declare and participate
	The University of Liverpool offers a consultancy service by means of which external organisations, public and private, can obtain expert advice from senior academic staff (please see: https://www.liverpool.ac.uk/business/services/research-and-consultancy/). I am registered on this service to provide advice and collaborate to develop new treatments for pancreatitis, including a contract with Cypralis Ltd (http://www.cypralis.com) that begun on 1 August 2016 at £10,000 p.a..	Non specific Non personal Financial	Declare and participate
	Currently the work with Cypralis is entirely preclinical in nature (see also grant 9 above); if there is a promising lead candidate identified, Cypralis intend to undertake a full, regulatory preclinical toxicology work package. If approved by the regulatory bodies (including the Medicines and Healthcare products Regulatory Agency), this will be a prelude to first-in-man phase I studies of single and multiple ascending doses of their chosen compound, again years away from clinical application other than in phase I, phase IIa, phase IIb and phase III clinical trials. This work has no bearing on the evidence base for pancreatitis guidelines, and Cypralis do not market any approved product for the management of any disease.	Non specific Non personal Financial	Declare and participate
	Director, NIHR Liverpool Pancreas Biomedical Research Unit, 2008-2017 Co-opted member of Executive Committee, Pancreatic Society of Great Britain and Ireland (as Chair of Guideline Development Committee; previously member 1998-2001 and 2005-2014, President 2012-2013), 2014 et seq Faculty, American Pancreatic Association, 2004 et seq Member of Council, International Association of Pancreatology, 2008-2016 [MEMBERSHIPS]	Specific personal non-financial:	Declare and participate
	Director of Research, Development and Innovation, Royal Liverpool and Broadgreen University Hospital NHS Trust, 2009 et seq Director of Research, Liverpool Health Partners, 2013 et	Non-specific personal non-financial	Declare and participate

Meeting	Declaration	Classification	Action taken
	seq Research Awards Committee, CORE (Digestive Disorders Foundation), 2003 et seq Member, Association of UK University Hospitals Research Directors, 2011 et seq		
	Previously contributed to editorship within the Cochrane Collaboration as Joint Editor Cochrane Hepatobiliary Collaborative Review Group, 1996-2012; I have also contributed to peer reviewing for public funding organisation and peer-reviewed journals for 30 years.	Non-specific personal non-financial	Declare and participate
	Has published the following original articles in 2015 and 2016: (1) Chvanov M, Huang W, Jin T, Wen L, Armstrong J, Elliot V, Alston B, Burdyga A, Criddle DN, Sutton R, Tepikin AV. Novel lipophilic probe for detecting near-membrane reactive oxygen species responses and its application for studies of pancreatic acinar cells: effects of pyocyanin and L-ornithine. Antioxid Redox Signal 2015; 22: 451-464. (2) Jenkinson C, Elliott V, Menon U, Apostolidou S, Fourkala OE, Gentry-Maharaj A, Pereira SP, Jacobs I, Cox TF, Greenhalf W, Timms JF, Sutton R, Neoptolemos JP, Costello E. Evaluation in pre-diagnosis samples discounts ICAM-1 and TIMP-1 as biomarkers for earlier diagnosis of pancreatic cancer. J Proteomics 2015; 113: 400-402. (3) Voronina S, Collier D, Chvanov M, Middlehurst B, Beckett AJ, Prior IA, Criddle DN, Begg M, Mikoshiba K, Sutton R, Tepikin AV. The role of Ca2+ influx in endocytic vacuole formation in pancreatic acinar cells. Biochem J 2015; 465: 405-412. (4) Wang YC, Szatmary P, Zhu JQ, Xiong JJ, Huang W, Gomatos I, Nunes QM, Sutton R, Liu XB. Prophylactic intra-peritoneal drain placement following pancreaticoduodenectomy: a systematic review and meta-analysis. World J Gastroenterol 2015; 21: 2510-2521. (5) Nicholson JA, Greenhalf W, Jackson R, Cox TF, Butler JV, Hanna T, Harrison S, Grocock CJ, Halloran CM, Howes NR, Raraty MG, Ghaneh P, Johnstone M, Sarkar S, Smart HL, Evans JC, Aithal GP, Sutton R, Neoptolemos JP, Lombard MG. Incidence of post-ERCP pancreatitis from direct pancreatic juice collection in hereditary pancreatitis and familial pancreatic cancer before and after the introduction of prophylactic pancreatic stents and rectal diclofenac. Pancreas 2015; 44: 260-265. (6) Huang W, Cash N, Wen L, Szatmary P, Mukherjee R, Armstrong J, Chvanov M, Tepikin AV, Murphy MP, Sutton R, Criddle DN. Effects of the mitochondria-targeted antioxidant mitoquinone in murine acute pancreatitis. Mediators Inflamm 2015; 2015:901780.	Non-specific personal non-financial	Declare and participate

Meeting	Declaration	Classification	Action taken
	(7) Huang W, Xiong JJ, Wan MH, Szatmary P, Bharucha S, Gomatos I, Nunes QM, Xia Q, Sutton R, Liu XB. Meta-analysis of subtotal stomach-preserving pancreaticoduodenectomy vs pylorus preserving pancreaticoduodenectomy. World J Gastroenterol 2015; 21: 6361-6373. (8) Wen L, Voronina S, Javed MA, Awais M, Szatmary P, Latawiec D, Chvanov M, Collier D, Huang W, Barrett J, Begg M, Stauderman K, Roos J, Grigoryev S, Ramos S, Rogers E, Whitten J, Velicelebi G, Dunn M, Tepikin AV, Criddle DN, Sutton R. Inhibitors of ORAI1 Prevent Cytosolic Calcium-Associated Injury of Human Pancreatic Acinar Cells and Acute Pancreatitis in 3 Mouse Models. Gastroenterology 2015; 149: 481-492. (9) Ou X, Cheng Z, Liu T, Tang Z, Huang W, Szatmary P, Zheng S, Sutton R, Toh CH, Zhang N, Wang G. Circulating histone levels reflect disease severity in animal models of acute pancreatitis. Pancreas 2015; 44: 1089-1095. (10) Gomatos IP, Halloran CM, Ghaneh P, Raraty MG, Polydoros F, Evans JC, Smart HL, Yagati-Satchidanand R, Garry JM, Whelan PA, Hughes FE, Sutton R, Neoptolemos JP. Outcomes from minimal access retroperitoneal and open pancreatic necrosectomy in 394 patients with necrotizing pancreatitis. Ann Surg 2015 Oct 22. [Epub ahead of print] (11) Huang W, Cane MC, Mukherjee R, Szatmary P, Zhang X, Elliott V, Ouyang Y, Chvanov M, Latawiec D, Wen L, Booth D, Haynes AC, Petersen OH, Tepikin AV, Criddle DN, Sutton R. Caffeine protects against experimental acute pancreatitis by inhibition of inositol 1,4,5-trisphosphate receptor-mediated Ca2+ release. Gut 2015 Dec 7. [Epub ahead of print] (12) Sultana A, Jackson R, Tim G, Bostock E, Psarelli EE, Cox TF, Sutton R, GhanehP, Raraty MG, Neoptolemos JP, Halloran CM. What is the best way to identify malignant transformation within pancreatic IPMN: a systematic review and meta-analyses. Clin Transl Gastroenterol 2015 Dec 10;6:e130. doi:10.1038/ctg.2015.60. (13) Okeke E, Parker T, Dingsdale H, Concannon M, Awais M, Voronina S, Molgo J, Begg M, Metcalf D, Knight AE, Sutton R, Haynes L, Tepikin AV. Epithelial- mesenchymal transition, IP3 receptors and ER-PM junctions: translocation of Ca2+ signalling complexes and regulation of migration. Biochem J 2016 Jan 12 [Epub ahead of print] (14) Gomatos IP, Halloran C, Ghaneh P, Raraty M, Polydoros F, Campbell F, Evans J, Sutton R, Garry J, Whelan P, Neoptolemos JP. Management and outcome of 64 patients with pancreatic serous cystic neoplasms. Dig Surg 2016; 33: 203-212.		

Meeting	Declaration	Classification	Action taken
	(15) Shore E, Awais M, Kershaw N, Gibson R, Pandalaneni S, Latawiec D, Wen L, Javed M, Criddle D, Berry N, O'Neill P, Lian L-Y, Sutton R. Small molecule inhibitors of cyclophilin D to protect mitochondrial function as a potential treatment for acute pancreatitis. J Med Chem 2016; 59: 2596-2611. (16) Xiong JJ, Szatmary P, Huang W, Iglesia-Garcia D, Nunes QM, Xia Q, Hu WM, Sutton R, Liu XB, Raraty MG. Enhanced recovery after surgery program in patients undergoing pancreaticoduodenectomy: A PRISMA-compliant systematic review and meta-analysis. Medicine 2016; 95: e3497. (17) Mukherjee R, Mareninova OA, Odinokova IV, Huang W, Murphy J, Chvanov M, Javed MA, Wen L, Booth DM, Cane MC, Awais M, Gavillet B, Pruss RM, Schaller S, Molkentin JD, Tepikin AV, Petersen OH, Pandol SJ, Gukovsky I, Criddle DN, Gukovskaya AS, Sutton R; and NIHR Pancreas Biomedical Research Unit. Mechanism of mitochondrial permeability transition pore induction and damage in the pancreas: inhibition prevents acute pancreatitis by protecting production of ATP. Gut 2016; 65: 1333-1346.		
	Has published the following review articles and book chapters in 2015 and 2016:		
	(1) Awais M, Voronina SG, Sutton R. An efficient method is required to transfect non-dividing cells with genetically encoded optical probes for molecular imaging. Anal Sci 2015; 31: 293-298.	Non-specific personal non-financial	Declare and participate
	(2) Afghani E, Pandol S, Shimosegawa T, Sutton R, Wu B, Vege SS, Gorelick F, Hirota M, Windsor J, Lo SK, Freeman M, Lerch MM, Tsuji Y, Melmed GY, Wassef W, Mayerle J. Acute pancreatitis: progress and challenges. A report on an international symposium. Pancreas 2015; 44: 1195-210.	Specific personal non-financial	Declare and participate
	(3) Cummings M, Bodansky J, Hicks D, Hopkins D, Kirby M, Sutton R. Pancreatic exocrine insufficiency in diabetes: why it is important and what are the practicalities in diagnosis and management. Diabetes Digest 2015; 13 (Suppl 3):2-8.	Non-specific personal non-financial	Declare and participate
	(4) Huang W, Szatmary P, Wan M, Bharucha S, Awais M, Tang W, Criddle DN, Xia Q, Sutton R. Translational insights into peroxisome proliferator-activated receptors in experimental acute pancreatitis. Pancreas 2015 Nov 17. [Epub ahead of print]	Non-specific personal non-financial	Declare and participate
	(5) Wen L, Javed MA, Altaf K, Szatmary P and Sutton R. Specific treatment for acute pancreatitis. In: Adams DB, Cotton PB, Zyromski NJ, Windsor J, eds. Pancreatitis: medical and surgical management. Oxford: Wiley, in press.	Specific personal Non-financial	Declare and participate

Meeting	Declaration	Classification	Action taken
	(6) Mukherjee R, Sutton R. Pharmaceutical developments for chronic pancreatitis: pipelines and future options. Pancreapedia: Exocrine Pancreas Knowledge Base, DOI: 10.3998/panc.2016.12.	Non-specific personal financial	Declare and participate
	(7) Wen L, Mukherjee R, Huang W, Sutton R. Calcium signaling, mitochondria and acute pancreatitis: avenues for therapy. Pancreapedia: Exocrine Pancreas Knowledge Base, DOI: 10.3998/panc.2016.15.	Non-specific personal financial	Declare and participate
GC 01	None		
GC 02	None	-	-
GC 03	None	-	-
GC 04	International Chair of the West China Pancreas International Forum 15th – 16th October 2016 held at the Ritz Carlton Hotel, Chengdu, China with expenses paid by West China Hospital. Member of the NHS England Hepato-Pancreato-Billiary Clinical Reference Group as representative of the Pancreatic Society of Great Britain and Ireland from 6th October 2016.	Non Specific personal financial	Declare and participate.
GC 05	None	-	-
GC 06	None	-	-
GC 07	None	-	-
GC 08	None	-	-
GC 09	A new grant form Innovate UK (£300,000) with Cypralis PLC on testing molecules that inhibit cyclophilin D for the treatment of chronic pancreatitis (preclinical). 01/08/17 – 31/07/18.	Personal Non specific financial	Declare and participate
GC 10	None	-	-
GC 11	None	-	-
GC 12	None	-	-

B.13 Stacey Munnelly (nurse)

Meeting	Declaration	Classification	Action taken
Initial application	I am currently working as part of a project team to develop and launch a virtual internet based clinic for patients with stable chronic pancreatitis to access follow up care in place of their traditional face to face outpatient clinic appointment for my employer (CMFT NHS Trust). The work involves collaborating with a commercial sector IT company who will provide a bespoke computer	Non-specific Personal Non-financial	Declare and participate

Meeting	Declaration	Classification	Action taken
	package which will help clinicians to perform health consultations and assess patients remotely by asking a series of set questions related to symptoms. Decisions regarding further investigations required or changes to treatment will then be made and communicated to the patients and their GPs by the responsible clinician via telephone/letter. The computer package simply allows patients to submit data related to their condition and does not make clinical decisions or replace the clinical expertise/judgement of the reviewing clinician. The aim of the virtual clinic is to use technology to facilitate a new innovative way to access healthcare that is convenient and safe and will free up traditional clinic spaces for new patients, consequently reducing waiting times for new referrals in line with new 2015 British Society of Gastroenterology targets for referral to consultation and improving patient engagement and satisfaction. There will be no personal financial rewards. The Trust will incur a financial recompense from local commissioners in the same way that it does for traditional outpatient clinic appointments. I have made no publications or public statements regarding the project but may do so in the future if the project aims are achieved.		
GC 01	None	-	-
GC 02	None	-	-
GC 03	None	-	-
GC 04	None	-	-
GC 05	None	-	-
GC 06	From March 2017, I have been recruited to contribute to and deliver the content of a degree level module for post registration Nurses/Allied Health Care Professionals by the University of Manchester. Topics will include the anatomy, physiology, pathophysiology, management and evidence/research to support management of GI diseases including liver diseases, pancreatic and biliary diseases. I will not receive financial payment for this work.	Specific personal non-financial	Declare and participate.
GC 07	None	-	-
GC 08	None	-	-
GC 09	None	-	-
GC 10	None	-	-
GC 11	None	-	-

Meeting	Declaration	Classification	Action taken
GC 12	None	-	-

B.14 Stuart Wood (lay member)

Meeting	Declaration	Classification	Action taken
Initial application	None	-	-
GC 01	None	-	-
GC 02	None	-	-
GC 03	None	-	-
GC 04	None	-	-
GC 05	None	-	-
GC 06	Attended a meeting of the Liverpool Clinical Trial Unit PPI Group on 28th April 2017. The only payment that I received was for travel expenses. I have been invited to join the committee for which I will, on future occasions, receive a fee as well as expenses.	Non-specific personal financial	Declare and participate
GC 07	None	-	-
GC 08	None	-	-
GC 09	None	-	-
GC 10	None	-	-
GC 11	None	-	-
GC 12	None	-	-

B.15 Tassos Grammatikopoulos (paediatrician)

Meeting	Declaration	Classification	Action taken
Initial application	Children's Liver Disease Foundation research grants in portal hypertension (x2)	Non-specific non-personal financial	Declare and participate
	Papers: Mutations in DCDC2 (doublecortin domain containing protein 2) in neonatal sclerosing cholangitis. Grammatikopoulos T, Sambrotta M, Strautnieks S, Foskett P, Knisely AS, Wagner B, Deheragoda M, Starling C, Mieli-Vergani G, Smith J; University of Washington Center for Mendelian Genomics, Bull L, Thompson RJ. J Hepatol. 2016 Jul 25. pii: S0168-8278(16)30342-7. doi:	Non-specific Personal Non-financial	Declare and participate

Meeting	Declaration	Classification	Action taken
	10.1016/j.jhep.2016.07.017. [Epub ahead of print]. PMID: 27469900. Financial support for above work(non-personal). Funding for this project included NIH R01 DK094828 to L.N.B. and R.J.T., the UCSF-King's. College Health Partners Faculty Fellowship Travel Grant (UCSF Academic Senate) to L.N.B., and NIH U01 DK062500 to P. Rosenthal, as well as a gift of funds from A.S. Knisely. WES was undertaken by the University of Washington Center for Mendelian. Genomics (UW CMG) and was funded by the National Human Genome Research Institute and the National Heart, Lung, and Blood Institute grant 1U54HG006493 to Drs. Debbie Nickerson, Jay Shendure, and Michael Bamshad.		
GC 01	None	-	-
GC 02	None	-	-
GC 03	None	-	-
GC 04	Travel sponsored by Nutricia for lecturing on neonatal cholestasis in December 2016.	Non-specific personal financial	Declare and Participate
GC 05	None	-	-
GC 06	The department was sponsored for organising an international symposium in paediatric liver transplantation at King's College Hospital, London by the International Liver Transplantation Society and pharmaceutical companies Alexion, Intercept and Gilead. I was the symposium organiser.	Non-specific non-personal financial	Declare and participate.
GC 07	None	-	-
GC 08	None	-	-
GC 09	None	-	-
GC 10	None	-	-
GC 11	None	-	-
GC 12	None	-	-

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1 Appendix C: Clinical review protocols

2 C.1 Patient information

Review question	What information and support should people with acute or chronic pancreatitis, their family and carers receive after diagnosis?
Guideline condition and its definition/method of assessment	Acute or chronic pancreatitis, including hereditary
Objective	To determine what type of information and support should be provided to people with acute or chronic pancreatitis, their family and carers after diagnosis. Patient support refers here to direct patient or carer interaction or engagement designed to help management of medication or disease outcomes (for example, adherence, awareness and education), or to provide healthcare professionals with support for their patients.
Population and setting	People with acute or chronic pancreatitis Adults (>16 years) Children (≤ 16 years) Family and carers of people with acute or chronic pancreatitis. Including young carers (<18 years)
Context	Any type of information and support of people with acute or chronic pancreatitis, their family and carers after diagnosis described by studies. For example: Content of information and support required and how this information and support is delivered Information and support to include pain relief, dietary advice Timing of information and support Information for family and carers
Exclusions	Papers that do not report a qualitative analysis
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL,PsychINFO Studies will be restricted to English language only.
Search terms	
The review strategy	Study designs to be considered: Qualitative studies (e.g., interviews, focus groups, observations) Appraisal of methodological quality The methodological quality of each study will be assessed using NCGC modified NICE checklists and the quality of the body of evidence as a whole will be assessed by a GRADE CerQual approach for each review finding. Data synthesis Synthesis of qualitative research: Thematic analysis - information synthesised into main review findings. Results presented in a detailed narrative with accompanying diagrams and in table format with summary statements of main review findings. Note: extract any themes around concerns about incorrect GP diagnosis.

Review question	What information and support should people with acute or chronic pancreatitis, their family and carers receive after diagnosis?
	For full details of the review methods please refer to chapter 4 of the full guideline.
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment)

C.2 Lifestyle interventions: stopping or reducing alcohol consumption

Review question	What is the clinical effectiveness and cost effectiveness of stopping or reducing alcohol consumption in reducing recurrent episodes of acute pancreatitis and improving quality of life in people with either chronic or acute pancreatitis?
Guideline condition and its definition/method of assessment	Pancreatitis
Objectives	To identify the most clinical and cost-effective method to support people with both chronic and acute pancreatitis in stopping or reducing alcohol consumption
Review population	People with acute or chronic pancreatitis
Major age categories	All age categories: Adults (>16) Young people (<16)
Setting	Primary, secondary and tertiary care
Intervention	Structured program to support people with both chronic and acute pancreatitis in stopping or reducing alcohol consumption
Comparator	No structured program/usual care (e.g. general advice)
Outcomes	Critical Quality of life (continuous) (no time cutoff) Mortality (dichotomous) (no time cutoff) Recurrent episodes of pancreatitis (dichotomous) (no time cutoff) Alcohol consumption (dichotomous or continuous) (no time cutoff) Important Nutritional status (continuous or dichotomous) (no time cutoff) Admissions to hospital (dichotomous) (no time cutoff) Morbidity (e.g. pancreatic function, pain) (continuous or dichotomous) (no time cutoff)
Study design	RCTs, systematic reviews of RCTs. If insufficient RCT evidence to form a recommendation is found, non-randomised comparative studies will be included.
Unit of randomisation	Patient or hospital randomised
Population stratification	None (young adults will be considered together with adults)
Review strategy/other analysis	Studies will only be included if they reported one of more of the outcomes listed above. For full details of the review methods please refer to chapter 4 of the full guideline.
Subgroup analyses if there is heterogeneity	Subgroup analyses will be conducted on the following if there is heterogeneity: Severity of pancreatitis (mild, moderate, severe)

Review question	What is the clinical effectiveness and cost effectiveness of stopping or reducing alcohol consumption in reducing recurrent episodes of acute pancreatitis and improving quality of life in people with either chronic or acute pancreatitis?
	Aetiology of pancreatitis (alcohol-related, other) Amount of alcohol consumed (high or low, as defined by national guidelines) Previous pancreatic surgery (previous surgery, no previous surgery) Type of program
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: 1990 Language: Restrict to English only
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment).

C.3 Aetiology of acute pancreatitis

Review question	What is the clinical effectiveness and cost effectiveness of assessing the aetiology of acute pancreatitis to prevent recurrent attacks in people in whom the aetiology is unconfirmed by first-line test results within normal ranges?
Guideline condition and its definition/method of assessment	Acute pancreatitis
Objectives	To identify what is the clinical and cost effectiveness of assessing the aetiology of acute pancreatitis to prevent recurrent attacks in people in which the aetiology is unconfirmed by first line test results within normal range (i.e. patient enquiry for alcohol and ultrasound (US) for gallstones, with or without patient enquiry for genetic causes, blood tests for hypercalcemia, hyperlipidemia).
Review population	People with a diagnosis of acute pancreatitis and aetiology unconfirmed by normal first line tests (i.e. patient enquiry for alcohol and genetic causes, US for gallstones and blood tests for metabolic causes).
Major age categories	Adults (>16 years old) Children (<16 years old)
Setting	All settings
Line of therapy	Not applicable
Interventions: generic/class; specific/drug	Testing for aetiology of acute pancreatitis with any of the following tests: History: drug history, specific questioning for Sphincter of Oddi dysfunction Blood tests: autoantibodies, antibodies, serological tests, tests for hypercalcaemia and hyperlipidaemia DNA test Endoscopic US of gall bladder and bile duct, EUS with duodenoscopy MRCP, secretin-MRCP Combinations of tests
Comparator	No test
Outcomes	Critical outcomes Quality of life (continuous)

Review question	What is the clinical effectiveness and cost effectiveness of assessing the aetiology of acute pancreatitis to prevent recurrent attacks in people in whom the aetiology is unconfirmed by first-line test results within normal ranges?
	Pancreatitis-related mortality (dichotomous) Number of repeated tests (dichotomous) Important outcomes Any pancreatitis-related admissions (including recurrent attacks) (dichotomous) Confirmation of aetiology/identification of a cause (dichotomous) Adverse events following investigations (dichotomous)
Study design	RCTs, systematic reviews of RCTs. If insufficient RCT evidence to form a recommendation is found, non-randomised controlled studies will be included.
Unit of randomisation	Patient or hospital randomised
Crossover study	Not permitted
Other inclusions	Only studies reporting one or more of the outcomes listed above will be included.
Other exclusions	Abstracts
Population stratification	Cause of acute pancreatitis Acute pancreatitis due to a genetic cause Gallstone-related (microlithiasis) acute pancreatitis Autoimmune acute pancreatitis Tumour-related pancreatitis Anatomical anomalies (pancreas divisum) Sphincter of Oddi dysfunction Infectious causes Drug-related pancreatitis Metabolic causes
Reasons for stratification	Different causes of acute pancreatitis are investigated with different tests
Review strategy/other analysis	Paper will only be included if they reported one or more of the outcomes listed above No time cut-off for outcomes was specified a priori. The GC felt it was not appropriate to impose a limit on outcomes for this review question, because consequences of testing could have a long-term effect. For full details of the review methods please refer to chapter 4 of the full guideline.
Subgroup analyses if there is heterogeneity	Causes (see above) Age (children/adults)
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: 1990 Language: English only
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment).

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C.4 Aetiology of chronic pancreatitis

Review question	What is the clinical effectiveness and cost effectiveness of performing genetic marker and autoantibody tests for identifying the aetiology of chronic pancreatitis in people with no known family history of pancreatitis, no significant alcohol history, and normal serum calcium and lipid levels?
Guideline condition and its definition/method of assessment	Chronic pancreatitis
Objectives	To identify what is the clinical and cost effectiveness of performing genetic markers and autoantibodies tests for identifying the aetiology of chronic pancreatitis in people with no known family history of pancreatitis, no significant alcohol history, and normal serum calcium and lipids
Review population	People with a diagnosis of chronic pancreatitis and no known family history of pancreatitis, no significant alcohol history, and normal serum calcium and lipids
Major age categories	Adults (>16 years old) Children (<16 years old)
Setting	All settings
Line of therapy	Not applicable
Interventions: generic/class; specific/drug	For the identification of autoimmune chronic pancreatitis Autoantibodies (for example, IgG4, ANA) For the identification of hereditary chronic pancreatitis (including CFTR) Genetic markers (for example, PRSS1, SPINK1, CFTR)
Comparator	No test
Outcomes	Critical outcomes Quality of life (continuous) Mortality (dichotomous) Number of repeated tests/any pancreatitis-related admissions (dichotomous) Important outcomes Early detection of cancer (for hereditary pancreatitis) (dichotomous) Early detection of extra-pancreatic involvement (for IgG4 related pancreatitis) (dichotomous) Confirmation of etiology/identification of a cause (dichotomous)
Study design	RCTs, systematic reviews of RCTs. If insufficient RCT evidence to form a recommendation is found, non-randomised comparative studies will be included.
Unit of randomisation	Patient or hospital randomised
Crossover study	Not permitted
Other inclusions	Only studies reporting one or more of the outcomes listed above will be included.
Other exclusions	Abstracts
Population stratification	Age: Adults and young people >16 years old children <16 years old
Reasons for stratification	The diagnosis of hereditary pancreatitis is more common in childhood.
Review strategy/other analysis	Paper will only be included if they reported one or more of the outcomes listed above

Review question	**What is the clinical effectiveness and cost effectiveness of performing genetic marker and autoantibody tests for identifying the aetiology of chronic pancreatitis in people with no known family history of pancreatitis, no significant alcohol history, and normal serum calcium and lipid levels?**
	No cut-off for outcomes was established. The GC felt it was not appropriate to impose a limit on outcomes for this review question, as consequences of testing could have a long-term effect. For full details of the review methods please refer to chapter 4 of the full guideline.
Subgroup analyses if there is heterogeneity	None
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: 1990 Language: English only
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment).

C.5 Diagnosing chronic pancreatitis

Review question	**In people with suspected (or under investigation for) chronic pancreatitis, whose diagnosis has not been confirmed by any of CT scan, ultrasound scan or upper GI endoscopy, what is the most accurate diagnostic test to identify whether chronic pancreatitis is present (as indicated by the reference standards: biopsy, clinical follow-up or subsequent CT scan)?**
Objectives	To evaluate and compare the accuracy of diagnostic tests to identify whether chronic pancreatitis is present, in people with suspected (or under investigation for) chronic pancreatitis whose diagnosis has not been confirmed by any of CT scan, US scan and/or upper GI endoscopy
Study design	Prospective and retrospective cohort studies, in which the index tests and the reference standard test are applied to the same patients in a cross-sectional design
Population	All people with suspected (or under investigation for) chronic pancreatitis whose diagnosis has not been confirmed by CT scan, US scan and/or upper GI endoscopy
Major age categories	Adults (>16 years old) Children (<16 years old)
Target condition	Chronic pancreatitis in people presenting with chronic abdominal pain, and normal or uncertain CT and/or US scan and/or upper GI endoscopy
Setting	All care settings (for example GP, hospital)
Index test	Breath tests (C13 mixed tryglicerides test) Endoscopic-based pancreatic function tests Faecal tests (stool tests): Faecal elastase (monoclonal or polyclonal tests) (<200 micrograms per gram) Faecal tests (stool tests): Faecal fat/coefficient of fat absorption (>7 gr per day, when people are on a 100 gr fat intake) Radiological imaging: MRI Radiological imaging: MRCP (= magnetic resonance cholangiopancreatography) Radiological imaging: Secretin-MRCP Endoscopic imaging: ERCP (= endoscopic retrograde cholangiopancreatography)

Review question	**In people with suspected (or under investigation for) chronic pancreatitis, whose diagnosis has not been confirmed by any of CT scan, ultrasound scan or upper GI endoscopy, what is the most accurate diagnostic test to identify whether chronic pancreatitis is present (as indicated by the reference standards: biopsy, clinical follow-up or subsequent CT scan)?**
	Endoscopic imaging: Endoscopic US (cut-off: Rosemont criteria: presence of chronic pancreatitis if >5) (including elastography) Combinations of the tests above Where a cut-off is not indicated, the GC was not able to indicate one a priori.
Reference standard	Biopsy Clinical follow-up Subsequent CT scan
Statistical measures	Specificity Sensitivity Positive and / or Negative predictive value (influenced by prevalence of a condition) Positive and / or negative likelihood ratio (less dependent on the prevalence of the condition) ROC curve or Area under Curve The committee agreed that sensitivity would be the primary measure for decision making.
Other exclusions	Two-gate studies
Search Strategy	Databases: Cochrane, Medline Date limits for search: 1990 Language: English only
Review Strategy	Prospective diagnostic cohorts; if none identified, retrospective diagnostic cohorts Stratum: Age (Children; adults) – children rarely undergo invasive procedures for diagnosis. There is also an issue with radiation protection for imaging. Subgroups (to be investigated if heterogeneity is identified): none identified. Appraisal of methodological quality: The methodological quality of each study will be assessed using the QUADAS-2 checklist (per target condition). Synthesis of data: Diagnostic meta-analysis will be conducted where appropriate and if sufficient data available (when there are 3 or more studies where 2x2 data are available for the same threshold, or agreed similar threshold) using hierarchical methods. For full details of the review methods please refer to chapter 4 of the full guideline.
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment).

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Review question	**In people with suspected (or under investigation for) chronic pancreatitis, in whom other causes have not been excluded by the use of CT scan, ultrasound scan or upper GI endoscopy, what is the most clinically effective and cost effective test to identify whether chronic pancreatitis is present, when each is followed by the appropriate treatment, in order to improve patient outcomes?**
Objectives	To evaluate the clinical effectiveness of different tests in improving patients' outcomes when followed up by appropriate treatment for chronic pancreatitis, in people with suspected (or under investigation for) chronic pancreatitis whose diagnosis has not been confirmed by CT scan, US scan and/or upper GI endoscopy
Population and target condition	People with suspected (or under investigation for) chronic pancreatitis whose diagnosis has not been confirmed by CT scan, US scan and/or upper GI endoscopy
Major age categories	Adults (>16 years old) Children (<16 years old)
Index diagnostic test + treatment	Tests Breath tests (C13 mixed tryglicerides test) Endoscopic-based pancreatic function tests Faecal tests (stool tests): Faecal elastase (monoclonal or polyclonal tests) (<200 micrograms per gram) Faecal tests (stool tests): Faecal fat/coefficient of fat absorption (>7 gr per day, when people are on a 100 gr fat intake) Radiological imaging: MRI Radiological imaging: MRCP (= magnetic resonance cholangiopancreatography) Radiological imaging: Secretin-MRCP Endoscopic imaging: ERCP (= endoscopic retrograde cholangiopancreatography) Endoscopic imaging: Endoscopic US (cut-off: Rosemont criteria: presence of chronic pancreatitis if >5) (including elastography) Combinations of the above tests Where a cut-off is not indicated, the GC was not able to indicate one a priori. Treatment Pancreatic enzyme replacement (PERT) and/or insulin; pain control; management of complications
Comparator index diagnostic tests + treatment or treatment alone (no test)	Tests Biopsy Clinical follow-up Subsequent CT scan Treatment Pancreatic enzyme replacement (PERT) and/or insulin; pain control; management of complications
Outcomes	Critical Quality of life Mortality Adverse events related to test (endoscopic complications) Adverse events related to treatment Important Hospital admission Number of people receiving treatment (i.e. including people who may not have needed it, such as those with false positive results) Patient/physician confidence in test

Review question	**In people with suspected (or under investigation for) chronic pancreatitis, in whom other causes have not been excluded by the use of CT scan, ultrasound scan or upper GI endoscopy, what is the most clinically effective and cost effective test to identify whether chronic pancreatitis is present, when each is followed by the appropriate treatment, in order to improve patient outcomes?**
	Repeat testing/additional testing
Study design	Diagnostic RCTs Systematic reviews of diagnostic RCTs
Unit of randomisation	Patient or hospital randomised
Review strategy	Stratification – groups that cannot be combined: Age (children; adults) Subgroups: N/A For full details of the review methods please refer to chapter 4 of the full guideline.
Search Strategy	Databases: Cochrane library, Medline, Date limits for search: 1990 Language: English only
Key paper	
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment).

C.6 Type of intravenous fluid for resuscitation in people with acute pancreatitis

Review question	**What is the most clinically effective and cost-effective type of intravenous fluid for resuscitation in people with acute pancreatitis?**
Guideline condition and its definition/method of assessment	Acute pancreatitis
Objectives	To identify what type of intravenous fluid is most clinically and cost-effective for people with acute pancreatitis who require fluid resuscitation.
Review population	Those admitted to hospital and receiving treatment for acute pancreatitis
Major age categories	All age categories: Adults and young people (>16) Children (<16)
Setting	Secondary care, tertiary care
Line of therapy	N/A
Interventions and comparators: generic/class; specific/drug	The following types of intravenous fluid: Albumin Synthetic colloids Balanced crystalloids (eg Ringer) Saline
Outcomes	Critical Quality of life (continuous) (<1 year) Mortality (dichotomous) (<1 year) Length of stay (in critical care or hospital) (continuous or dichotomous) Important

Review question	What is the most clinically effective and cost-effective type of intravenous fluid for resuscitation in people with acute pancreatitis?
	Local complications (fluid collection; cystic collection; pancreas necrosis; peri-pancreatic necrosis; local infection) (dichotomous) (<6 months) Systemic complications (persistent organ failure; fluid overload) (dichotomous) (during admission) Serious adverse events (dichotomous) (during admission)
Key confounders	Severity of AP Aetiology Age
Study design	RCTs, systematic reviews of RCTs. If insufficient RCT evidence to form a recommendation is found, non-randomised comparative studies will be included.
Other exclusions	Abstracts Hydroxyethyl starches, as they are not recommended for use by the Medicines and Healthcare products Regulatory Agency due to significant risk of acute kidney injury
Unit of randomisation	Patient or hospital randomised
Population stratification	Age: Adults and young people >16 years old Children <16 years old
Reasons for stratification	Different strategies of fluid resuscitation are used in children
Other stratifications	None
Review strategy/other analysis	Studies will only be included if they reported one of more of the outcomes listed above. For full details of the review methods please refer to chapter 4 of the full guideline.
Subgroup analyses if there is heterogeneity	Elderly (>75) Severity of pancreatitis (as defined by studies; information on the classification of severity used by single studies will be extracted) Type of fluid within class
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: 1990 Language: Restrict to English only
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment).

C.7 Speed of intravenous fluid for resuscitation in people with acute pancreatitis

Review question	What is the most clinically effective and cost-effective speed of administration of intravenous fluid for resuscitation in people with acute pancreatitis?
Guideline condition and its definition/method of assessment	Acute pancreatitis

Review question	What is the most clinically effective and cost-effective speed of administration of intravenous fluid for resuscitation in people with acute pancreatitis?
Objectives	To identify what speed of administration of intravenous fluid is most clinically and cost-effective for people with acute pancreatitis who require fluid resuscitation.
Review population	Those admitted to hospital and receiving treatment for acute pancreatitis who require fluid resuscitation
Major age categories	All age categories: Adults and young people (>16) Children (<16)
Setting	Secondary care, tertiary care
Interventions and comparators: generic/class; specific/drug	'Aggressive' fluid administration (as defined by studies, including goal-directed therapies; for example: 15 ml/kg body weight per hour, ≥ 33% of total volume in 72h of infusion performed in the first 24 hrs., >3.1 L given in first 24hrs) 'Conservative' fluid administration (as defined by studies, including goal-directed therapies; for example, 5-10 ml/kg body weight per hour) Studies in the following fluids will be considered: albumin, synthetic colloids, balanced crystalloids (e.g. Ringer), saline. Only studies where both arms use the same type of fluid will be included.
Outcomes	Critical Quality of life (continuous) (<1 year) Mortality (dichotomous) (<1 year) Length of stay (in critical care or hospital) (continuous or dichotomous) Achievement of pre-specified target for resuscitation (for example, target central venous pressure, urine output, lactate levels, PiCCO measurement) Important Local complications (fluid collection; cystic collection; pancreas necrosis; peri-pancreatic necrosis; local infection) (dichotomous) (<6 months) Systemic complications (persistent organ failure; fluid overload) (dichotomous) (during admission) Serious adverse events (dichotomous) (during admission)
Key confounders	Severity of AP Aetiology Age
Study design	RCTs, systematic reviews of RCTs. If insufficient RCT evidence to form a recommendation is found, non-randomised comparative studies will be included.
Other exclusions	Abstracts Studies where arms use different types of fluids Maintenance fluid administration. For studies in patients receiving fluids for resuscitation and then maintenance (for example, bolus plus maintenance strategies), only outcomes at a time-point that is relevant to the resuscitation therapy given (i.e. after 24hrs) will be extracted. In such studies, outcomes reported at one time point (e.g. CCU or hospital mortality) rather than after the "resuscitation" period (e.g. 24hrs) will not be extracted. Hydroxyethyl starches, as they are not recommended for use by the Medicines and Healthcare products Regulatory Agency due to significant risk of acute kidney injury

Review question	What is the most clinically effective and cost-effective speed of administration of intravenous fluid for resuscitation in people with acute pancreatitis?
Unit of randomisation	Patient or hospital randomised
Population stratification	Age: Adults and young people >16 years old Children <16 years old
Reasons for stratification	Different strategies of fluid resuscitation are used in children
Other stratifications	None
Review strategy/other analysis	As there is no universally accepted definition of 'aggressive' or 'conservative' fluid management, the definition given by the studies will be used. For full details of the review methods please refer to chapter 4 of the full guideline.
Subgroup analyses if there is heterogeneity	Age (Elderly >75 years; <75 years) Severity of pancreatitis (as defined by studies; information on the classification of severity used by single studies will be extracted)
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: 1990 Language: Restrict to English only
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment).

C.8 Route of feeding in people with severe acute pancreatitis

Review question	What is the most clinically effective and cost effective route of feeding at time of admission to the hospital in people with severe acute pancreatitis?
Guideline condition and its definition/method of assessment	Acute pancreatitis
Objectives	To identify the most clinically and cost-effective route of feeding in people with acute pancreatitis
Review population	People with severe or moderately severe acute pancreatitis admitted to hospital
Major age categories	Adults (>16 years old) Children (<16 years old)
Setting	Secondary and tertiary care
Interventions and comparators: generic/class; specific/drug	The following routes of administration will be considered: Oral feeding Enteral feeding (+/- oral feeding), where separate data are available this will be stratified as: Gastric, or jejunal/duodenal Parenteral feeding (+/- oral feeding) Compared to each other Early versus late
Outcomes	Critical

Review question	What is the most clinically effective and cost effective route of feeding at time of admission to the hospital in people with severe acute pancreatitis?
	Quality of life (continuous) (≤ 1 year) Mortality (dichotomous) (≤1 year) Length of stay (in critical care or hospital) (continuous or dichotomous) (≤1 year) Achieving nutrition (meeting nutritional requirements; at least 20-25 kcal/kg (dichotomous) (≤1 year) Requiring total parenteral nutrition (dichotomous) (≤1 year) Important Infections (dichotomous) (≤1 year) Serious adverse events (dichotomous) (≤1 year) Adverse events (dichotomous) (eg tube displacements, aspirational pneumonia, ischemic gut and central line infections – in PN group) Weight loss (continuous or dichotomous) (≤1 year)
Key confounders	Predicted severity on admission Presence of organ failure Vomiting
Study design	RCTs, systematic reviews of RCTs. If insufficient RCT evidence to form a recommendation is found, non-randomised controlled studies will be included.
Other exclusions	Mild acute pancreatitis
Unit of randomisation	Patient or hospital randomised
Population stratification	Age: Adults and young people >16 years old Children <16 years old
Reasons for stratification	Children do not tolerate prolonged periods of nil by mouth in the way adults do and so the routes of feeding routinely used differ from those in adults.
Review strategy/other analysis	Studies will only be included if they reported one of more of the outcomes listed above. Regarding enteral feeding,gastric and jejunal/duodenal will be considered as two different interventions where they are clearly defined in the studies, and comparisons between these two enteral routes will be included. However, if studies describe an intervention as enteral (including a combination of both gastric and jejunal/duodenal) compared with a different feeding route this will also be included. We will accept 'severe' as defined by the author, but acknowledge that there is also a moderately severe category, which will also be included. A network meta-analysis will be considered if sufficient data are available. For full details of the review methods please refer to chapter 4 of the full guideline.
Subgroup analyses if there is heterogeneity	Subgroup analyses will be conducted on the following if there is heterogeneity: Patients in critical care
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: 1990 Language: Restrict to English only
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to

Review question	What is the most clinically effective and cost effective route of feeding at time of admission to the hospital in people with severe acute pancreatitis?
	completion. 10% of papers will be double reviewed (sift and quality assessment)

C.9 Early versus late nutritional intervention in people with chronic pancreatitis

Review question	What is the clinical effectiveness and cost-effectiveness of early compared with late nutritional intervention (for example, food supplements, enzyme supplements) in people with chronic pancreatitis and signs of malnutrition or malabsorption?
Guideline condition and its definition/method of assessment	Chronic pancreatitis
Objectives	To identify the most clinical and cost-effective timing of nutritional intervention in people with chronic pancreatitis and signs of malnutrition or malabsorption.
Review population	Individuals with chronic pancreatitis
Major age categories	All age categories: Adults and young people (>16) Children (<16)
Setting	Primary, secondary and tertiary care
Interventions and comparators: generic/class; specific/drug	Early intervention (as defined by studies, e.g. <5% weight loss) Late intervention (as defined by studies, e.g. ≥5% weight loss) The following interventions will be considered: Nutrition advice Food supplements Enzyme supplements
Outcomes	Critical Quality of life (continuous) (≤ 1 year) Mortality (dichotomous) (≤1 year) Weight loss/BMI (change from baseline or final score; continuous or dichotomous) (≤1 year) Osteoporosis or biochemical deficiencies (dichotomous) (≤1 year) Hospital admissions (dichotomous) (≤1 year) Important Signs of vitamin and mineral deficiency (e.g. skin problems, swollen tongue, poor vision at night, breathlessness, bone and joint pain) (dichotomous) (≤1 year)
Study design	RCTs, systematic reviews of RCTs. If insufficient RCT evidence to form a recommendation is found, non-randomised comparative studies will be included.
Minimum duration of study	1 month
Other exclusions	People with no signs of malnutrition.
Unit of randomisation	Patient or hospital randomised

Review question	What is the clinical effectiveness and cost-effectiveness of early compared with late nutritional intervention (for example, food supplements, enzyme supplements) in people with chronic pancreatitis and signs of malnutrition or malabsorption?
Population stratification	Age: Adults and young people >16 years old Children <16 years old
Reasons for stratification	There may be more long term effects of malnourishment in children undergoing development.
Review strategy/other analysis	Studies will only be included if they reported one of more of the outcomes listed above. For full details of the review methods please refer to chapter 4 of the full guideline.
Subgroup analyses if there is heterogeneity	Subgroup analyses will be conducted on the following if there is heterogeneity: Nutrition advice Food supplements Enzyme supplements
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: 1990 Language: Restrict to English only
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment)

C.10 Specialist versus non-specialist nutritional assessment in people with chronic pancreatitis

Review question	What is the clinical effectiveness and cost-effectiveness of a specialist nutritional assessment compared with a non-specialist assessment for managing malabsorption or malnutrition in people with chronic pancreatitis?
Guideline condition and its definition/method of assessment	Chronic pancreatitis
Objectives	To identify what is the clinical and cost effectiveness of a specialist nutritional assessment compared to a non-specialist assessment for managing malabsorption or malnutrition in people with chronic pancreatitis
Review population	Individuals with chronic pancreatitis
Major age categories	Adults (>16 years old) Children (<16 years old)
Setting	All settings (primary, secondary and tertiary care)
Interventions: generic/class; specific/drug	Specialist nutritional assessment
Comparator	Non-specialist nutritional assessment
Outcomes	Critical Quality of life (continuous) (≤ 1 year)

Review question	What is the clinical effectiveness and cost-effectiveness of a specialist nutritional assessment compared with a non-specialist assessment for managing malabsorption or malnutrition in people with chronic pancreatitis?
	Mortality (dichotomous) (≤1 year) Weight loss/BMI (change from baseline or final score; continuous or dichotomous) (≤1 year) Osteoporosis or biochemical deficiencies (dichotomous) (≤1 year) Hospital admissions (dichotomous) (≤1 year) Unnecessary dietary restriction (low fat diets) (dichotomous) (≤1 year) Important Signs of vitamin and mineral deficiency (e.g. skin problems, swollen tongue, poor vision at night, breathlessness, bone and joint pain) (dichotomous) (≤1 year)
Study design	RCTs, systematic reviews of RCTs. If insufficient RCT evidence to form a recommendation is found, non-randomised comparative studies will be included.
Unit of randomisation	Patient or hospital randomised
Crossover study	Not permitted
Other inclusions	Only studies reporting one or more of the outcomes listed above will be included.
Other exclusions	Abstracts
Population stratification	Age: Adults and young people >16 years old Children <16 years old
Reasons for stratification	There may be more long term effects of malnourishment in children undergoing development so they may require specialist assessment to a different extent from adults.
Review strategy/other analysis	Paper will only be included if they reported one or more of the outcomes listed above For some outcomes, no time cut-off was specified a priori. The GC felt it was not appropriate to impose a limit on some outcomes for this review question, because consequences of testing could have a long-term effect. For full details of the review methods please refer to chapter 4 of the full guideline.
Subgroup analyses if there is heterogeneity	Subgroup analyses will be conducted on the following if there is heterogeneity: Pancreatic exocrine insufficiency / no pancreatic exocrine insufficiency Requiring enteral nutrition / not requiring enteral nutrition
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: 1990 Language: English only
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment)

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C.11 Prophylactic antimicrobial agents to prevent infection in people with acute pancreatitis

Review question	What is the clinical effectiveness and cost effectiveness of prophylactic antimicrobial agents to prevent infection in people with acute pancreatitis?
Guideline condition and its definition/method of assessment	Acute pancreatitis
Objectives	To identify whether or not the use of prophylactic antimicrobial agents to prevent infection in people with acute pancreatitis is clinically and cost effective.
Review population	Those admitted to hospital with acute pancreatitis.
Major age categories	All age categories: Adults and young people (>16) Children (<16)
Setting	Secondary care, tertiary care
Interventions and comparators: generic/class; specific/drug	Intervention: Any antimicrobial therapy administered prophylactically, including antifungals, for example: Antibiotics Penicillins (Ampicillin, Amoxicillin, Amoxicillin/Clavulinic acid, Piperacillin/Tazobactam) Chephalosporins (Cefuroxime, Ceftriaxone, Cefalexin, Ceftazidime, Cefotaxime) Carbapenems (Meropenem, Imipenem/cilastatin, Ertapenem) Fluoroquinolones (Ciprofloxacin, Ofloxacin, Levofloxacin, Pefloxacin) Imidazole (Metronidazole) Oxazolidinones (Linezolid) Tetracyclines (Tigecycline) Other antibiotics (Vancomycin, Teicoplanin, Clindamycin, Aztreonam) Antifungals: Azoles (Caspofungin, Anidulafungin, Micafungin) Azoles (Fluconazole, Miconazole, Econazole, Clotrimazole, Tioconazole, Omoconazole, Ketoconazole, Voriconazole, Posaconazole, Epoxiconazole) Other antifungals (Amphoterecin) Comparison: No antimicrobial therapy (usual care) Placebo Any antimicrobial therapy
Outcomes	Critical Quality of life (continuous) (≤ 1 year) Mortality (dichotomous) (≤1 year) Length of stay (in critical care or hospital) (continuous or dichotomous) Infected necrosis (dichotomous) (≤1 year) Important Extra-pancreatic infection (dichotomous) (≤1 year) Colonisation of resistant organisms (≤6 months, >6 months) Serious adverse events (≤ 6 months, >6 months)
Study design	RCTs, systematic reviews of RCTs.

Review question	What is the clinical effectiveness and cost effectiveness of prophylactic antimicrobial agents to prevent infection in people with acute pancreatitis?
	If insufficient RCT evidence to form a recommendation is found, non-randomised comparative studies will be included for the children strata only.
Other exclusions	People with known infection or already on antibiotics People who are immunosuppressed Abstracts
Unit of randomisation	Patient or hospital randomised
Reasons for stratification	Children with pancreatitis show lower mortality and morbidity rates, lower risk of complications, and lower risk of pancreatic necrosis
Review strategy/other analysis	Antimicrobial agents will be pooled across drug classes and doses. Both inter-class and intra-class comparison allowed For full details of the review methods please refer to chapter 4 of the full guideline.
Subgroup analyses if there is heterogeneity	Subgroup analyses will be conducted on the following if there is heterogeneity: Severity of pancreatitis (as defined by studies; information on the classification of severity used by single studies will be extracted) Drug class / dose / route / duration of therapy
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: 1990 Language: Restrict to English only
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. This question will be double reviewed in full including double sift and quality assessment.

C.12 Methods of management of infected necrosis in people with acute pancreatitis

Review question	What is the most clinically effective and cost-effective method for managing (suspected) infected necrosis in people with acute pancreatitis?
Guideline condition and its definition/method of assessment	Acute pancreatitis
Objectives	To identify what method is the most clinical and cost-effective type of intervention for managing (suspected) infected necrosis in people with acute pancreatitis.
Review population	Individuals with (suspected) infected necrosis in acute pancreatitis.
Major age categories	All age categories: Adults and young people (>16) Children (<16)
Setting	Secondary care, tertiary care
Interventions and comparators: generic/class; specific/drug	Any of the following interventions: Minimally invasive surgery: percutaneous Minimally invasive surgery: endoscopic

Review question	What is the most clinically effective and cost-effective method for managing (suspected) infected necrosis in people with acute pancreatitis?
	Open surgery Percutaneous drainage (radiological) Antibiotic treatment Combination of intervention techniques: combined approach upfront Combination of intervention techniques: step-up approach No treatment
Outcomes	Critical Quality of life (continuous) (≤ 1 year) Mortality (dichotomous) (≤1 year) Length of stay (in critical care or hospital) (continuous or dichotomous) (≤1 year) Important Number of procedures (repeated procedures) (≤1 year) Recurrence of infection (≤1 year) Complications (for example bleeding, fistulae) (≤1 year) Pancreatic function (for example development of diabetes) (≤1 year)
Key confounders	Percentage necrosis Positive bacteriology Presence of organ failure
Study design	RCTs, systematic reviews of RCTs. If insufficient RCT evidence to form a recommendation is found, non-randomised comparative studies will be included.
Other exclusions	None
Unit of randomisation	Patient or hospital randomised
Review strategy/other analysis	Studies will only be included if they reported one of more of the outcomes listed above. For full details of the review methods please refer to chapter 4 of the full guideline.
Subgroup analyses if there is heterogeneity	Subgroup analysis will be conducted on the following if there is heterogeneity: Severity of infection Severity of pancreatitis Type of minimally invasive surgery Procalcitonin-led antibiotic treatment
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: 1990 Language: Restrict to English only
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment).

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C.13 Timing of management of infected necrosis in people with acute pancreatitis

Review question	What is the most clinically effective and cost-effective timing of intervention for managing (suspected) infected necrosis in people with acute pancreatitis?
Guideline condition and its definition/method of assessment	Acute pancreatitis
Objectives	To identify what timing of intervention is the most clinical and cost-effective method for managing (suspected) infected necrosis in people with acute pancreatitis.
Review population	Individuals with (suspected) infected necrosis in acute pancreatitis.
Major age categories	All age categories: Adults and young people (>16) Children (<16)
Setting	Secondary care, tertiary care
Interventions and comparators: generic/class; specific/drug	Early intervention (as defined by studies) Late intervention (as defined by studies) The following interventions will be considered: No treatment Minimally invasive surgery: percutaneous Minimally invasive surgery: endoscopic Open surgery Percutaneous drainage (radiological) Antibiotic treatment Combination of intervention techniques: combined approach upfront Combination of intervention techniques: step-up approach Only studies where both arms use the same type of intervention will be included.
Outcomes	Critical Quality of life (continuous) (≤ 1 year) Mortality (dichotomous) (≤1 year) Length of stay (in critical care or hospital) (continuous or dichotomous) (≤1 year) Important Number of procedures (repeated procedures) (≤1 year) Recurrence of infection (≤1 year) Complications (for example bleeding, fistulae) (≤1 year) Pancreatic function (for example development of diabetes) (≤1 year)
Key confounders	Percentage necrosis Positive bacteriology Presence of organ failure
Study design	RCTs, systematic reviews of RCTs. If insufficient RCT evidence to form a recommendation is found, non-randomised comparative studies will be included.
Other exclusions	None

Review question	What is the most clinically effective and cost-effective timing of intervention for managing (suspected) infected necrosis in people with acute pancreatitis?
Unit of randomisation	Patient or hospital randomised
Review strategy/other analysis	Studies will only be included if they reported one of more of the outcomes listed above For full details of the review methods please refer to chapter 4 of the full guideline.
Subgroup analyses if there is heterogeneity	Subgroup analysis will be conducted on the following if there is heterogeneity: Severity of infection Severity of pancreatitis Type of intervention Procalcitonin-led antibiotic treatment
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: 1990 Language: Restrict to English only
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment).

C.14 Management of pain in people with chronic pancreatitis

Review question	What is the most clinically effective and cost-effective intervention for managing chronic pain in people with chronic pancreatitis?
Guideline condition and its definition/method of assessment	Chronic pancreatitis
Objectives	To identify what type of intervention is most clinically and cost-effective for managing pain in people with chronic pancreatitis.
Review population	People with chronic pancreatitis presenting with chronic pain
Major age categories	All age categories: Adults and young people (>16) Children (<16)
Setting	Primary care, secondary care, tertiary care
Line of therapy	N/A
Interventions	Nerve blocks Opioids Pharmacological therapies (including antioxidants; excluding opioids) Psychological interventions e.g. Psychotherapy Enzyme replacement therapy Surgery Endoscopic treatment Combinations of the above
Comparator	Standard treatment Placebo To each other No pain relief

Review question	What is the most clinically effective and cost-effective intervention for managing chronic pain in people with chronic pancreatitis?
Outcomes	Critical Quality of life (continuous) (no time cutoff) Mortality (dichotomous) (no time cutoff) Pain – acute or chronic (duration of pain, reduction in pain, medication reduction) (continuous or dichotomous) (no time cutoff) Important Serious adverse events (dichotomous) (≤ 1 year) Adverse events (dichotomous) (≤ 1 year) Return to usual activities (continuous or dichotomous) (no time cutoff) Pancreatic function (endocrine and exocrine) (no time cutoff)
Study design	RCTs, systematic reviews of RCTs If insufficient RCT evidence to form a recommendation is found, non-randomised comparative studies will be included.
Other exclusions	Abstracts Pharmacological treatment for neuropathic pain (for example, gabapentin). The Pancreatitis guideline will cross-refer to the Neuropathic pain guideline CG173.
Unit of randomisation	Patient or hospital randomised
Population stratification	Age: Adults and young people >16 years old Children <16 years old
Review strategy/other analysis	Studies will only be included if they reported one of more of the outcomes listed above. Where not specified above, a time cut off for outcomes was not defined a priori. For this review question the GC felt it was not appropriate to impose a limit on some outcomes, because consequences of pain relief could have long-term effects. Acute and chronic pain outcomes will be analysed separately. Note: Presentation with chronic pain is the area where the difficulty of pain control exists (although patients with CP occasionally get acute episodes). A network meta-analysis will be considered if sufficient data are available. For full details of the review methods please refer to chapter 4 of the full guideline.
Subgroup analyses if there is heterogeneity	Severity of pain Types of surgery Types of nerve blocks Drug class Types of psychological therapies
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: 1990 Language: Restrict to English only
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment)

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C.15 Management of pancreatic duct obstruction in people with chronic pancreatitis

Review question	What is the most clinically effective and cost-effective intervention for managing pancreatic duct obstruction, with or without an inflammatory mass, in people with chronic pancreatitis presenting with chronic pain?
Guideline condition and its definition/method of assessment	Chronic pancreatitis
Objectives	To identify what type of intervention is most clinically and cost-effective for managing pancreatic duct obstruction, with or without an inflammatory mass, in people with chronic pancreatitis presenting with chronic pain.
Review population	People with chronic pancreatitis and pancreatic duct obstruction, with or without an inflammatory mass, presenting with pain
Major age categories	All age categories: Adults and young people (>16) Children (<16)
Setting	Secondary care, tertiary care
Line of therapy	N/A
Interventions	Pancreatic endotherapy (endoscopic techniques – pancreatic stent (plastic or metal), pancreatic sphincterotomy, drainage) Pancreatic ESWL (extracorporeal shock wave lithotripsy [ESWL]) – with or without ERCP Surgery (Resection and/or surgical drainage procedure) Combination of techniques (eg ESWL + pancreatic endotherapy)
Comparator	Standard treatment / no treatment To each other
Outcomes	Critical Quality of life (continuous) no time cutoff) Mortality (dichotomous) (no time cutoff) Complications (dichotomous) (≤ 1 year) Pain – acute or chronic (duration of pain, reduction in pain, medication reduction) (continuous or dichotomous) (no time cutoff) Important Length of stay (in critical care or hospital) (continuous) (≤ 1 year) Repeated procedures (dichotomous) (no time cutoff) Pancreatic function (endocrine and exocrine) (no time cutoff)
Study design	RCTs, systematic reviews of RCTs If insufficient RCT evidence to form a recommendation is found, non-randomised comparative studies will be included.
Other exclusions	Abstracts
Unit of randomisation	Patient or hospital randomised
Population stratification	Age: adults >16 years old children and young people <16 years old
Review strategy/other analysis	Studies will only be included if they reported one of more of the outcomes listed above. Where not specified above, a time cut off for outcomes was not defined a priori. For this review question the GC felt it was not appropriate to impose a limit on some outcomes, because consequences of surgery (for example,

Review question	What is the most clinically effective and cost-effective intervention for managing pancreatic duct obstruction, with or without an inflammatory mass, in people with chronic pancreatitis presenting with chronic pain?
	stents) could and have long-term effects. Acute and chronic pain outcomes will be analysed separately. Note: Presentation with chronic pain is the area where the difficulty of pain control exists (although patients with CP occasionally get acute episodes). A network meta-analysis will be considered if sufficient data are available. For full details of the review methods please refer to chapter 4 of the full guideline.
Subgroup analyses if there is heterogeneity	Presence of an inflammatory mass (yes/no) Type of surgery (resection/surgical drainage) Types of endotherapy
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: 1990 Language: Restrict to English only
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment).

C.16 Management of small-duct disease in people with chronic pancreatitis

Review question	What is the most clinically effective and cost-effective intervention for managing small-duct disease (in the absence of pancreatic duct obstruction, inflammatory mass or pseudocyst) in people with chronic pancreatitis presenting with chronic pain?
Guideline condition and its definition/method of assessment	Chronic pancreatitis
Objectives	To identify what type of intervention is most clinically and cost-effective for managing small-duct disease in people with chronic pancreatitis presenting with chronic pain.
Review population	People with chronic pancreatitis and small-duct disease presenting with pain
Major age categories	All age categories: Adults and young people (>16) Children (<16)
Setting	Secondary care, tertiary care
Line of therapy	N/A
Interventions	Surgery (partial or total resection, resection and drainage operation,) Endoscopic treatment
Comparator	Standard care treatment (for example, pharmacological treatment only/enzyme replacement therapy/nerve blocks) / no treatment To each other
Outcomes	Critical Quality of life (continuous) (no time cutoff) Mortality (dichotomous) (no time cutoff)

Review question	**What is the most clinically effective and cost-effective intervention for managing small-duct disease (in the absence of pancreatic duct obstruction, inflammatory mass or pseudocyst) in people with chronic pancreatitis presenting with chronic pain?**
	Complications (dichotomous) (≤ 1 year) Pain – acute or chronic (duration of pain, reduction in pain, medication reduction) (continuous or dichotomous) (no time cutoff) Important Length of stay (in critical care or hospital) (continuous) (≤ 1 year) Repeated procedures (dichotomous) (no time cutoff) Pancreatic function (endocrine and exocrine) (no time cutoff)
Key confounders	Presence of diabetes; Opiates for pain; Presence of pancreatic calcification; Continued alcohol consumption; Continued smoking.
Study design	RCTs, systematic reviews of RCTs If insufficient RCT evidence to form a recommendation is found, non-randomised comparative studies will be included.
Other exclusions	Abstracts
Unit of randomisation	Patient or hospital randomised
Population stratification	Age: Adults and young people >16 years old Children <16 years old
Review strategy/other analysis	Studies will only be included if they reported one of more of the outcomes listed above. Where not specified above, a time cut off for outcomes was not defined a priori. For this review question the GC felt it was not appropriate to impose a limit on some outcomes, because consequences of treatment could have long-term effects. Acute and chronic pain outcomes will be analysed separately. Note: Presentation with chronic pain is the area where the difficulty of pain control exists (although patients with CP occasionally get acute episodes). A network meta-analysis will be considered if sufficient data are available. For full details of the review methods please refer to chapter 4 of the full guideline.
Subgroup analyses if there is heterogeneity	Type of surgery Type of endotherapy
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: 1990 Language: Restrict to English only
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment).

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C.17 Management of pseudocysts

Review question	What is the most clinically effective and cost-effective intervention for managing pseudocysts in people with pancreatitis presenting with or without pain?
Guideline condition and its definition/method of assessment	Acute or chronic pancreatitis
Objectives	To identify what type of intervention is most clinically and cost-effective for managing pseudocysts in people with acute or chronic pancreatitis with or without pain.
Review population	People with acute or chronic pancreatitis and pseudocysts presenting with or without pain
Major age categories	All age categories: Adults and young people (>16) Children (<16)
Setting	Secondary care, tertiary care
Line of therapy	N/A
Interventions	Pancreatic endoscopic stent Endoscopic drainage (EUS-guided) Laparoscopic drainage Percutaneous drainage Open surgery (resection/drainage) Combination of techniques
Comparator	Standard treatment/no treatment To each other
Outcomes	Critical Quality of life (continuous) no time cutoff) Mortality (dichotomous) (≤ 1 year) Complications – bleeding, perforation and infection or overall rate of complications (dichotomous) (no time cutoff) Resolution of presenting symptoms (e.g Pain, nutritional status, gastric outlet obstruction) (continuous or dichotomous) (no time cutoff) Resolution or recurrence of pseudocysts (dichotomous) (no time cutoff) Important Length of stay (in critical care or hospital) (continuous or dichotomous) (≤ 1 year) Repeated procedures (dichotomous) (no time cutoff)
Study design	RCTs, systematic reviews of RCTs If insufficient RCT evidence to form a recommendation is found, non-randomised comparative studies will be included.
Other exclusions	Abstracts
Unit of randomisation	Patient or hospital randomised
Population stratification	Age: Adults and young people >16 years old Children <16 years old
Review strategy/other analysis	Studies will only be included if they reported one of more of the outcomes listed above. Where not specified above, a time cut off for outcomes was not defined a priori. For this review question the GC felt it was not appropriate to impose a limit on some outcomes, because consequences of surgery (for example,

Review question	What is the most clinically effective and cost-effective intervention for managing pseudocysts in people with pancreatitis presenting with or without pain?
	stents) could have long-term effects A network meta-analysis will be considered if sufficient data are available. For full details of the review methods please refer to chapter 4 of the full guideline.
Subgroup analyses if there is heterogeneity	Presence of pain (people presenting with pain; people presenting without pain) Pancreatitis (acute pancreatitis; chronic pancreatitis) Type of stent Type of surgery
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: 1990 Language: Restrict to English only
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment)

C.18 Management of pancreatic ascites and pleural effusion secondary to pancreatitis

Review question	What are the most clinically effective and cost-effective interventions for treating pancreatic ascites and pleural effusion secondary to acute or chronic pancreatitis?
Guideline condition and its definition/method of assessment	Acute or chronic pancreatitis
Objectives	To identify what method is the most clinical and cost-effective type of intervention for treating pancreatic ascites and pleural effusion secondary to acute or chronic pancreatitis
Review population	People with ascites and pleural effusion, including fistulae and intra-abdominal collections, secondary to acute or chronic pancreatitis
Major age categories	All age categories: Adults and young people (>16) Children (<16)
Setting	Secondary care, tertiary care
Interventions and comparators: generic/class; specific/drug	Percutaneous intervention (e.g. aspiration and/or drainage) Surgery (e.g. resection or drainage procedure) Pharmacological treatment (e.g. somatostatin analogue, for example octreotide, lanreotide; diuretics e.g. spironolactone) Nutritional supplements (enteral or parenteral) Pancreatic endotherapy Combinations
Comparator	To each other No treatment

Review question	What are the most clinically effective and cost-effective interventions for treating pancreatic ascites and pleural effusion secondary to acute or chronic pancreatitis?
	Usual care
Outcomes	Critical Quality of life (continuous) (no time cutoff) Mortality (dichotomous) (no time cutoff) Length of stay (in critical care or hospital) (continuous or dichotomous) (no time cutoff) Resolution (e.g. resolution of fluid collection, resolution of fistulae) (no time cutoff) Important Number of procedures (repeated procedures) (time cutoff) Recurrence (time cutoff) Complications (no time cutoff)
Study design	RCTs, systematic reviews of RCTs. If insufficient RCT evidence to form a recommendation is found, non-randomised comparative studies will be included.
Other exclusions	None
Unit of randomisation	Patient or hospital randomised
Review strategy/other analysis	Studies will only be included if they reported one of more of the outcomes listed above. No time cutoff – this is a recurrent condition For full details of the review methods please refer to chapter 4 of the full guideline.
Subgroup analyses if there is heterogeneity	Subgroup analysis will be conducted on the following if there is heterogeneity: Acute or chronic pancreatitis (Ascites and pleural effusion related to chronic pancreatitis are more likely to be associated with pancreatic duct disruption and so may influence the definitive treatment required.)
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: 1990 Language: Restrict to English only
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment).

C.19 Management of biliary obstruction in people with chronic pancreatitis

Review question	What is the most clinically effective and cost-effective intervention for treating biliary obstruction in people with chronic pancreatitis?
Guideline condition and its definition/method of assessment	Chronic pancreatitis
Objectives	To identify what method is the most clinical and cost-effective type of intervention for treating biliary obstruction in people with chronic pancreatitis.

Review question	What is the most clinically effective and cost-effective intervention for treating biliary obstruction in people with chronic pancreatitis?
Review population	People with biliary obstruction and chronic pancreatitis
Major age categories	All age categories: Adults and young people (>16) Children (<16)
Setting	Secondary care, tertiary care
Interventions	Plastic stents (single, multiple) Metal stents (uncovered, partially covered, fully covered) Surgery (for example, hepatojejunostomy, choledocho-jejunostomy, biliary-enteric anastomosis) Combination stent + surgery (eg step-up approach as defined by studies)
Comparator	To each other
Outcomes	Critical Quality of life (continuous) Mortality (dichotomous) (≤1 year) Recurrence of biliary obstruction (including failed stent, both removal and additional stents) (dichotomous) Biliary infections (dichotomous) Important Number of procedures (repeated procedures) (dichotomous) Length of stay (in critical care or hospital) (continuous or dichotomous) Complications (for example, bleeding, fistulae) (dichotomous)
Key confounders	Presence of pancreatic head mass Portal hypertension or portal vein thrombosis Previous biliary stent
Study design	RCTs, systematic reviews of RCTs. If insufficient RCT evidence to form a recommendation is found, non-randomised controlled studies will be included.
Other exclusions	None
Unit of randomisation	Patient or hospital randomised
Reasons for stratification	Treatment modalities are different in children.
Review strategy/other analysis	Studies will only be included if they reported one of more of the outcomes listed above. Where not specified above, a time cut off for outcomes was not defined a priori. For this review question the GC felt it was not appropriate to impose a limit on some outcomes, because consequences of surgery (for example, stents) could have long-term effects A network meta-analysis will be considered if sufficient data are available. For full details of the review methods please refer to chapter 4 of the full guideline.
Subgroup analyses if there is heterogeneity	Subgroup analysis will be conducted on the following if there is heterogeneity: Timing of intervention (prophylactic surgery/on demand surgery) Type of stent (endoscopic vs percutaneous insertion of stent; single/multiple; uncovered/partially covered/fully covered) Type of surgery
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: 1990

Review question	What is the most clinically effective and cost-effective intervention for treating biliary obstruction in people with chronic pancreatitis?
	Language: Restrict to English only
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment)

C.20 Management of type 3c diabetes secondary to pancreatitis

Review question	What is the most clinically effective and cost-effective insulin regimen strategy specifically for type 3c diabetes secondary to pancreatitis?
Guideline condition and its definition/method of assessment	People with acute and chronic pancreatitis
Objectives	To identify the most clinically and cost-effective insulin regimen strategy for diabetes secondary to pancreatitis (type 3c diabetes)
Review population	Individuals diagnosed with diabetes secondary to pancreatitis C peptide-positive people only Includes chronic pancreatitis in people with Cystic fibrosis mutations
Major age categories	All age categories: Adults and young people (>16 years) Children (<16 years)
Setting	Primary, secondary and tertiary care
Interventions: generic/class; specific/drug	Multiple daily injection therapy (basal-bolus)
Comparator	Twice daily insulin regimen Insulin pump
Outcomes	Critical Quality of life (continuous) (≤ 1 year) HbA1c levels (continuous) (no time cutoff) Hospital admissions (for example related to diabetic ketoacidosis or decompensated high glucose levels) (dichotomous)(no time cutoff) Severe hypoglycemia (as defined by the American Diabetes association: an event requiring assistance of another person to actively administer carbohydrates, glucagon, or take other corrective actions. Plasma glucose concentrations may not be available during an event, but neurological recovery following the return of plasma glucose to normal is considered sufficient evidence that the event was induced by a low plasma glucose concentration) (dichotomous) (no time cutoff) Important Mortality (dichotomous) (≤1 year) Hyperglycaemic hyperosmolar nonketotic coma (HONK) (dichotomous) (≤1 year) Fear of hypoglycemia according to known validated scoring systems (for example, Hypoglycemia fear survey) (no time cutoff) Impaired awareness of hypoglycemia according to known validated scoring systems (for example, Gold score, Clarke score, Ryan score (Hypoglycaemia burden score) , Pedersen-Bjergaard score) (dichotomous) (no time cutoff)
Study design	RCTs, systematic reviews of RCTs. If insufficient RCT evidence to form a

Review question	What is the most clinically effective and cost-effective insulin regimen strategy specifically for type 3c diabetes secondary to pancreatitis?
	recommendation is found, non-randomised comparative studies will be included.
Unit of randomisation	Patient or hospital randomised
Other exclusions	Abstracts Type 3c diabetes secondary to pancreatic cancer C-peptide negative patients Once-daily insulin therapy (± oral glucose lowering agents) Comparisons of insulin with oral agents (this would not be of value as likely to reflect different severity of disease, eg C-peptide insufficiency) Management of decompensated glucose levels during acute pancreatitis hospital admission Studies comparing specific types of insulin against each other (for example, different types of long-acting insulin compared to each other)
Population stratification	All age categories: Adults and young people (>16 years) Children (<16 years)
Reasons for stratification	Treatment modalities are different in children.
Review strategy/other analysis	Studies will only be included if they reported one of more of the outcomes listed above. For full details of the review methods please refer to chapter 4 of the full guideline.
Subgroup analyses if there is heterogeneity	Severity of disease (as assessed by presence of calcification in pancreas) Complications of chronic pancreatitis Previous pancreatic surgery Current insulin therapy (yes/no)
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: 1990 Language: Restrict to English only
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment)

C.21 Receiving specialist input in people with acute pancreatitis

Review question	What is the clinical effective and cost-effectiveness of receiving specialist input in people with acute pancreatitis?
Guideline condition and its definition/method of assessment	Pancreatitis
Objectives	To determine the clinical and cost-effectiveness of receiving specialist input in people with acute pancreatitis
Review population	People with acute pancreatitis
Major age categories	All age categories: Adults and young people (>16 years) Children (<16 years)
Setting	Primary, secondary and tertiary care

Review question	What is the clinical effective and cost-effectiveness of receiving specialist input in people with acute pancreatitis?
Interventions: generic/class; specific/drug	Specialist input in the diagnosis, management or follow-up of acute pancreatitis (regardless of setting; e.g., specialist consultation in a secondary setting)
Comparator	No specialist input in the diagnosis, management or follow-up of acute pancreatitis
Outcomes	Critical Quality of life (continuous) (no time cutoff) Mortality (dichotomous) (no time cutoff) Length of stay (continuous) (no time cutoff) Important Hospital admissions (dichotomous) (no time cutoff) Complications (dichotomous) (no time cutoff)
Study design	RCTs, systematic reviews of RCTs. If insufficient RCT evidence to form a recommendation is found, non-randomised comparative studies will be included.
Other exclusions	Abstracts
Unit of randomisation	Patient or hospital randomised
Population stratification	Age: Adults and young people (>16 years) Children (<16 years)
Reasons for stratification	Treatment modalities are different in children.
Review strategy/other analysis	Studies will only be included if they reported one of more of the outcomes listed above. Specialist input was defined as: A tertiary centre; or Consultation with a pancreatitis specialist (either in person or by teleconference); or Consultation in person with a GI specialist For full details of the review methods please refer to chapter 4 of the full guideline.
Subgroup analyses if there is heterogeneity	Severity of disease, as assessed by the revised Atlanta criteria 2012: Mild: no organ failure; no local complications; Moderate: transient organ failure <48h with or without local complications Severe: persistent organ failure >48h Previous pancreatic surgery Presence of necrosis Presence of recurrent acute pancreatitis Aetiology Worsening or persistent organ failure (>48 hours) Presence of ductal changes Age at diagnosis
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: 1990 Language: Restrict to English only
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment)

C.22 Follow-up of pancreatic exocrine function in people with chronic pancreatitis

Review question	How often should follow up to assess pancreatic exocrine function and any secondary health issues, if any, be carried out in people with chronic pancreatitis?
Guideline condition and its definition/method of assessment	Chronic pancreatitis
Objectives	To identify the frequency that investigations should be conducted during follow-up in people with chronic pancreatitis
Review population	People with a diagnosis of chronic pancreatitis
Major age categories	All age categories: Adults and young people (>16 years) Children (<16 years)
Setting	Primary, secondary, tertiary settings
Interventions: generic/class; specific/drug	Follow up (with any of the following tests, alone or in combination: faecal elastase; assessment of nutritional status (for example, measurement of fat-soluble vitamins ADEK; iron; body weight; anthropometrics (for example Z scores); PTH); bone density (DEXA scan)) 6-monthly (or at intervals of ≤ 6 months) Yearly (or at intervals of 6 months - 1 year) At intervals >1 year No follow-up
Comparison	Follow-up versus no follow-up (or follow-up on demand) Different frequency of same follow up investigation
Outcomes	Critical Quality of life (continuous) Mortality (dichotomous) Exocrine function (as measured by for example faecal elastase) Low impact fractures (dichotomous) Changes in nutritional status Important Hospital admissions (dichotomous) Return to usual activities (dichotomous)
Study design	RCTs, systematic reviews of RCTs. If insufficient RCT evidence to form a recommendation is found, non-randomised comparative studies will be included.
Unit of randomisation	Patient or hospital randomised
Other exclusions	Abstracts
Population stratification	Etiology of pancreatitis: hereditary pancreatitis any other etiology Age: Adults and young people >16 years old Children <16 years old
Reasons for stratification	People with hereditary pancreatitis are at higher risk of developing pancreatic cancer; they are also currently followed up as per EUROPAC

Review question	How often should follow up to assess pancreatic exocrine function and any secondary health issues, if any, be carried out in people with chronic pancreatitis?
	guidance Hereditary pancreatitis is more common as aetiology in children
Review strategy/other analysis	Papers will only be included if they reported one or more of the outcomes above. No cut-off for outcomes was established. The GC felt it was not appropriate to impose a limit on outcomes for this review question, as consequences of testing could have a long-term effect. For full details of the review methods please refer to chapter 4 of the full guideline.
Subgroup analyses if there is heterogeneity	Type of investigation (eg imaging) Type of genetic mutation (in hereditary pancreatitis)
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: 1990 Language: Restrict to English only
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment).

C.23 Follow-up to identify diabetes in people with chronic pancreatitis

Review question	How often should follow up to identify the development of diabetes be carried out in people with chronic pancreatitis?
Guideline condition and its definition/method of assessment	Chronic pancreatitis
Objectives	To identify the frequency that investigations should be conducted during follow-up in people with chronic pancreatitis
Review population	People with a diagnosis of chronic pancreatitis
Major age categories	All age categories: Adults and young people (>16 years) Children (<16 years)
Setting	Primary, secondary, tertiary settings
Interventions: generic/class; specific/drug	Surveillance (with HbA1c; fasting glucose; OGTT) 6-monthly (or at intervals of ≤ 6 months) Yearly (or at intervals of 6 months - 1 year) At intervals >1 year No surveillance
Comparison	Follow-up versus no follow-up (or follow-up on demand) Different frequency of same follow up investigation
Outcomes	Critical Quality of life (continuous) Mortality (dichotomous) Important People requiring insulin (dichotomous) Diabetic complications (for example, retinopathy, peripheral neuropathy, CKD) (dichotomous)

Review question	How often should follow up to identify the development of diabetes be carried out in people with chronic pancreatitis?
	Diagnosis of diabetes (dichotomous)
Study design	RCTs, systematic reviews of RCTs. If insufficient RCT evidence to form a recommendation is found, non-randomised comparative studies will be included.
Unit of randomisation	Patient or hospital randomised
Other inclusions	Define
Other exclusions	Abstracts
Population stratification	Etiology of pancreatitis: hereditary pancreatitis any other etiology Age: Adults and young people >16 years old Children <16 years old
Reasons for stratification	People with hereditary pancreatitis are at higher risk of developing pancreatic cancer; they are also currently followed up as per EUROPAC guidance Hereditary pancreatitis is more common as aetiology in children
Review strategy/other analysis	Papers will only be included if they reported one or more of the outcomes above. No cut-off for outcomes was established. The GC felt it was not appropriate to impose a limit on outcomes for this review question, as consequences of testing could have a long-term effect. For full details of the review methods please refer to chapter 4 of the full guideline.
Subgroup analyses if there is heterogeneity	Type of investigation (eg imaging) Type of genetic mutation (in hereditary pancreatitis)
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: 1990 Language: Restrict to English only
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment).

C.24 Follow-up to identify pancreatic cancer in people with chronic pancreatitis

Review question	How often should follow up to identify the development of pancreatic cancer be carried out in people with chronic pancreatitis?
Guideline condition and its definition/method of assessment	Chronic pancreatitis
Objectives	To identify the frequency that investigations should be conducted during follow-up in people with chronic pancreatitis
Review population	People with a diagnosis of chronic pancreatitis
Major age categories	All age categories: Adults and young people (>16 years)

Review question	How often should follow up to identify the development of pancreatic cancer be carried out in people with chronic pancreatitis?
	Children (<16 years)
Setting	Primary, secondary, tertiary settings
Interventions: generic/class; specific/drug	Surveillance (with any of the following tests, alone or in combination: tumour markers (eg CA19.9); MRI; EUS; CT) 6-monthly (or at intervals of ≤ 6 months) Yearly (or at intervals of 6 months - 1 year) At intervals >1 year No surveillance
Comparison	Follow-up versus no follow-up (or follow-up on demand) Different frequency of same follow up investigation
Outcomes	Critical Quality of life (continuous) Mortality (dichotomous) Cancer-related mortality (dichotomous) Important Stage of cancer at diagnosis Serious adverse events (dichotomous)
Study design	RCTs, systematic reviews of RCTs. If insufficient RCT evidence to form a recommendation is found, non-randomised comparative studies will be included.
Unit of randomisation	Patient or hospital randomised
Other exclusions	Abstracts
Population stratification	Etiology of pancreatitis: hereditary pancreatitis any other etiology Age: Adults and young people >16 years old Children <16 years old
Reasons for stratification	People with hereditary pancreatitis are at higher risk of developing pancreatic cancer; they are also currently followed up as per EUROPAC guidance Hereditary pancreatitis is more common as aetiology in children
Review strategy/other analysis	Papers will only be included if they reported one or more of the outcomes above. No cut-off for outcomes was established. The GC felt it was not appropriate to impose a limit on outcomes for this review question, as consequences of testing could have a long-term effect. For full details of the review methods please refer to chapter 4 of the full guideline.
Subgroup analyses if there is heterogeneity	Type of investigation (eg imaging) Type of genetic mutation (in hereditary pancreatitis)
Search criteria	Databases: Medline, Embase, the Cochrane Library Date limits for search: 1990 Language: Restrict to English only
Quality assurance measures	Quality assurance will be undertaken by a senior research fellow prior to completion. 10% of papers will be double reviewed (sift and quality assessment).

1

Appendix D: Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	Populations, interventions and comparators must be as specified in the clinical review protocols in appendix D above. Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) Unpublished reports will not be considered unless submitted as part of a call for evidence. Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix G.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2001, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[787] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation as excluded health economic studies in appendix M. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France,

Review question	All questions – health economic evidence
	Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example, Switzerland). • Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2001 or later but that depend on unit costs and resource data entirely or predominantly from before 2001 will be rated as 'Not applicable'. • Studies published before 2001 will be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

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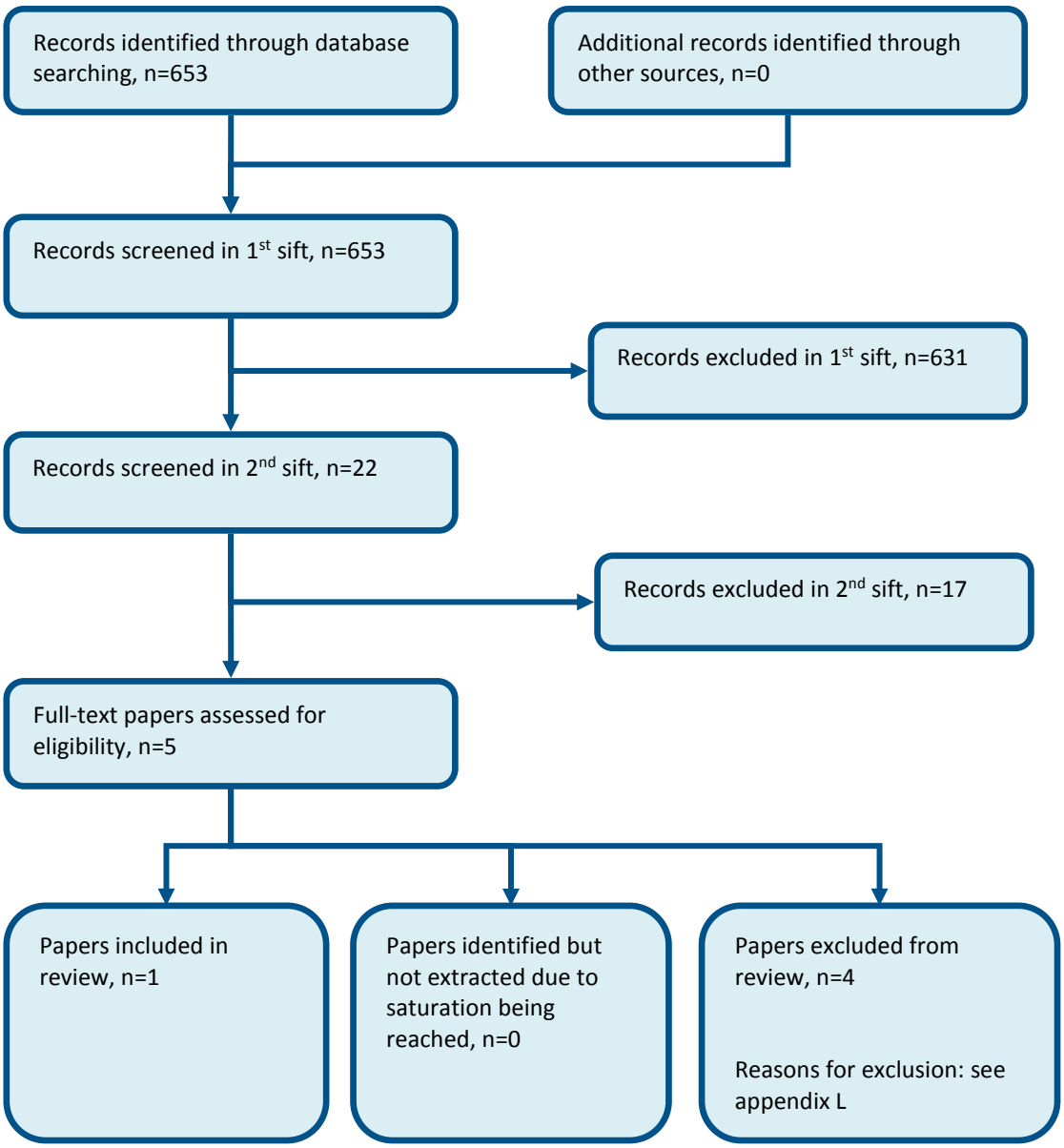
Appendix E: Clinical study selection

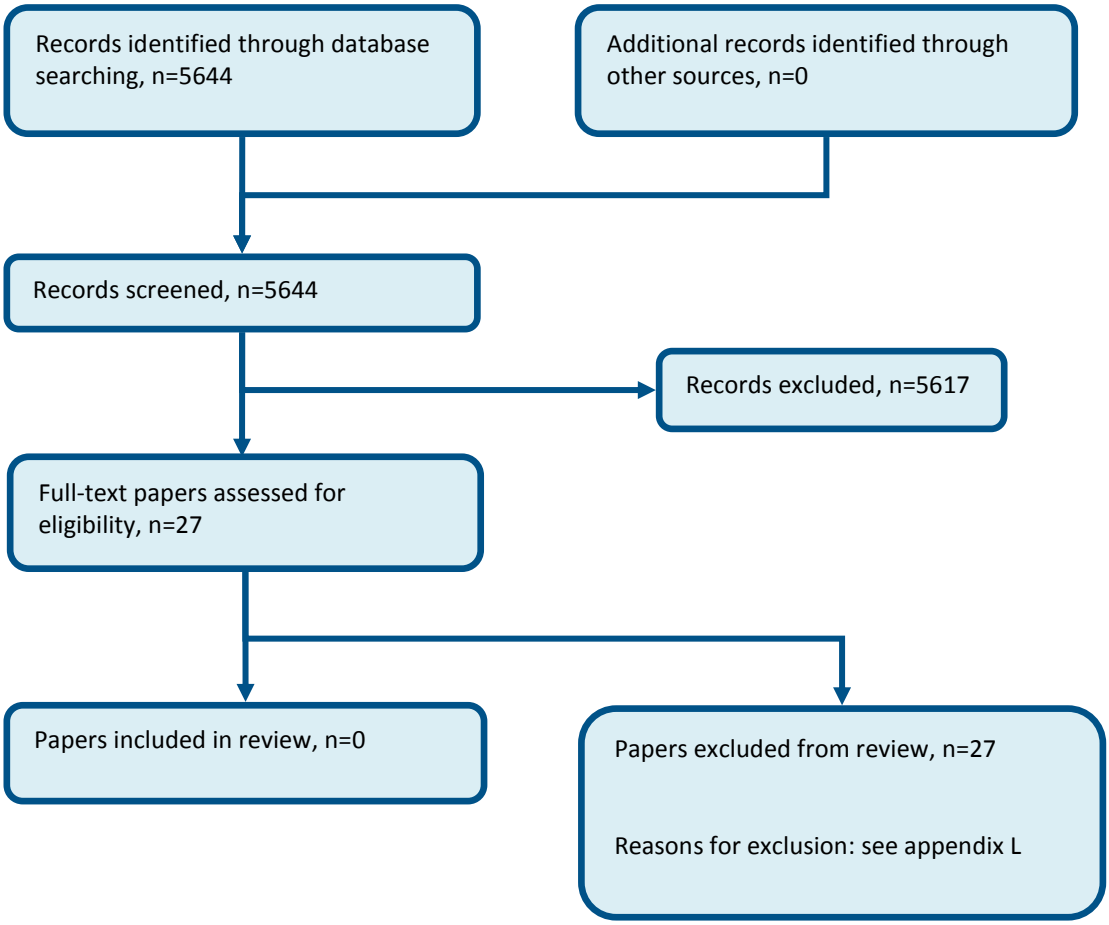
E.1 Patient information (qualitative study selection)

Figure 1: Flow chart of qualitative study selection for the review of information and support



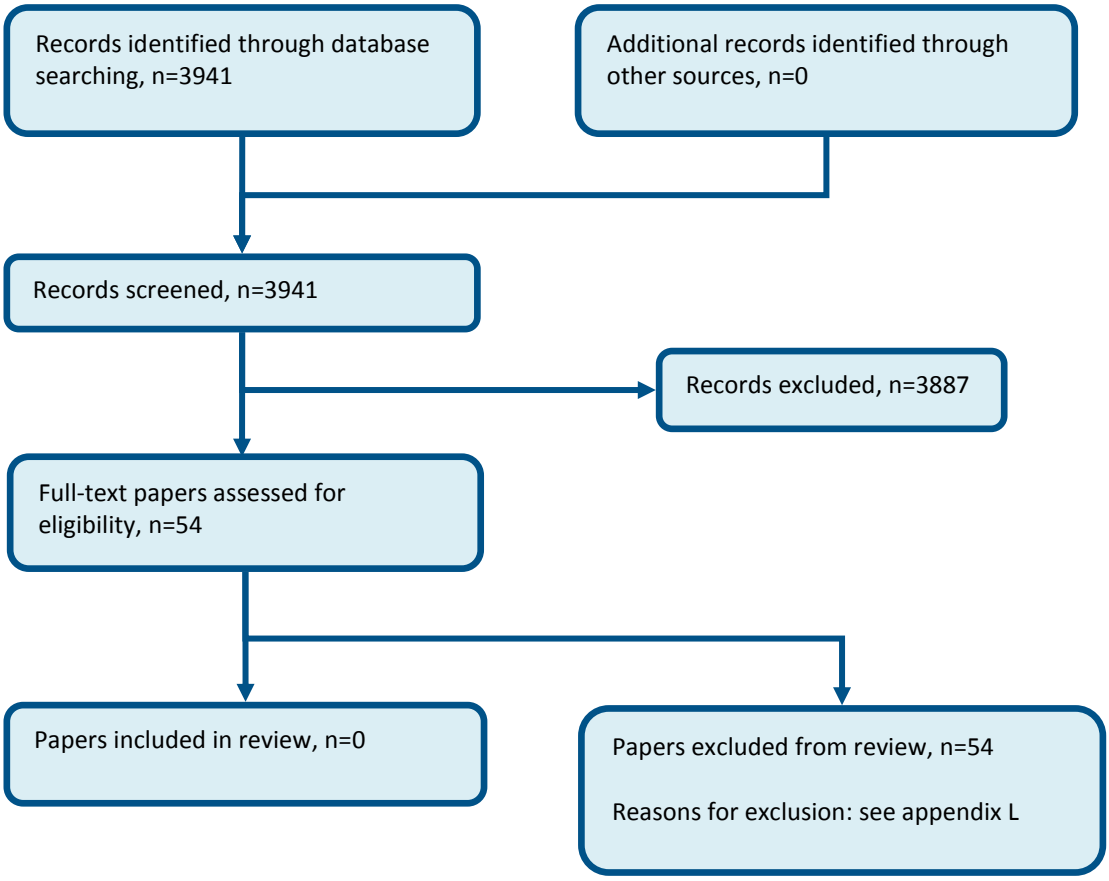
E.2 Aetiology of acute pancreatitis

Figure 2: Flow chart of clinical study selection for the review of aetiology of acute pancreatitis



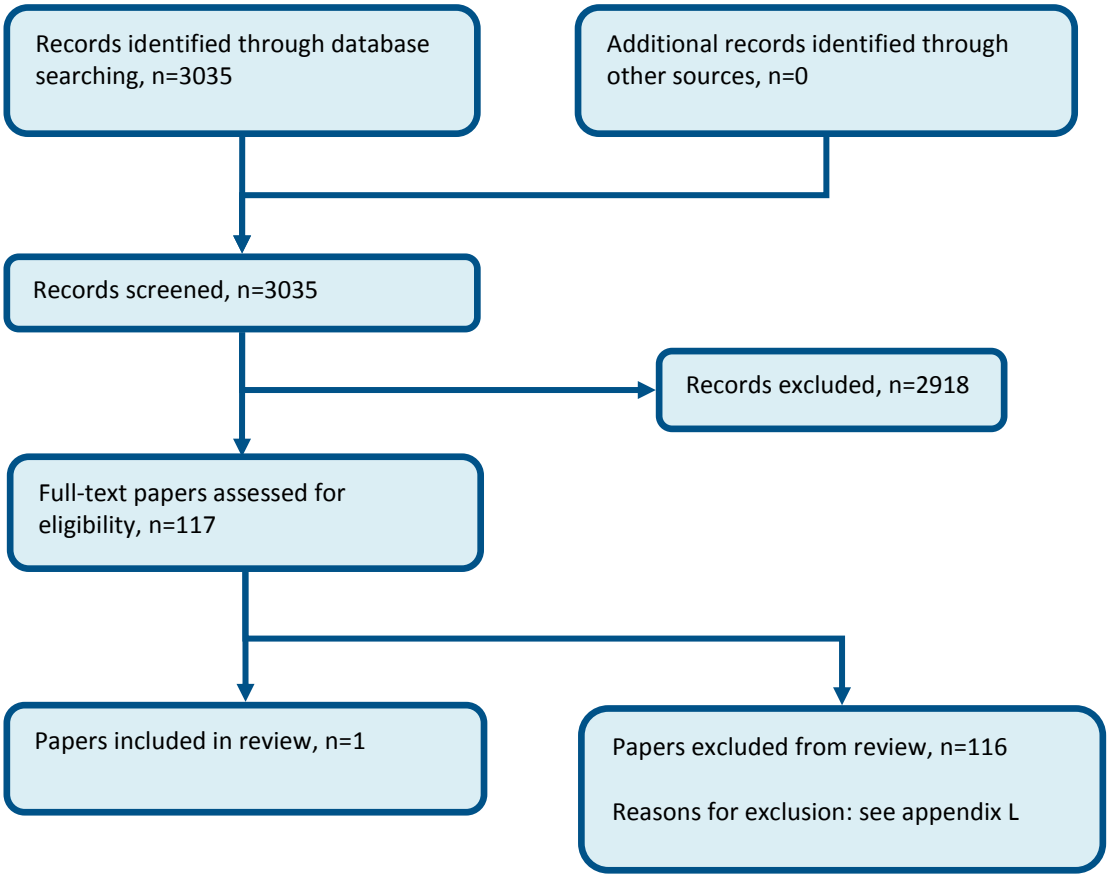
E.3 Aetiology of chronic pancreatitis

Figure 3: Flow chart of clinical study selection for the review of aetiology of chronic pancreatitis



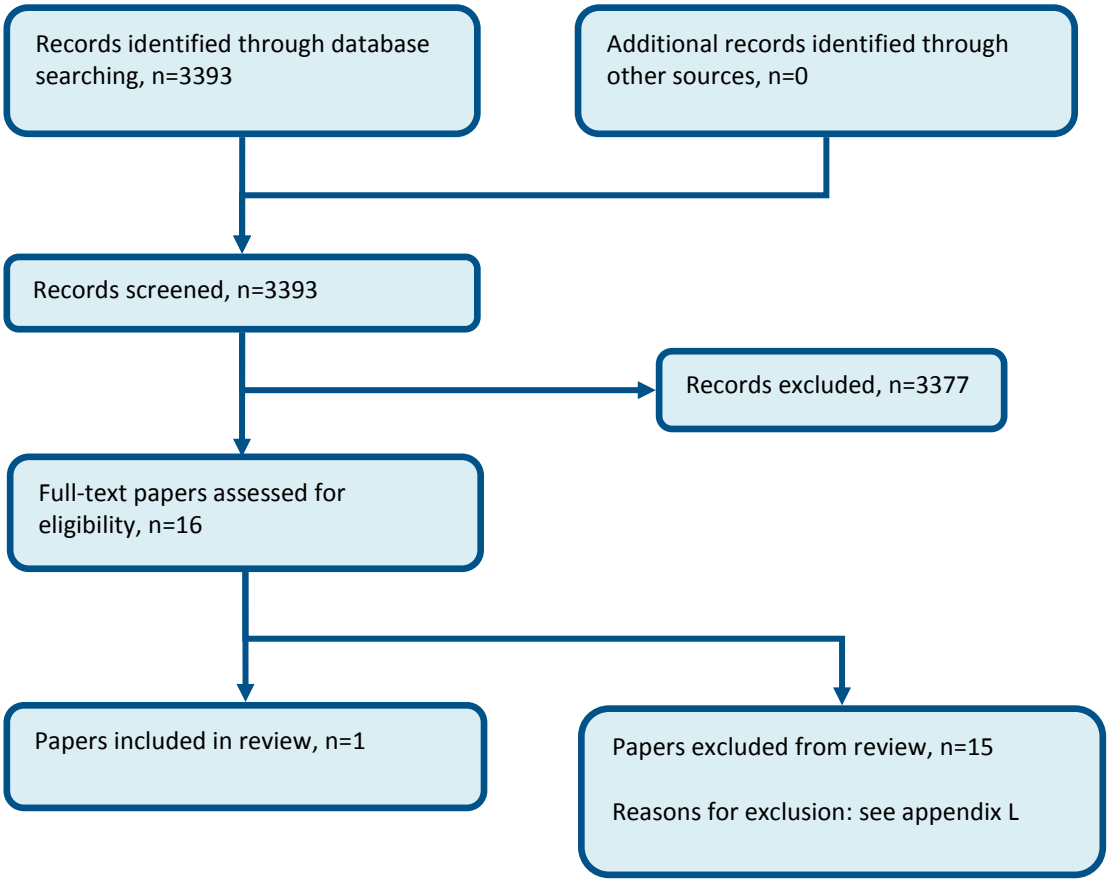
E.4 Diagnosing chronic pancreatitis

Figure 4: Flow chart of clinical study selection for the review of Diagnosis of chronic pancreatitis



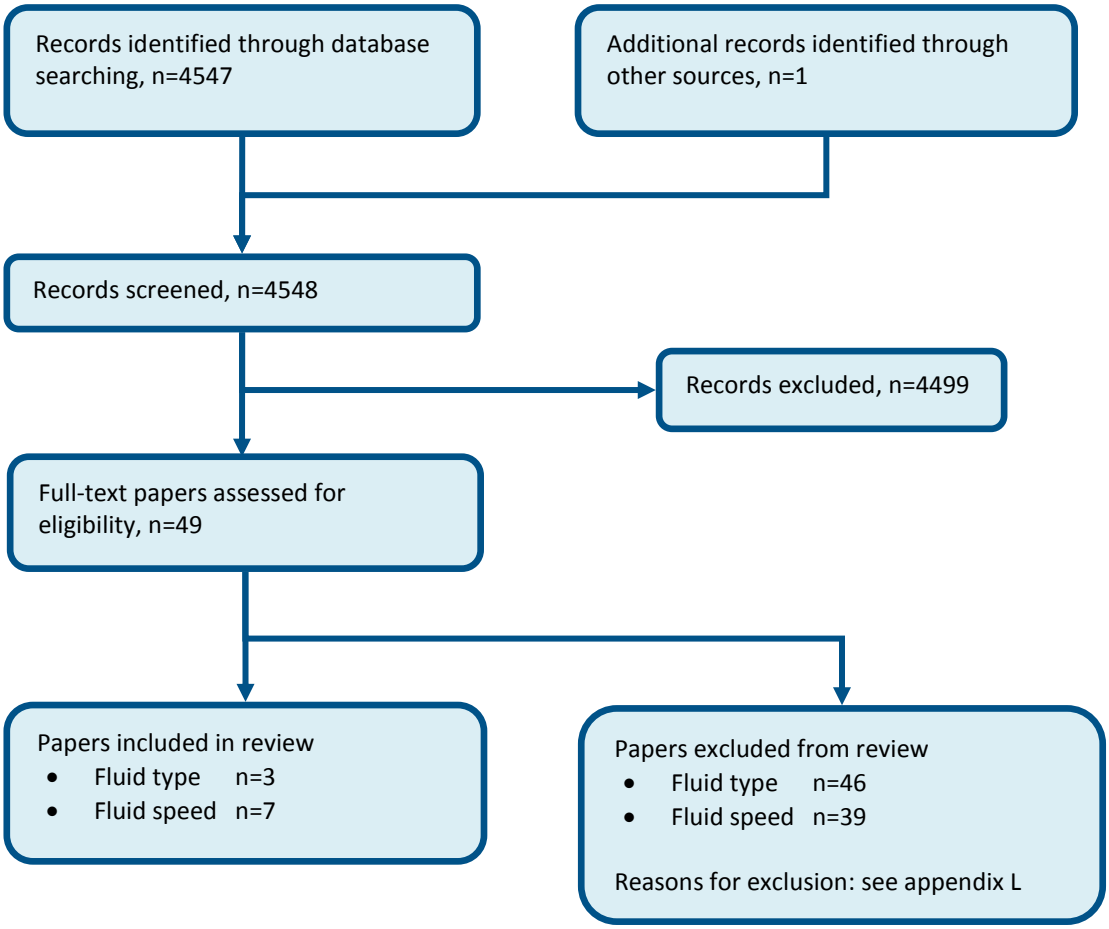
E.5 Lifestyle interventions: stopping or reducing alcohol consumption

Figure 5: Flow chart of clinical study selection for the review of lifestyle intervention (alcohol consumption)



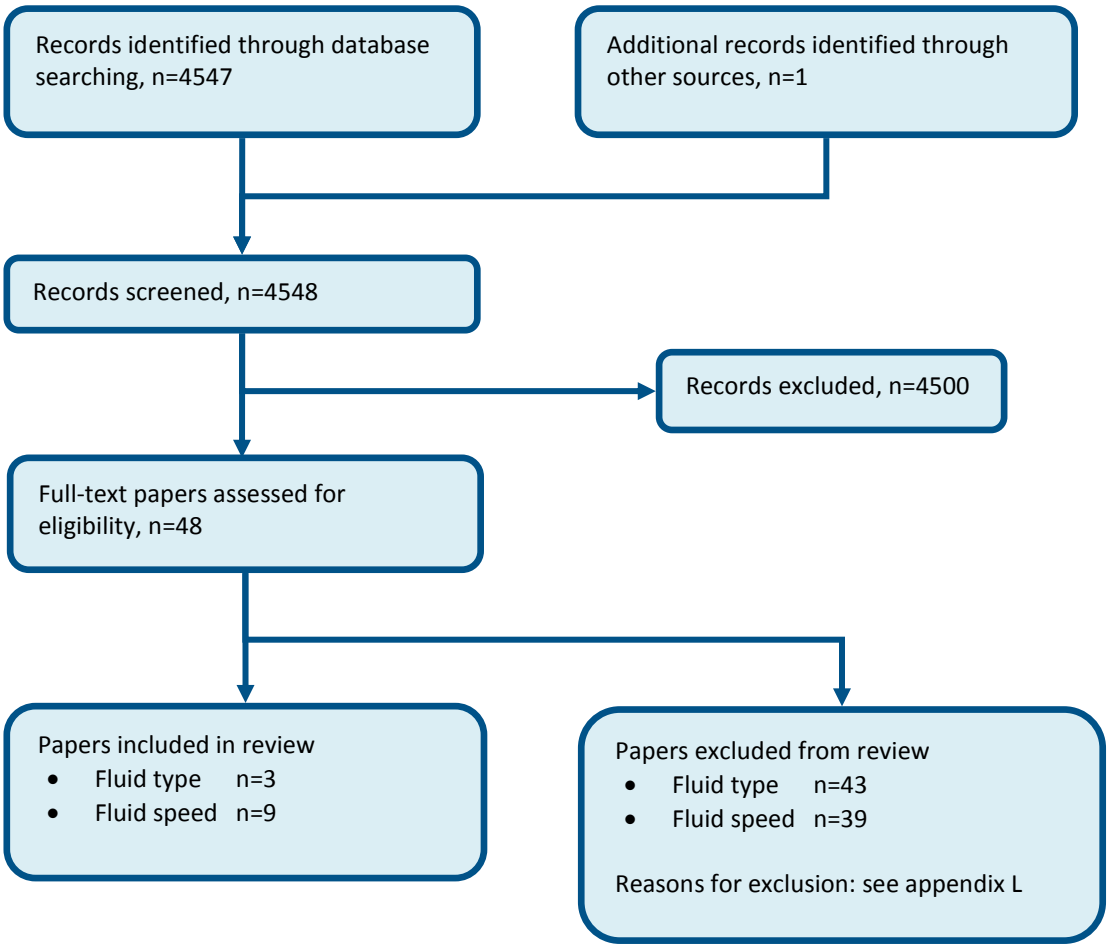
E.6 Fluid Resuscitation - Type

Figure 6: Flow chart of clinical study selection for the reviews of IV fluid for resuscitation in acute pancreatitis



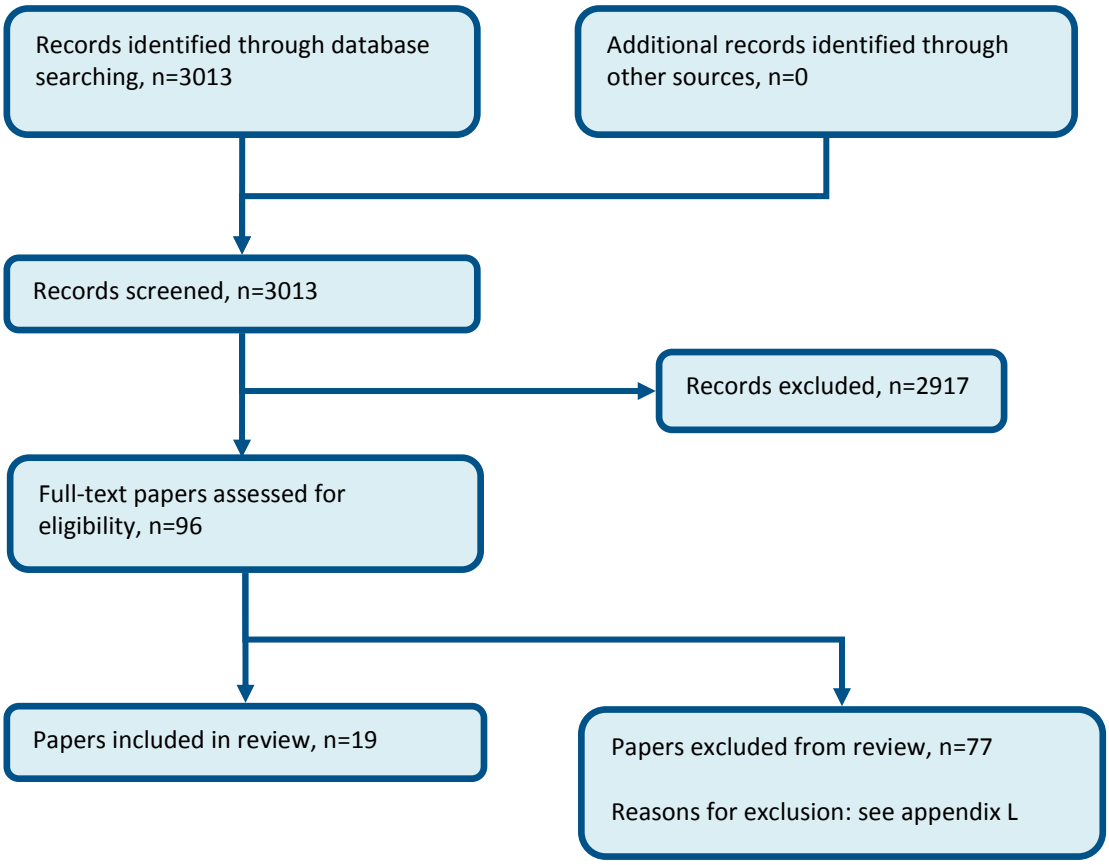
E.7 Speed of intravenous fluid for resuscitation in people with acute pancreatitis

Figure 7: Flow chart of clinical study selection for the review of IV fluid resuscitation in acute pancreatitis



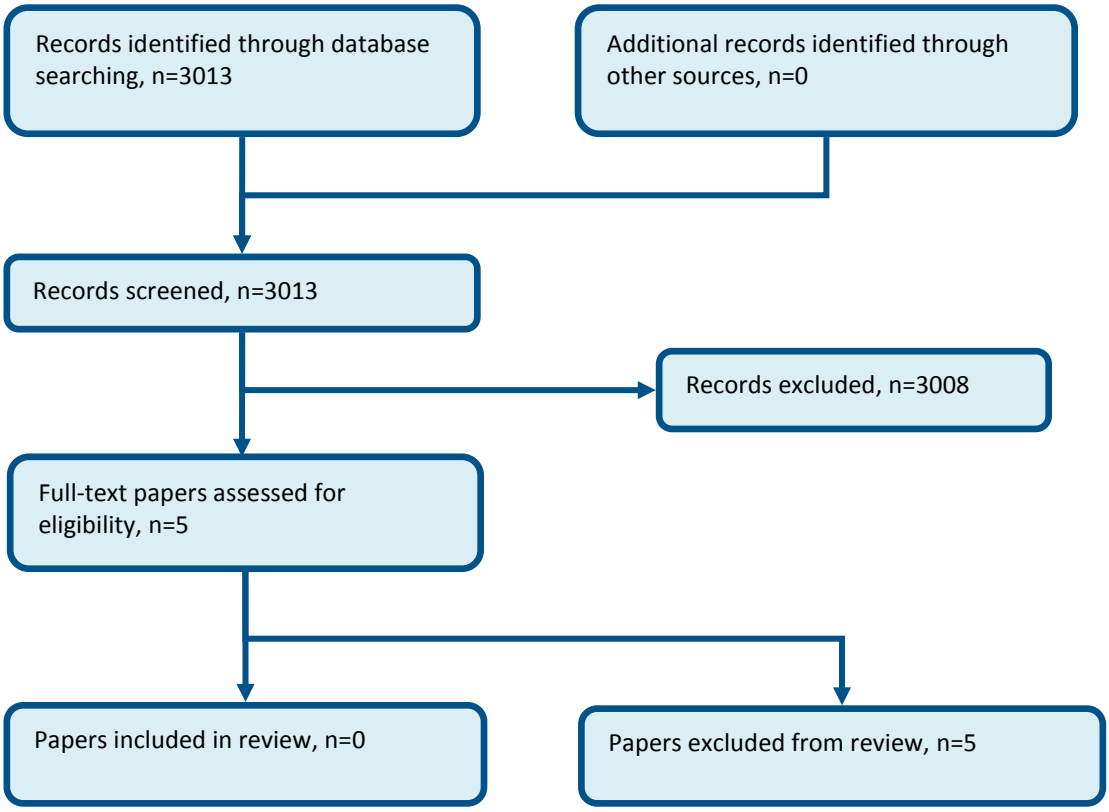
E.8 Route of feeding in people with severe acute pancreatitis

Figure 8: Flow chart of clinical study selection for the review of route of feeding for severe acute pancreatitis



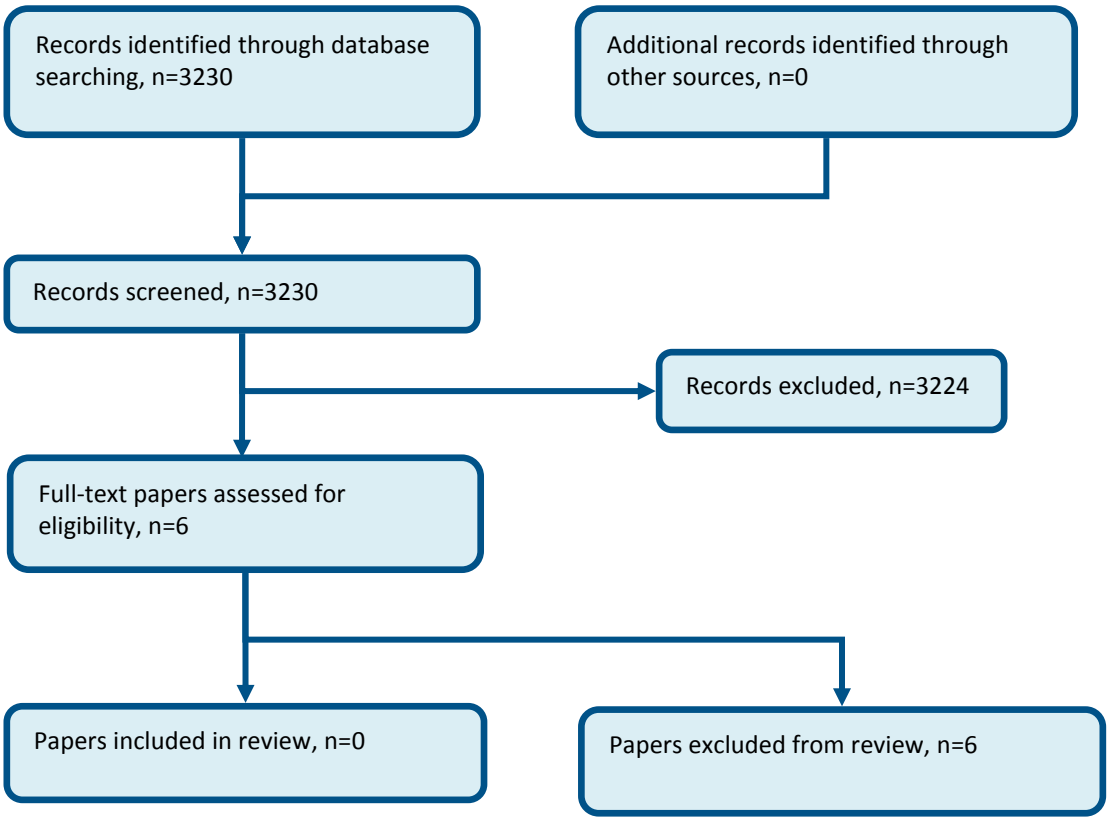
E.9 Early versus late nutritional intervention in people with chronic pancreatitis

Figure 9: Flow chart of clinical study selection for the review of the timing of nutritional intervention



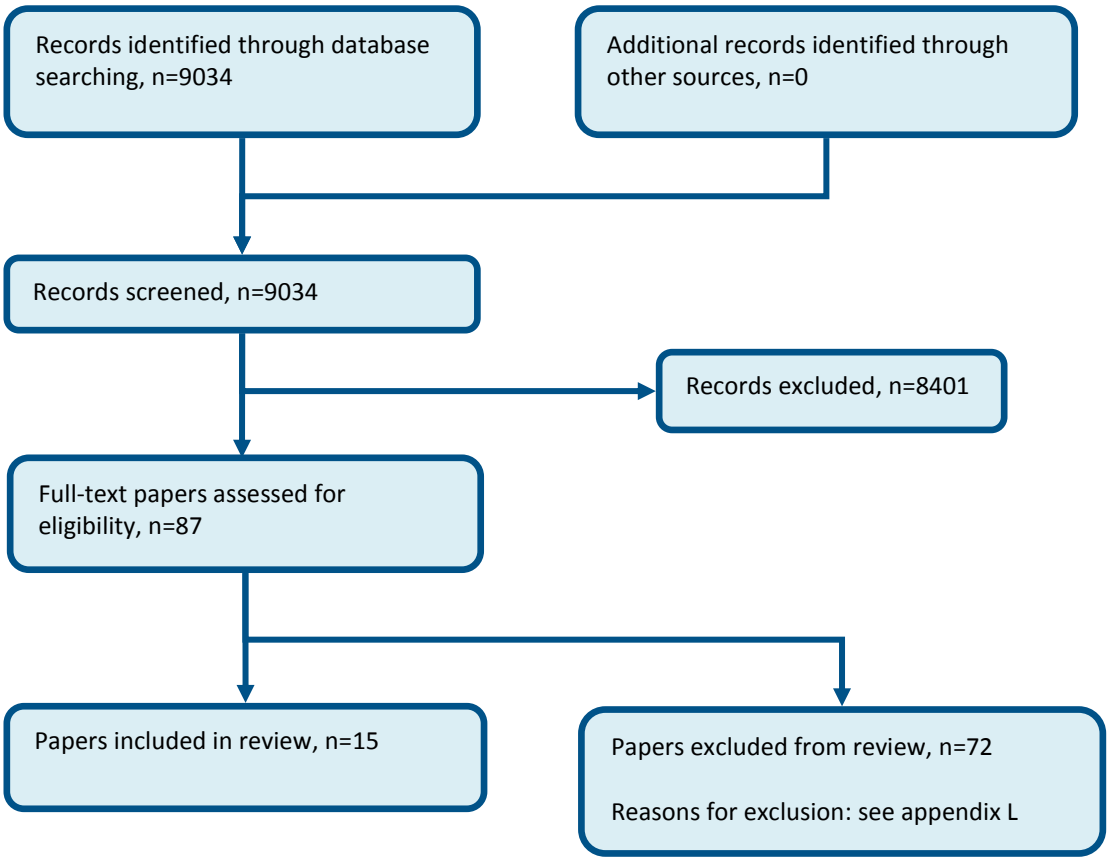
E.10 Specialist versus non-specialist nutritional assessment in people with chronic pancreatitis

Figure 10: Flow chart of clinical study selection for the review of specialist versus non-specialist nutritional assessment



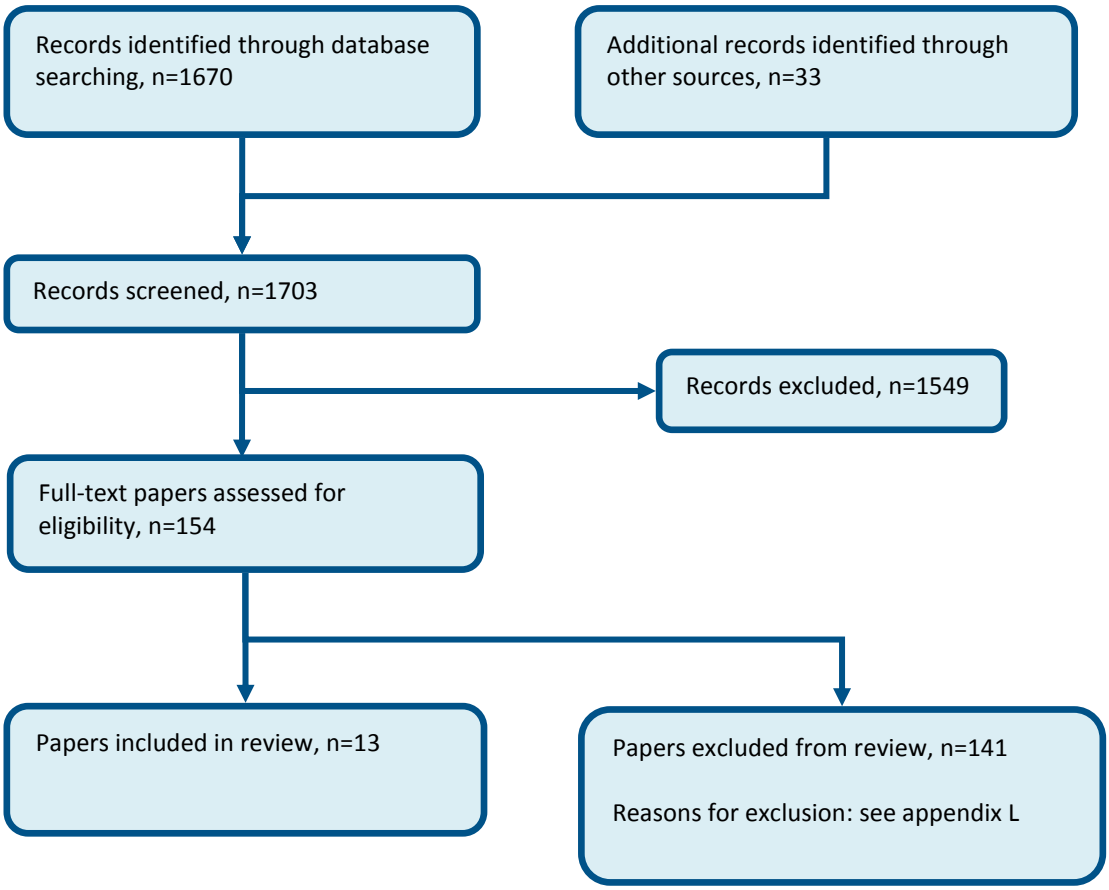
E.11 Prophylactic antimicrobial agents to prevent infection in people with acute pancreatitis

Figure 11: Flow chart of clinical study selection for the review of antimicrobial prophylaxis for acute pancreatitis



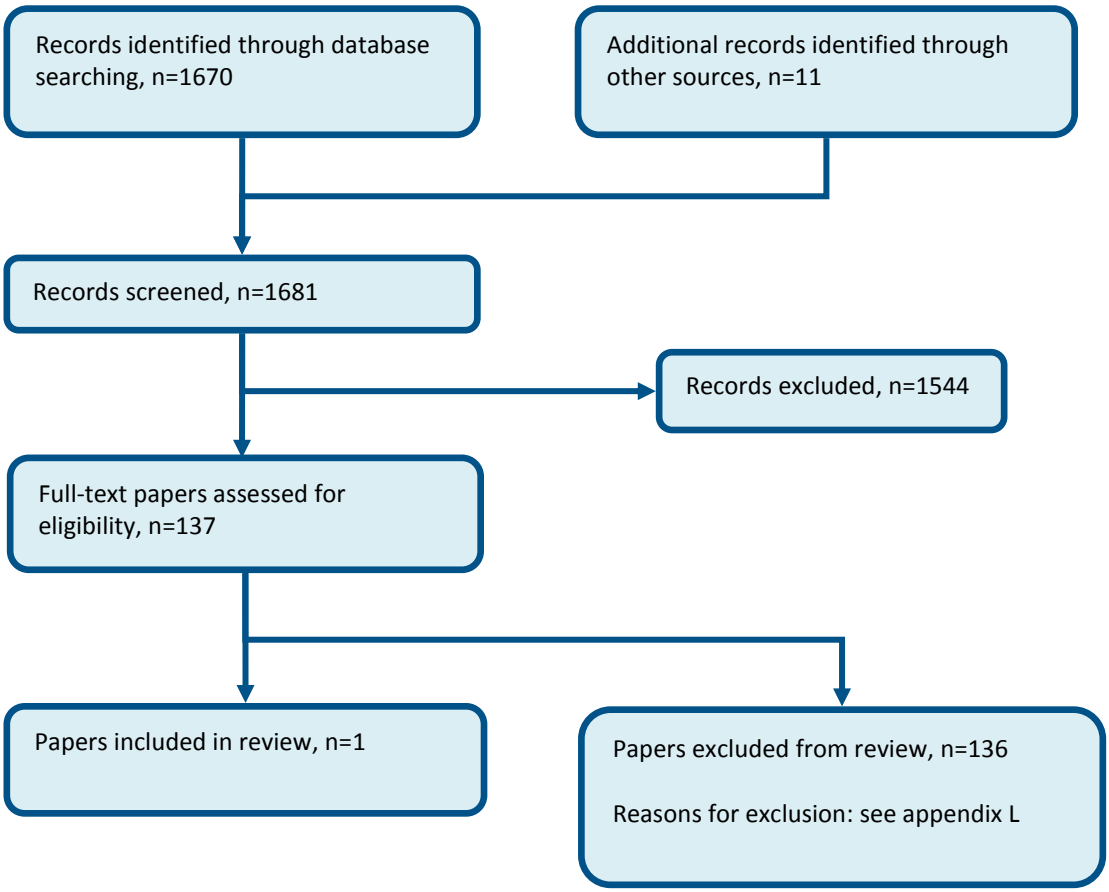
E.12 Methods of management of infected necrosis in people with acute pancreatitis

Figure 12: Flow chart of clinical study selection for the review of what is the most clinical and cost-effective method for managing (suspected) infected necrosis in people with acute pancreatitis?



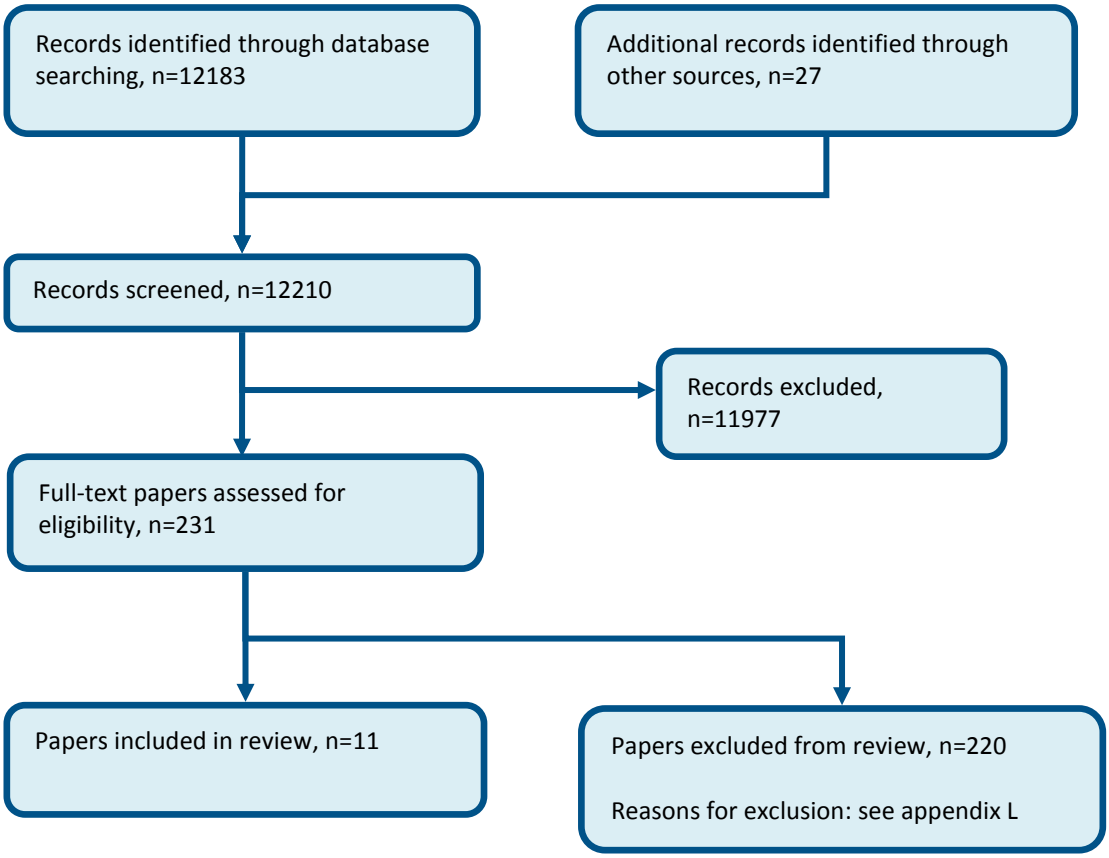
E.13 Timing of management of infected necrosis in people with acute pancreatitis

Figure 13: Flow chart of clinical study selection for the review of the timing of intervention for managing infected necrosis in people with acute pancreatitis



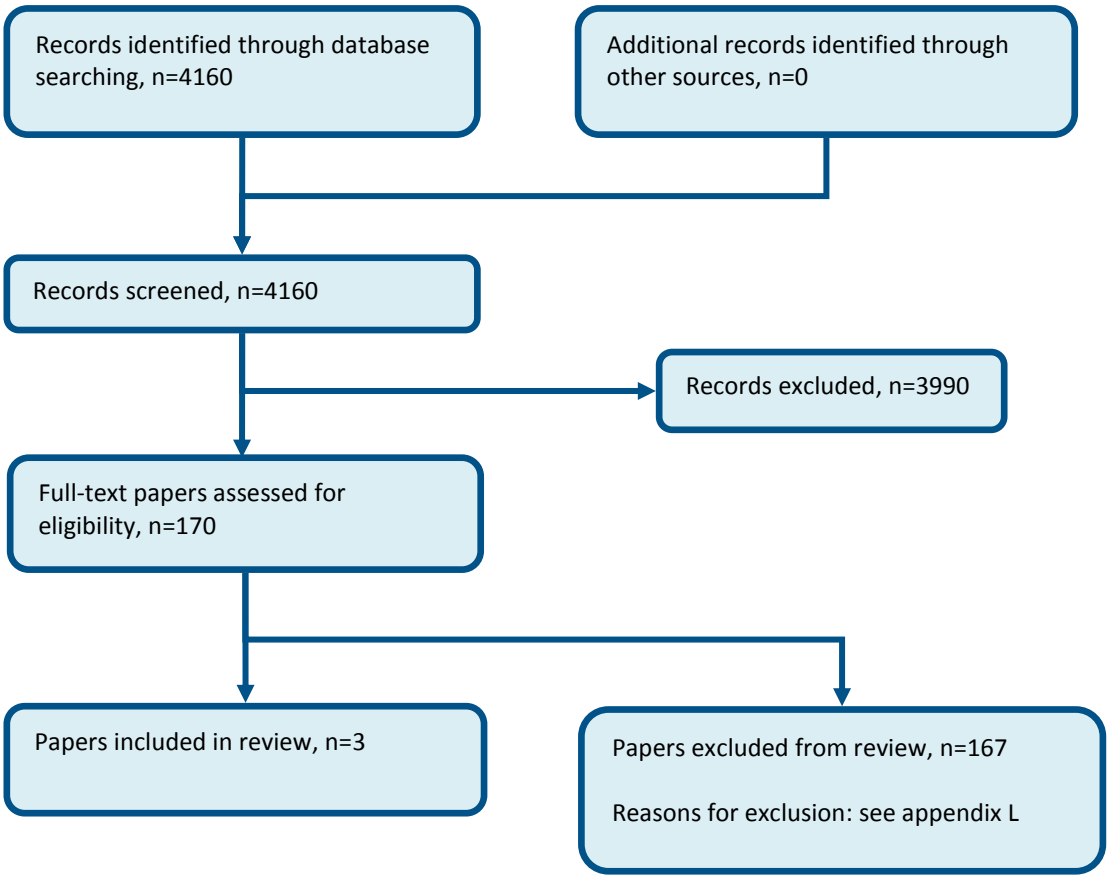
E.14 Management of pain in people with chronic pancreatitis

Figure 14: Flow chart of clinical study selection for the review of management of pain in people with chronic pancreatitis



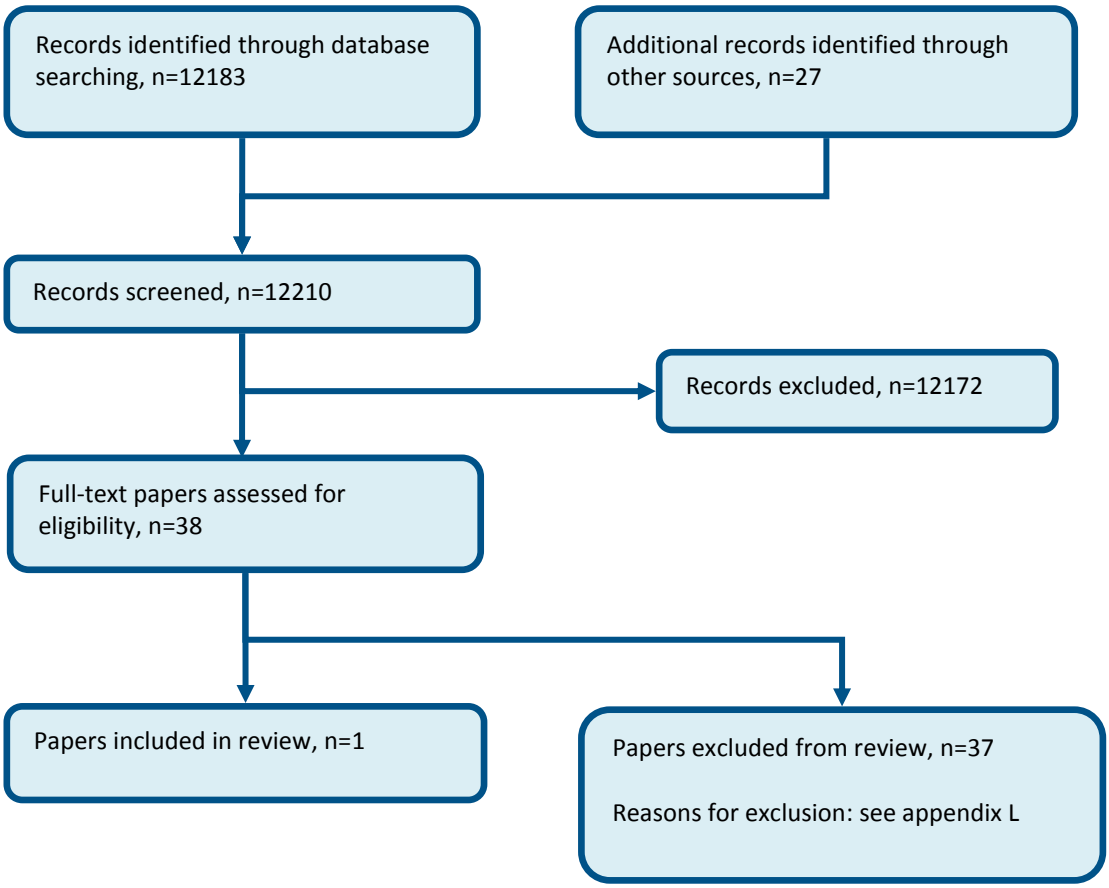
E.15 Management of pancreatic duct obstruction in people with chronic pancreatitis

Figure 15: Flow chart of clinical study selection for the review of what is the most clinically and cost-effective intervention for managing pancreatic duct obstruction, with or without an inflammatory mass, in people with chronic pancreatitis presenting with pain?



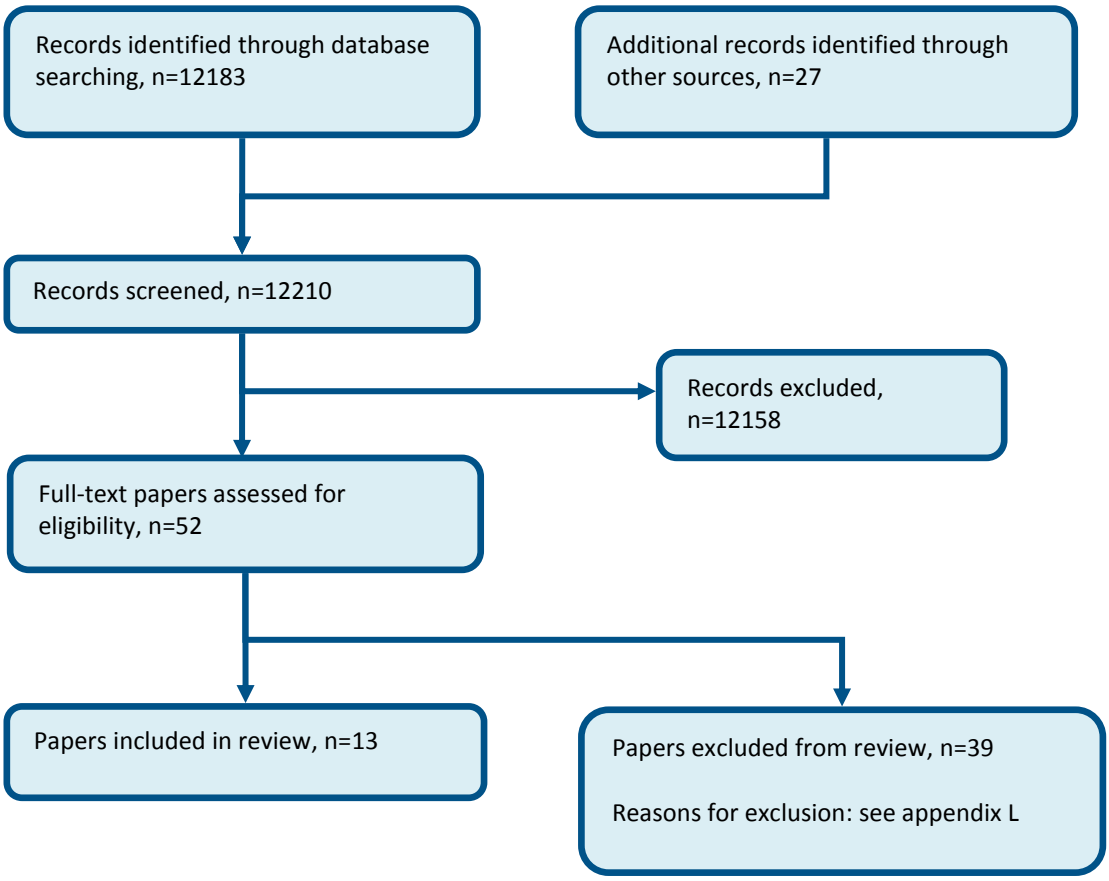
E.16 Management of small-duct disease in people with chronic pancreatitis

Figure 16: Flow chart of clinical study selection for the review of pain management in small duct disease



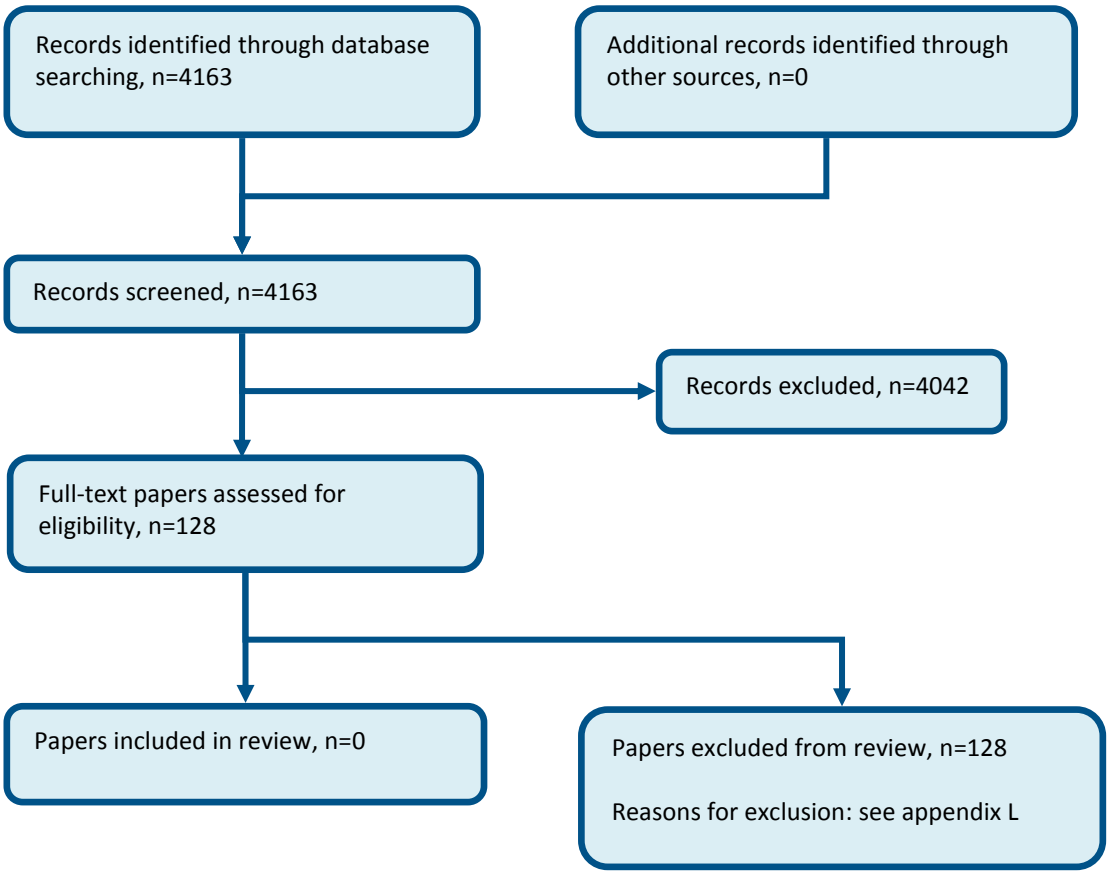
E.17 Management of pseudocysts

Figure 17: Flow chart of clinical study selection for the review of pseudocysts



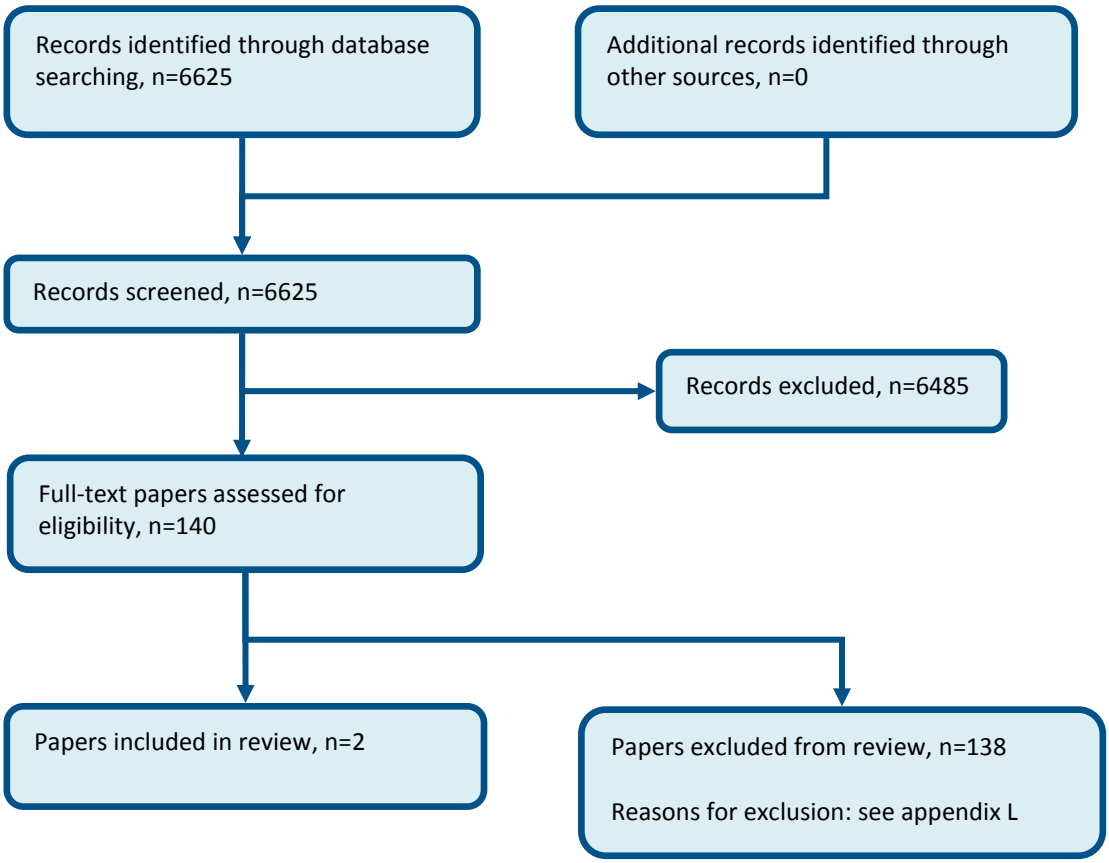
E.18 Management of pancreatic ascites and pleural effusion secondary to pancreatitis

Figure 18: Flow chart of clinical study selection for the review of managing pancreatic ascites and pleural effusion



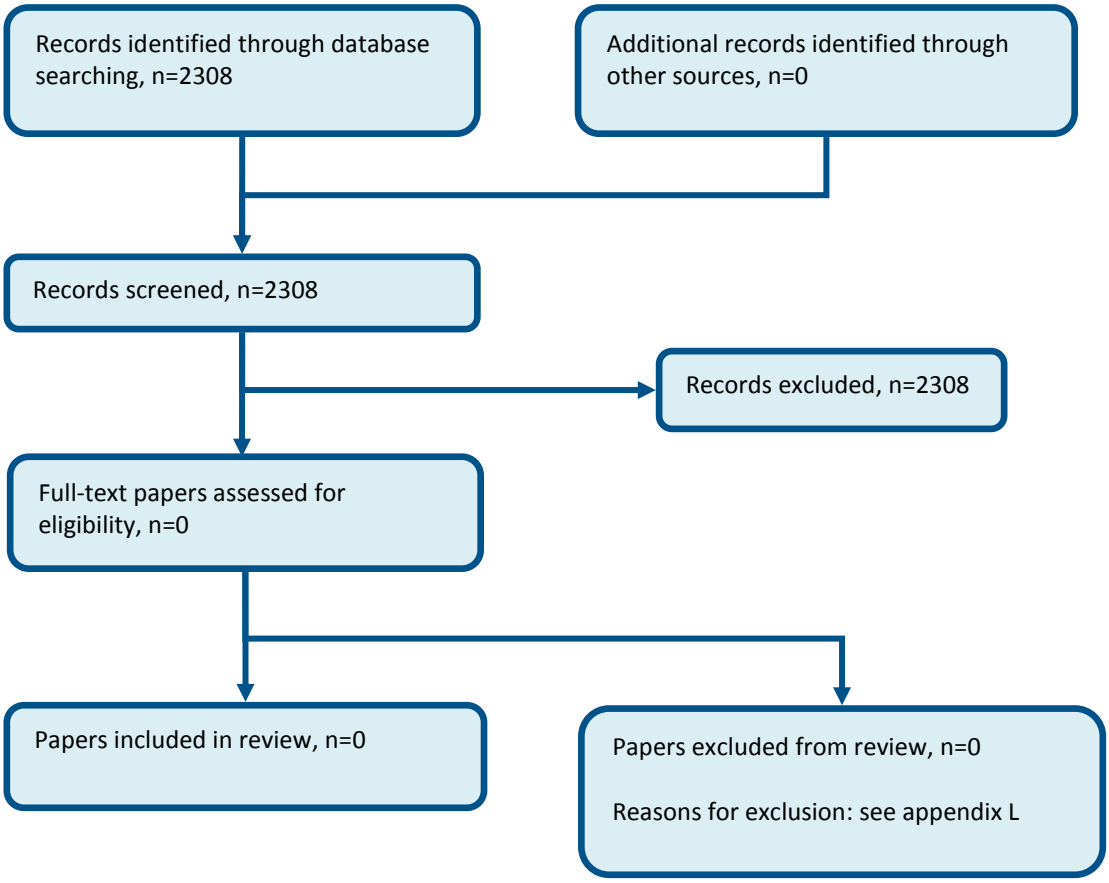
E.19 Management of biliary obstruction in people with chronic pancreatitis

Figure 19: Flow chart of clinical study selection for the review of interventions for treating biliary obstruction in people with chronic pancreatitis



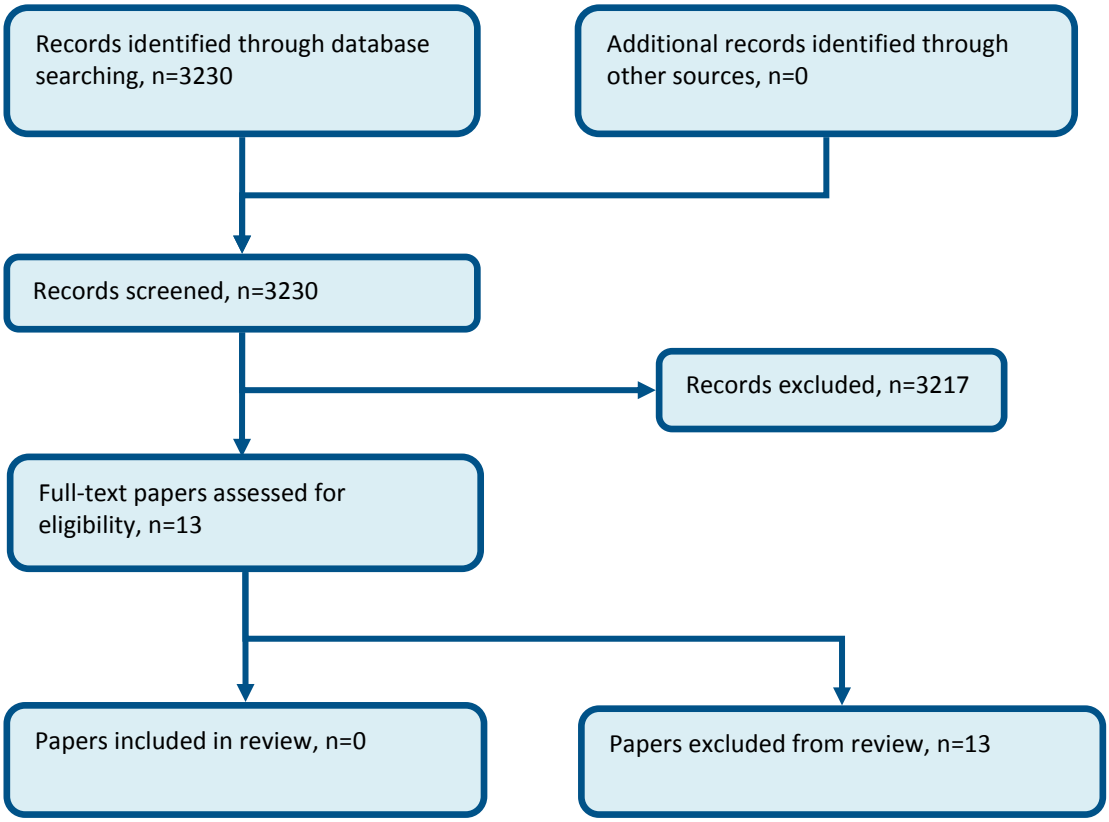
E.20 Management of type 3c diabetes secondary to pancreatitis

Figure 20: Flow chart of clinical study selection for the review of insulin management for type 3c diabetes



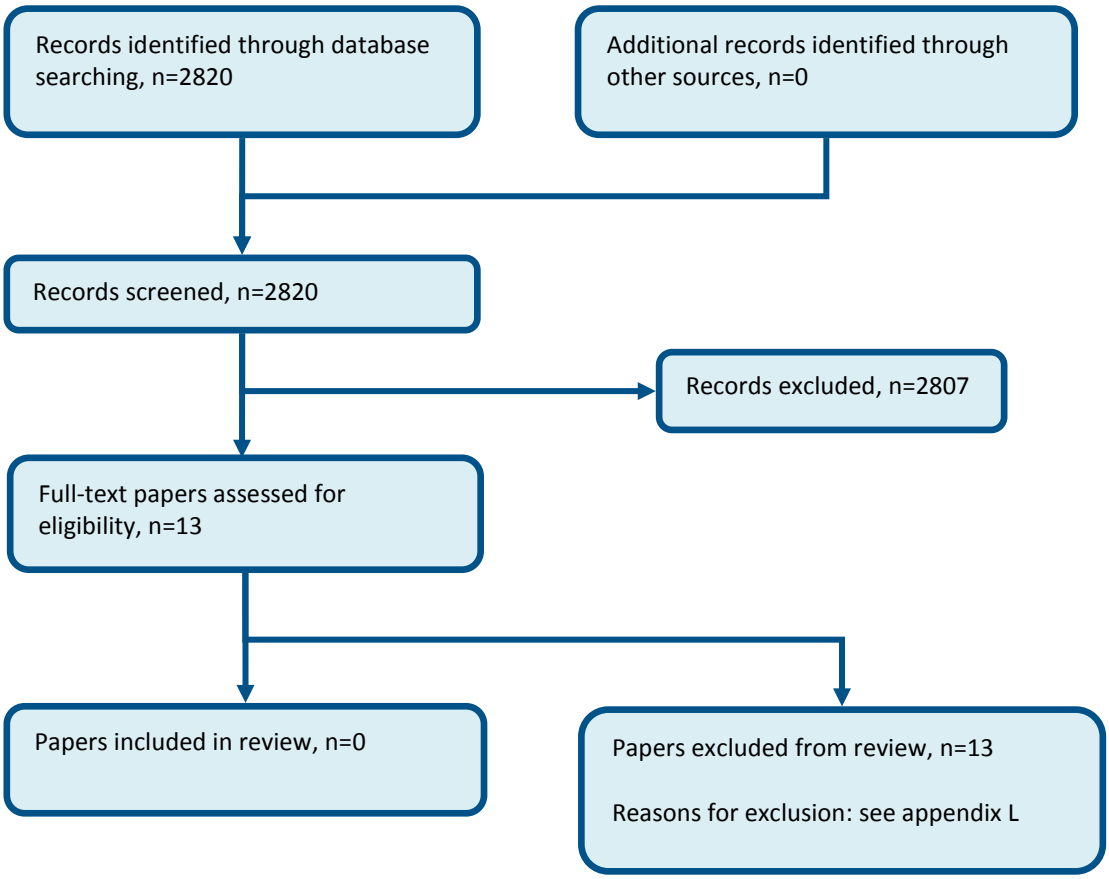
E.21 Receiving specialist input in people with acute pancreatitis

Figure 21: Flow chart of clinical study selection for the review of receiving specialist input



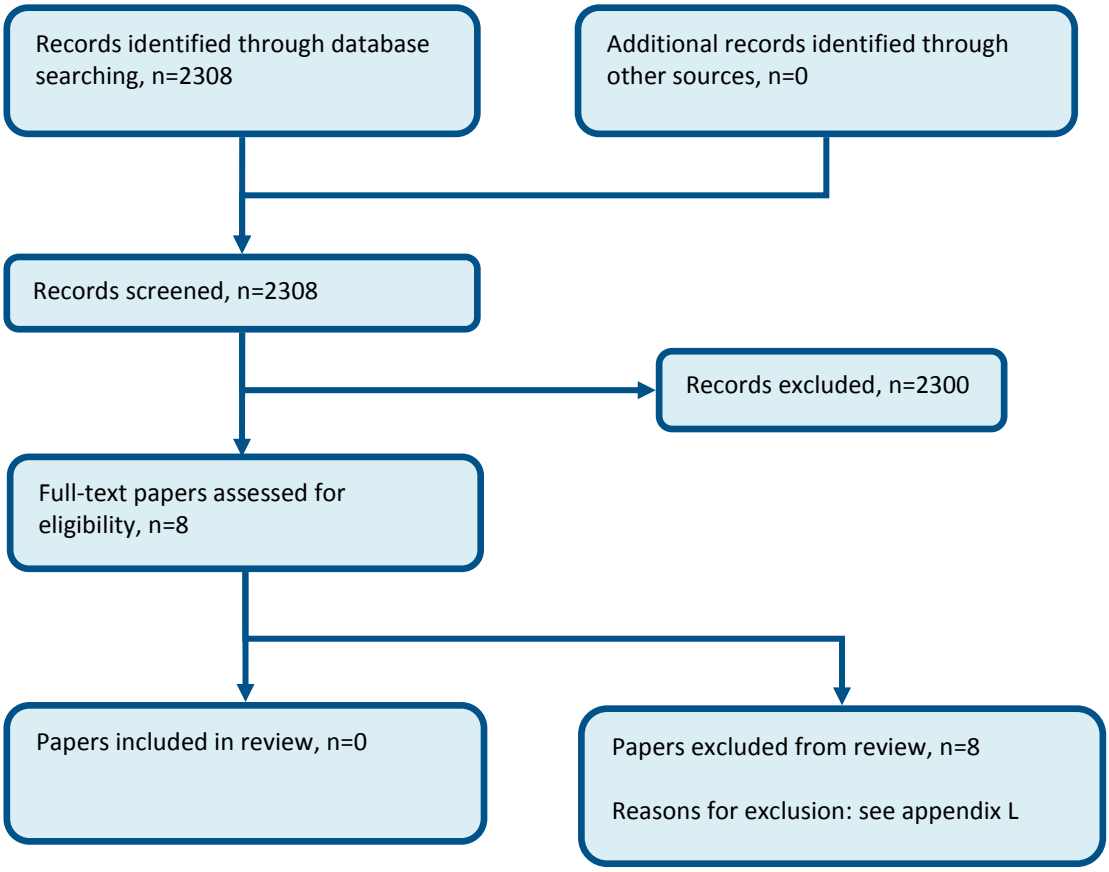
E.22 Follow-up of pancreatic exocrine function in people with chronic pancreatitis

Figure 22: Flow chart of clinical study selection for the review of follow-up to assess pancreatic exocrine function



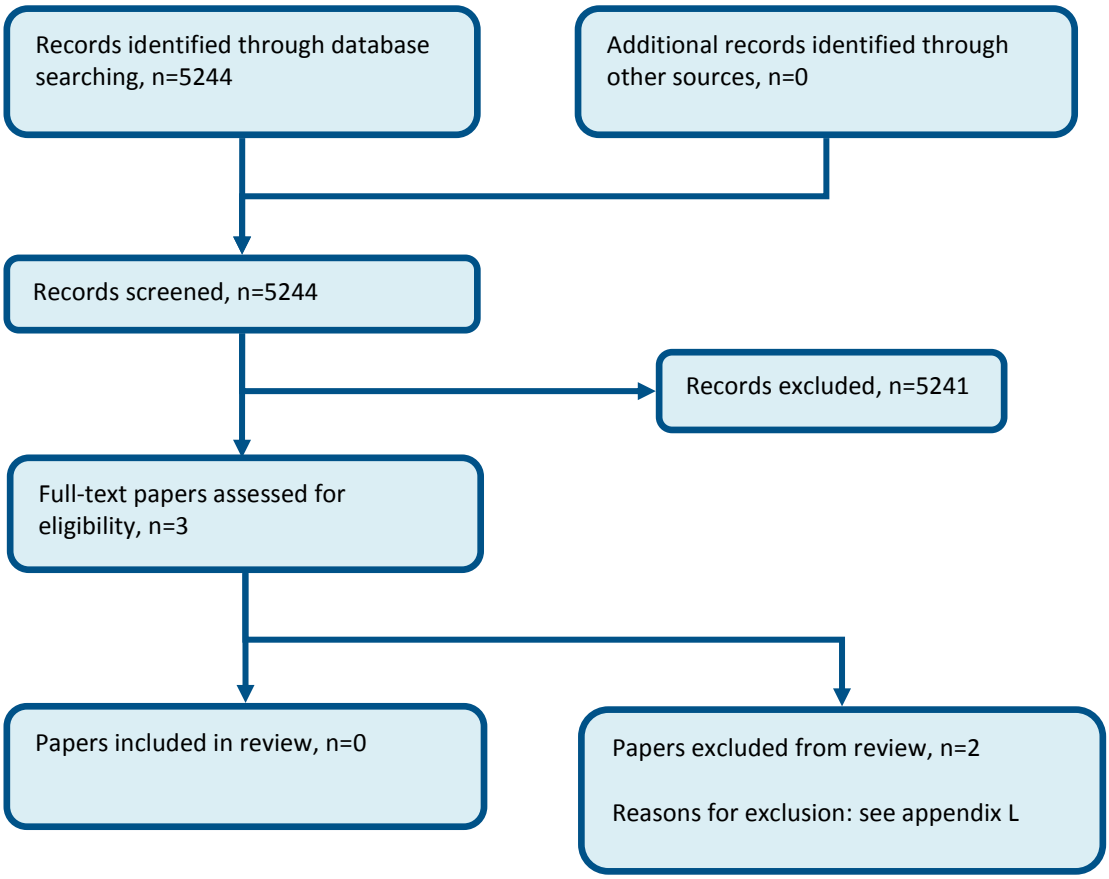
E.23 Follow-up to identify diabetes in people with chronic pancreatitis

Figure 23: Flow chart of clinical study selection for the review of follow-up of diabetes



E.24 Follow-up to identify pancreatic cancer in people with chronic pancreatitis

Figure 24: Flow chart of clinical study selection for the review of follow-up of pancreatic cancer



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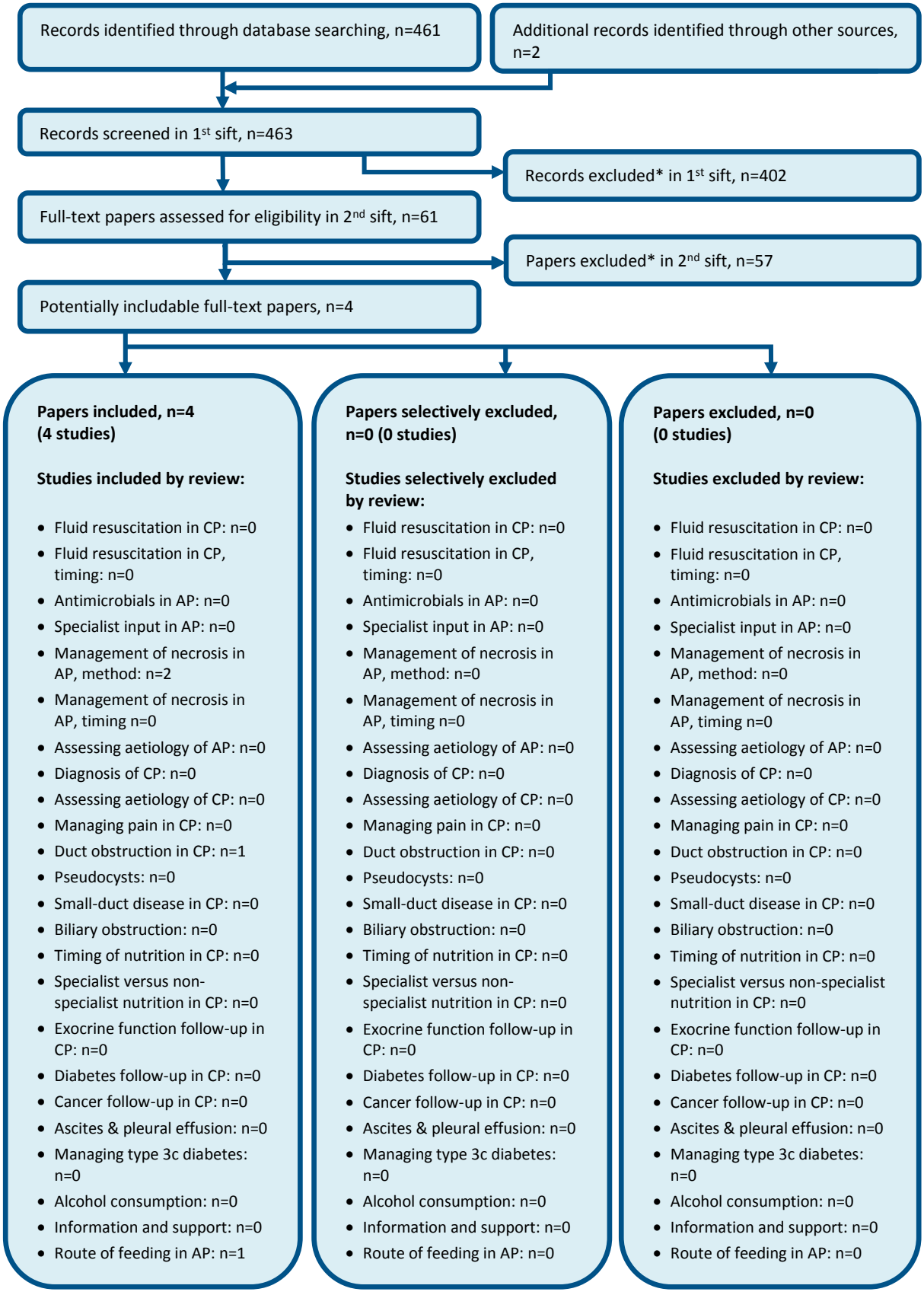
Appendix F: Health economic study selection

Figure 25: Flow chart of health economic study selection for the guideline



Appendix G: Literature search strategies

G.1 Contents

Search strategies used for the pancreatitis guideline are outlined below and were run in accordance with the methodology in the NICE guidelines manual 2014, available from https://www.nice.org.uk/article/pmg20/. All searches were run up to 28 September 2017 unless otherwise stated. Any studies added to the databases after this date (even those published prior to

this date) were not included unless specifically stated in the text. Where possible searches were limited to retrieve material published in English.

Table 1: Database date parameters

Database	Dates searched
Medline	1990 – 28 September 2017
Embase	1990 – 28 September 2017
The Cochrane Library	Cochrane Reviews from 1990 to 2017 Issue 10 of 12 CENTRAL from 1990 to 2017 Issue 9 of 12 DARE and NHSEED to from 1990 to 2015 Issue 2 of 4 HTA from 1990 to 2016 Issue 4 of 4
CINAHL	1990– 28 September 2017
PsycINFO	1990– 28 September 2017

Searches for the **clinical reviews** were run in Medline (OVID), Embase (OVID) and the Cochrane Library (Wiley). Additional searches were run in CINAHL, Current Nursing and Allied Health Literature (EBSCO)and PsycINFO (ProQuest). Searches for **intervention and diagnostic studies** were usually constructed using a PICO format where population (P) terms were combined with Intervention (I) and sometimes Comparison (C) terms. An intervention can be a drug, a procedure or a diagnostic test. Outcomes (O) are rarely used in search strategies for interventions. Search filters were also added to the search where appropriate.

Searches for **patient views** were run in Medline, Embase, CINAHL and PsycINFO. Searches were constructed by adding a patient views search filter to the population terms.

Table 2: Databases searched

Question	Question number	Databases
Acute aetiology	0	Medline, Embase, The Cochrane Library, PsycINFO
Antimicrobial prophylaxis	0	Medline, Embase, The Cochrane Library, PsycINFO
Biliary obstruction	0	Medline, Embase, The Cochrane Library, PsycINFO
Chronic aetiology	0	Medline, Embase, The Cochrane Library, PsycINFO
Chronic diagnosis	0	Medline, Embase, The Cochrane Library, PsycINFO
Diabetes	0	Medline, Embase, The Cochrane Library, PsycINFO
Follow up: pancreatic cancer	0	Medline, Embase, The Cochrane Library, PsycINFO
Follow up: pancreatic function	0	Medline, Embase, The Cochrane Library, PsycINFO
Information and support	G.4.1	Medline, Embase, CINAHL, PsycINFO
IV fluid management	G.4.6	Medline, Embase, The Cochrane Library, PsycINFO
Lifestyle: alcohol	0	Medline, Embase, The Cochrane Library, PsycINFO
Necrosis	0	Medline, Embase, The Cochrane

Question	Question number	Databases
		Library, PsycINFO
Nutrition support	0	Medline, Embase, The Cochrane Library, PsycINFO
Pain management	0	Medline, Embase, The Cochrane Library, PsycINFO
Pancreatic ascites and pleural effusion	0	Medline, Embase, The Cochrane Library, PsycINFO
Specialist assessment	0	Medline, Embase, The Cochrane Library, PsycINFO

Searches for the health economic reviews were run in Medline, Embase, the NHS Economic Evaluations Database (NHS EED) and the Health Technology Assessment (HTA) database. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). The NHS EED database has not been updated since 2015.

For Medline and Embase an economic filter (instead of a study type filter) was added to the same clinical search strategy. Searches in CRD were constructed using population terms only.

G.2 Population search strategies

G.2.1 Standard pancreatitis population

The standard population was not used in questions 0 and 0. Question 0 used both the standard population and the chronic pancreatitis population.

Medline and Embase search terms

1.	exp pancreatitis/
2.	exp pancreas/
3.	inflammation/
4.	2 and 3
5.	pancreatitis.ti,ab.
6.	(pancrea* adj3 inflam*).ti,ab.
7.	or/1,4-6

Cochrane search terms

#1.	MeSH descriptor: (pancreatitis) explode all trees
#2.	MeSH descriptor: (pancreas) explode all trees
#3.	MeSH descriptor: (inflammation) this term only
#4.	#2 and #3
#5.	pancreatitis:ti,ab
#6.	(pancrea* near/3 inflam*):ti,ab
#7.	#1 or #4 or #5 or #6

CINAHL search terms

S1.	(MH "pancreatitis+")
S2.	(MH "pancreas+")
S3.	(MH "inflammation+")
S4.	S2 and S3
S5.	TI pancreatitis or AB pancreatitis

S6.	AB (pancrea* n3 inflam*) or TI (pancrea* n3 inflam*)
S7.	S1 or S4 or S5 or S6

PsycINFO search terms

1.	pancrea*

CRD search terms

1.	MeSH descriptor pancreatitis explode all trees
2.	MeSH descriptor pancreas explode all trees
3.	MeSH descriptor inflammation explode all trees
4.	#2 and #3
5.	(pancreatitis)
6.	((pancrea* adj3 inflam*))
7.	#1 or #4 or #5 or #6

G.2.2 Chronic pancreatitis population

This population was used in questions 0, 0 and 0

Medline search terms

1.	exp pancreatitis, chronic/ or exp pancreatitis, alcoholic/
2.	exp pancreas/
3.	inflammation/
4.	2 and 3
5.	chronic pancreatitis.ti,ab.
6.	(pancrea* adj3 (autoimmun* or heredit* or inflam*)).ti,ab.
7.	or/1,4-6

Embase search terms

1.	exp alcoholic pancreatitis/ or exp chronic pancreatitis/
2.	exp autoimmune pancreatitis/
3.	exp pancreas/
4.	inflammation/
5.	3 and 4
6.	chronic pancreatitis.ti,ab.
7.	(pancrea* adj3 (heredit* or inflam*)).ti,ab.
8.	1 or 2 or 5 or 6 or 7

Cochrane search terms

#1.	MeSH descriptor: (pancreatitis, chronic) explode all trees
#2.	MeSH descriptor: (pancreatitis, alcoholic) explode all trees
#3.	MeSH descriptor: (pancreas) explode all trees
#4.	MeSH descriptor: (inflammation) explode all trees
#5.	#3 and #4
#6.	chronic pancreatitis:ti,ab
#7.	(pancrea* near/3 (autoimmun* or heredit* or inflam*)):ti,ab
#8.	#1 or #2 or #5 or #6 or #7

G.3 Study filter search terms

G.3.1 Excluded study designs and publication types

The following study designs and publication types were removed from retrieved results using the NOT operator.

Medline search terms

1.	letter/
2.	editorial/
3.	news/
4.	exp historical article/
5.	anecdotes as topic/
6.	comment/
7.	case report/
8.	(letter or comment*).ti.
9.	or/1-8
10.	randomized controlled trial/ or random*.ti,ab.
11.	9 not 10
12.	animals/ not humans/
13.	exp animals, laboratory/
14.	exp animal experimentation/
15.	exp models, animal/
16.	exp rodentia/
17.	(rat or rats or mouse or mice).ti.
18.	or/11-17

Embase search terms

1.	letter.pt. or letter/
2.	note.pt.
3.	editorial.pt.
4.	case report/ or case study/
5.	(letter or comment*).ti.
6.	or/1-5
7.	randomized controlled trial/ or random*.ti,ab.
8.	6 not 7
9.	animal/ not human/
10.	nonhuman/
11.	exp animal experiment/
12.	exp experimental animal/
13.	animal model/
14.	exp rodent/
15.	(rat or rats or mouse or mice).ti.
16.	or/8-15

CINAHL search terms

S1.	pt anecdote or pt audiovisual or pt bibliography or pt biography or pt book or pt book review

	or pt brief item or pt cartoon or pt commentary or pt computer program or pt editorial or pt games or pt glossary or pt historical material or pt interview or pt letter or pt listservs or pt masters thesis or pt obituary or pt pamphlet or pt pamphlet chapter or pt pictorial or pt poetry or pt proceedings or pt "questions and answers" or pt response or pt software or pt teaching materials or pt website

PsycINFO (ProQUEST) search terms

1.	(su.exact.explode("rodents") or su.exact.explode("mice") or (su.exact("animals") not (su.exact("human males") or su.exact("human females"))) or ti(rat or rats or mouse or mice))
2.	Limits applied: Books, Letter; Dissertation Abstract; Comment/Reply; Obituary; Editorial

G.3.2 Randomised controlled trials (RCT)

Medline search terms

(Based on the sensitivity and precision maximising version reported in the Cochrane Handbook (http://handbook.cochrane.org/)).

1.	randomized controlled trial.pt.
2.	controlled clinical trial.pt.
3.	randomi#ed.ti,ab.
4.	placebo.ab.
5.	randomly.ab.ti
6.	clinical trials as topic.sh.
7.	trial.ti.
8.	or/1-7

Embase search terms

1.	random*.ti,ab.
2.	factorial*.ti,ab.
3.	(crossover* or cross over*).ti,ab.
4.	((doubl* or singl*) adj blind*).ti,ab.
5.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
6.	crossover procedure/
7.	double blind procedure/
8.	single blind procedure/
9.	randomized controlled trial/
10.	or/1-9

G.3.3 Systematic reviews (SR)

Medline search terms

1.	meta-analysis/
2.	meta-analysis as topic/
3.	(meta analy* or metanaly* or metaanaly*).ti,ab.
4.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
5.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
6.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
7.	(search* adj4 literature).ab.

8.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
9.	cochrane.jw.
10.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
11.	or/1-10

Embase search terms

1.	systematic review/
2.	meta-analysis/
3.	(meta analy* or metanaly* or metaanaly*).ti,ab.
4.	((systematic or evidence) adj3 (review* or overview*)).ti,ab.
5.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
6.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
7.	(search* adj4 literature).ab.
8.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
9.	cochrane.jw.
10.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
11.	or/1-10

G.3.4 Health economic studies (HE)

Medline search terms

1.	economics/
2.	value of life/
3.	exp "costs and cost analysis"/
4.	exp economics, hospital/
5.	exp economics, medical/
6.	economics, nursing/
7.	economics, pharmaceutical/
8.	exp "fees and charges"/
9.	exp budgets/
10.	budget*.ti,ab.
11.	cost*.ti.
12.	(economic* or pharmaco?economic*).ti.
13.	(price* or pricing*).ti,ab.
14.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
15.	(financ* or fee or fees).ti,ab.
16.	(value adj2 (money or monetary)).ti,ab.
17.	or/1-16

Embase search terms

1.	health economics/
2.	exp economic evaluation/
3.	exp health care cost/
4.	exp fee/
5.	budget/

6.	funding/
7.	budget*.ti,ab.
8.	cost*.ti.
9.	(economic* or pharmaco?economic*).ti.
10.	(price* or pricing*).ti,ab.
11.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
12.	(financ* or fee or fees).ti,ab.
13.	(value adj2 (money or monetary)).ti,ab.
14.	or/1-13

G.3.5 Quality of life studies (QoL)

Medline search terms

1.	quality-adjusted life years/
2.	sickness impact profile/
3.	(quality adj2 (wellbeing or well-being)).ti,ab.
4.	sickness impact profile.ti,ab.
5.	disability adjusted life.ti,ab.
6.	(qal* or qtime* or qwb* or daly*).ti,ab.
7.	(euroqol* or eq5d* or eq 5d*).ti,ab.
8.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
9.	(health utility* or utility score* or disutilit*).ti,ab.
10.	(hui or hui1 or hui2 or hui3).ti,ab.
11.	health* year* equivalent*.ti,ab.
12.	(hye or hyes).ti,ab.
13.	rosser.ti,ab.
14.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
15.	(sf36 or sf 36 or short form 36 or shortform 36 or shortform36).ti,ab.
16.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
17.	(sf12 or sf 12 or short form 12 or shortform 12 or shortform12).ti,ab.
18.	(sf8 or sf 8 or short form 8 or shortform 8 or shortform8).ti,ab.
19.	(sf6 or sf 6 or short form 6 or shortform 6 or shortform6).ti,ab.
20.	or/1-19

Embase search terms

1.	quality adjusted life year/
2.	"quality of life index"/
3.	short form 12/ or short form 20/ or short form 36/ or short form 8/
4.	sickness impact profile/
5.	(quality adj2 (wellbeing or well-being)).ti,ab.
6.	sickness impact profile.ti,ab.
7.	disability adjusted life.ti,ab.
8.	(qal* or qtime* or qwb* or daly*).ti,ab.
9.	(euroqol* or eq5d* or eq 5d*).ti,ab.
10.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
11.	(health utility* or utility score* or disutilit*).ti,ab.

12.	(hui or hui1 or hui2 or hui3).ti,ab.
13.	health* year* equivalent*.ti,ab.
14.	(hye or hyes).ti,ab.
15.	rosser.ti,ab.
16.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
17.	(sf36 or sf 36 or short form 36 or shortform 36 or shortform36).ti,ab.
18.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
19.	(sf12 or sf 12 or short form 12 or shortform 12 or shortform12).ti,ab.
20.	(sf8 or sf 8 or short form 8 or shortform 8 or shortform8).ti,ab.
21.	(sf6 or sf 6 or short form 6 or shortform 6 or shortform6).ti,ab.
22.	or/1-21

G.3.6 Diagnostic test accuracy studies (DIAG)

Medline search terms

1.	exp "sensitivity and specificity"/
2.	(sensitivity or specificity).ti,ab.
3.	((pre test or pretest or post test) adj probability).ti,ab.
4.	(predictive value* or ppv or npv).ti,ab.
5.	likelihood ratio*.ti,ab.
6.	likelihood function/
7.	(roc curve* or auc).ti,ab.
8.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
9.	gold standard.ab.
10.	or/1-9

Embase search terms

1.	exp "sensitivity and specificity"/
2.	(sensitivity or specificity).ti,ab.
3.	((pre test or pretest or post test) adj probability).ti,ab.
4.	(predictive value* or ppv or npv).ti,ab.
5.	likelihood ratio*.ti,ab.
6.	(roc curve* or auc).ti,ab.
7.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
8.	diagnostic accuracy/
9.	diagnostic test accuracy study/
10.	gold standard.ab.
11.	or/1-10

G.3.7 Observational studies (OBS)

Medline search terms

1.	epidemiologic studies/
2.	observational study/
3.	exp cohort studies/

4.	(cohort adj (study or studies or analys* or data)).ti,ab.
5.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
6.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
7.	controlled before-after studies/
8.	historically controlled study/
9.	interrupted time series analysis/
10.	(before adj2 after adj2 (study or studies or data)).ti,ab.
11.	or/1-10
12.	exp case control study/
13.	case control*.ti,ab.
14.	or/12-13
15.	11 or 14
16.	cross-sectional studies/
17.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
18.	or/16-17
19.	11 or 18
20.	11 or 15 or 18

1 **Embase search terms**

1.	Clinical study/
2.	Observational study/
3.	family study/
4.	longitudinal study/
5.	retrospective study/
6.	prospective study/
7.	cohort analysis/
8.	follow-up/
9.	cohort*.ti,ab.
10.	88 and 89
11.	(cohort adj (study or studies or analys* or data)).ti,ab.
12.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
13.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
14.	(before adj2 after adj2 (study or studies or data)).ti,ab.
15.	or/1-7,10-14
16.	exp case control study/
17.	case control*.ti,ab.
18.	or/16-17
19.	15 or 18
20.	cross-sectional study/
21.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
22.	or/20-21
23.	15 or 22

24.	15 or 18 or 22

G.3.8 Qualitative reviews (QUAL)

Medline search terms

1.	qualitative research/ or narration/ or exp interviews as topic/ or exp questionnaires/ or health care surveys/
2.	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*).ti,ab.
3.	(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* adj3 analys*) or theoretical sampl* or purposive sampl* or hermeneutic* or heidegger* or husserl* or colaizzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricoeur* or spiegelberg* or merleau*).ti,ab.
4.	or/1-3

Embase search terms

1.	health survey/ or exp questionnaire/ or exp interview/ or qualitative research/ or narrative/
2.	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*).ti,ab.
3.	(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* adj3 analys*) or theoretical sampl* or purposive sampl* or hermeneutic* or heidegger* or husserl* or colaizzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricoeur* or spiegelberg* or merleau*).ti,ab.
4.	or/1-3

CINAHL search terms

S1.	(mh "qualitative studies+")
S2.	(mh "qualitative validity+")
S3.	(mh "interviews+") or (mh "focus groups") or (mh "surveys") or (mh "questionnaires+")
S4.	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*)
S5.	(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* adj3 analys*) or theoretical sampl* or purposive sampl* or hermeneutic* or heidegger* or husserl* or colaizzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricoeur* or spiegelberg* or merleau*)
S6.	S1 or s2 or S3 or S4 or S5

G.4 Searches for specific questions

G.4.1 Information and support

What information and support should people with acute or chronic pancreatitis, their family and carers receive after diagnosis?

Medline search terms

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	caregivers/ or exp family/ or exp parents/ or exp legal-guardians/
6.	patients/ or inpatients/ or outpatients/

7.	or/5-6
8.	popular-works-publication-type/ or exp information-services/ or publications/ or books/ or pamphlets/ or counseling/ or directive-counseling/
9.	7 and 8
10.	patient education as topic/
11.	consumer health information/
12.	patient satisfaction/
13.	exp consumer-satisfaction/
14.	personal-satisfaction/
15.	patient participation/
16.	decision making/
17.	access to information/
18.	exp patient-acceptance-of-health-care/
19.	((caregiver* or carer* or client* or customer* or famil* or father* or guardian* or mother* or next of kin or parent* or patient* or relatives or spouse or user*) adj6 (attitude* or belief* or believe* or choice* or choos* or decid* or decision* or expectation* or feeling* or interpret* or involvement or misconception* or misconception* or mis-conception* or misunderstand* or mis-understand* or need or needs or opinion* or perception* or perspective* or preferen* or priorit* or satisfact* or understand* or view*)).ti,ab.
20.	((caregiver* or carer* or client* or customer* or famil* or father* or guardian* or mother* or next of kin or parent* or patient* or relatives or spouse or user*) adj6 (advi?e* or communicat* or consult* or convers* or counsel* or discuss* or educat* or inform* or involve* or knowledge or learn* or psycholog* or support*)).ti,ab.
21.	((advi?e* or communicat* or consult* or convers* or counsel* or discuss* or educat* facilitat* or inform* or involve* or knowledge or learn* or psycholog* or support*) adj6 (access* or arrang* or barrier* or deliver* or disseminat* or establish* or facilitat* or need or needs or offer* or provide* or provision* or requirement* or seek* or support)).ti,ab.
22.	((caregiver* or carer* or client* or customer* or famil* or father* or guardian* or mother* or next of kin or parent* or patient* or relatives or spouse or user*) adj6 (bluetooth or booklet* or brochure* or computer* or digital* or dvd* or email* or e-mail* or handout* or interactive* or internet or leaflet* or literature or manual* or mobile health or pamphlet* or phone* or program* or publication* or resource* or smartphone* or social media or social network* or sms or telephone* or text* or video* or web page* or web site* or webpage* or website* or wireless)).ti,ab.
23.	or/9-22
24.	Study filter QUAL (G.3.8)
25.	4 and 23 and 24
	Date parameters: 1946-28 September 2017

1 **Embase search terms**

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	patient/ or hospital patient/ or outpatient/
6.	caregiver/ or exp family/ or exp parent/
7.	5 or 6
8.	information service/ or information center/ or publication/ or book/ or counseling/ or directive counseling/
9.	7 and 8

10.	patient education/
11.	consumer health information/
12.	patient satisfaction/
13.	patient participation/
14.	decision making/
15.	patient preference/
16.	patient attitude/
17.	patient information/
18.	((caregiver* or carer* or client* or customer* or famil* or father* or guardian* or mother* or next of kin or parent* or patient* or relatives or spouse or user*) adj6 (attitude* or belief* or believe* or choice* or choos* or decid* or decision* or expectation* or feeling* or interpret* or involvement or misconception* or misconception* or mis-conception* or misunderstand* or mis-understand* or need or needs or opinion* or perception* or perspective* or preferen* or priorit* or satisfact* or understand* or view*)).ti,ab.
19.	((advi?e* or communicat* or consult* or convers* or counsel* or discuss* or educat* or inform* or involve* or knowledge or learn* or psycholog* or support*) adj6 (access* or arrang* or barrier* or deliver* or disseminat* or establish* or facilitat* or need or needs or offer* or provide* or provision* or requirement* or seek* or support)).ti,ab.
20.	((caregiver* or carer* or client* or customer* or famil* or father* or guardian* or mother* or next of kin or parent* or patient* or relatives or spouse or user*) adj6 (advi?e* or communicat* or consult* or convers* or counsel* or discuss* or educat* or inform* or involve* or knowledge or learn* or psycholog* or support*)).ti,ab.
21.	((caregiver* or carer* or client* or customer* or famil* or father* or guardian* or mother* or next of kin or parent* or patient* or relatives or spouse or user*) adj6 (bluetooth or booklet* or brochure* or computer* or digital* or dvd* or email* or e-mail* or handout* or interactive* or internet or leaflet* or literature or manual* or mobile health or pamphlet* or phone* or program* or publication* or resource* or smartphone* or social media or social network*or sms or telephone* or text* or video* or web page* or web site* or webpage* or website* or wireless)).ti,ab.
22.	or/9-21
23.	Study filter QUAL (G.3.8)
24.	4 and 22 and 23
	Date parameters: 1974-28 September 2017

1 **CINAHL search terms**

S1.	Standard population (G.2.1)
S2.	Excluded study designs and publication types (G.3.1)
S3.	1 not 2
S4.	Limit 3 to English language
S5.	(MH "caregivers")
S6.	(MH "family+")
S7.	(MH "parents+")
S8.	(MH "guardianship, legal+")
S9.	(MH "patients+")
S10.	(MH "inpatients")
S11.	(MH "outpatients")
S12.	S5 or S6 or S7 or S8 or S9 or S10 or S11
S13.	(MH "information services+")
S14.	(MH "books") or (MH "reference books") or (MH "literature") or (MH "pamphlets")

S15.	(MH "counseling")
S16.	S13 or S14 or S15
S17.	S12 and S16
S18.	(MH "patient education")
S19.	(MH "consumer health information")
S20.	(MH "patient satisfaction")
S21.	(MH "consumer satisfaction+")
S22.	(MH "personal satisfaction")
S23.	(MH "consumer participation")
S24.	(MH "decision making")
S25.	(MH "access to information")
S26.	TI (((caregiver* or carer* or client* or customer* or famil* or father* or guardian* or mother* or next of kin or parent* or patient* or relatives or spouse or user*) n6 (attitude* or belief* or believe* or choice* or choos* or decid* or decision* or expectation* or feeling* or interpret* or involvement or misconception* or misconception* or mis-conception* or misunderstand* or mis-understand* or need or needs or opinion* or perception* or perspective* or preferen* or priorit* or satisfact* or understand* or view*))) or AB (((caregiver* or carer* or client* or customer* or famil* or father* or guardian* or mother* or next of kin or parent* or patient* or relatives or spouse or user*) n6 (attitude* or belief* or believe* or choice* or choos* or decid* or decision* or expectation* or feeling* or interpret* or involvement or misconception* or misconception* or mis-conception* or misunderstand* or mis-understand* or need or needs or opinion* or perception* or perspective* or preferen* or priorit* or satisfact* or understand* or view*))
S27.	TI (((caregiver* or carer* or client* or customer* or famil* or father* or guardian* or mother* or next of kin or parent* or patient* or relatives or spouse or user*) n6 (advi?e* or communicat* or consult* or convers* or counsel* or discuss* or educat* or inform* or involve* or knowledge or learn* or psycholog* or support*))) or AB (((caregiver* or carer* or client* or customer* or famil* or father* or guardian* or mother* or next of kin or parent* or patient* or relatives or spouse or user*) n6 (advi?e* or communicat* or consult* or convers* or counsel* or discuss* or educat* or inform* or involve* or knowledge or learn* or psycholog* or support*)))
S28.	TI (((advi?e* or communicat* or consult* or convers* or counsel* or discuss* or educat* or facilitat* or inform* or involve* or knowledge or learn* or psycholog* or support*) n6 (access* or arrang* or barrier* or deliver* or disseminat* or establish* or facilitat* or need or needs or offer* or provide* or provision* or requirement* or seek* or support))) or AB (((advi?e* or communicat* or consult* or convers* or counsel* or discuss* or educat* or facilitat* or inform* or involve* or knowledge or learn* or psycholog* or support*) n6 (access* or arrang* or barrier* or deliver* or disseminat* or establish* or facilitat* or need or needs or offer* or provide* or provision* or requirement* or seek* or support)))
S29.	TI (((caregiver* or carer* or client* or customer* or famil* or father* or guardian* or mother* or next of kin or parent* or patient* or relatives or spouse or user*) n6 (bluetooth or booklet* or brochure* or computer* or digital* or dvd* or education sheet* or email* or e-mail* or handout* or information sheet* or interactive* or internet or leaflet* or literature or manual* or mobile health or pamphlet* or phone* or program* or publication* or resource* or smartphone* or social media or social network* or SMS or telephone* or text* or video* or web page* or web site* or webpage* or website* or wireless))) or AB ((caregiver* or carer* or client* or customer* or famil* or father* or guardian* or mother* or next of kin or parent* or patient* or relatives or spouse or user*) n6 (bluetooth or booklet* or brochure* or computer* or digital* or dvd* or email* or e-mail* or handout* or interactive* or internet or leaflet* or literature or manual* or mobile health or pamphlet* or phone* or program* or publication* or resource* or smartphone* or social media or social network* or SMS or telephone* or text* or video* or web page* or web site* or webpage* or website* or wireless)))

S30.	S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S9
S31.	S17 or S30
S32.	Study filter QUAL (G.3.8)
S33.	S4 or S31 or S32
	Date parameters: 1981-28 September 2017

PsycINFO search terms

1.	Standard population (A.2.1)
2.	Excluded study designs and publication types (A.3.1)
3.	1 not 2
4.	Limit 3 to English language
	Date parameters: see **Table 1**

G.4.2 Acute aetiology

- What is the clinical and cost effectiveness of assessing the aetiology of acute pancreatitis to prevent recurrent attacks in people in which the aetiology is unconfirmed by first line test results within normal ranges?

Medline search terms

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	((medic* or drug* or clinical or patient*) adj3 (history or record* or antecedent*)).ti,ab.
6.	medical history taking/
7.	5 or 7
8.	"sphincter of oddi"/
9.	((sphincter of oddi or hepatopancreatic sphincter or glisson's sphincter) adj3 (dysfunction* or failure* or disorder*)).ti,ab.
10.	cholangiopancreatography, endoscopic retrograde/
11.	(endoscopic retrograde cholangiopancreatograph* or ercp).ti,ab.
12.	10 or 11
13.	9 or (8 and 12)
14.	exp immunoglobulins/
15.	immunoglobulin*.ti,ab.
16.	igg*.ti,ab.
17.	exp antibodies, antinuclear/
18.	(autoantibod* or auto-antibod*).ti,ab.
19.	(anti-nuclear antibod* or antinuclear antibod* or ana).ti,ab.
20.	(antinuclear factor* or anti-nuclear factor* or anf).ti,ab.
21.	or/14-20
22.	serologic tests/
23.	hypercalcemia/
24.	hyperlipidemias/
25.	((test* or analysis) adj3 (hypercalc?emia or hyperlipid?emia or serolog* or blood)).ti,ab.
26.	or/22-25

27.	genetic markers/ or genetic testing/
28.	genetic predisposition to disease/
29.	(genetic* adj3 (marker* or test* or predisposition*)).ti,ab.
30.	trypsin/
31.	trypsinogen/
32.	(trypsinogen or trypsin or prss1).ti,ab.
33.	(tati or psti).ti,ab.
34.	chymotrypsin/
35.	(chymotrypsin* or ctrc or cldn2).ti,ab.
36.	cystic fibrosis transmembrane conductance regulator/
37.	(cystic fibrosis transmembrane conductance regulator or cftr).ti,ab.
38.	trypsin inhibitor, kazal pancreatic/
39.	(serine protease inhibitor kazal-type 1 or spink1).ti,ab.
40.	or/27-39
41.	endosonography/
42.	cholangiopancreatography, endoscopic retrograde/
43.	41 or 42
44.	exp biliary tract/
45.	43 and 44
46.	((endoscopic retrograde cholangiopancreatograph* or ercp or endoscopic ultraso* or eus or echo-endoscop* or endosonograph*) adj3 (gall bladder or gallbladder or bil* duct* or gallstone* or cbd or choledoch* or biliary)).ti,ab.
47.	45 or 46
48.	duodenoscopy/
49.	((endoscopic ultraso* or eus or echo-endoscop* or endosonograph*) adj3 ((endoscop* adj3 duodenum) or duodenoscop*)).ti,ab.
50.	or/47-49
51.	cholangiopancreatography, magnetic resonance/
52.	secretin/
53.	51 and 52
54.	(magnetic resonance cholangiopancreatograph* or mrcp or secretin-mrcp).ti,ab.
55.	smrcp.ti,ab.
56.	or/53-55
57.	pancreatitis, acute necrotizing/et (etiology)
58.	(pancrea* adj3 ?etiology).ti,ab.
59.	4 and (7 or 13 or 21 or 26 or 40 or 50 or 56 or 57 or 58)
60.	Study filters RCT (G.3.2) or SR (G.3.3) or OBS (G.3.7)
61.	59 and 60
	Date parameters: see **Table 1**

1 **Embase search terms**

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	((medic* or drug* or clinical or patient*) adj3 (history or record* or antecedent*)).ti,ab.

6.	anamnesis/
7.	5 or 6
8.	oddi sphincter/
9.	((sphincter of oddi or hepatopancreatic sphincter or glisson's sphincter) adj3 (dysfunction* or failure* or disorder*)).ti,ab.
10.	endoscopic retrograde cholangiopancreatography/
11.	(endoscopic retrograde cholangiopancreatograph* or ercp).ti,ab.
12.	10 or 11
13.	9 or (8 and 12)
14.	exp immunoglobulin/
15.	immunoglobulin*.ti,ab.
16.	igg*.ti,ab.
17.	exp antinuclear antibody/
18.	(anti-nuclear antibod* or antinuclear antibod* or ana).ti,ab.
19.	(antinuclear factor* or anti-nuclear factor* or anf).ti,ab.
20.	(autoantibod* or auto-antibod*).ti,ab.
21.	autoantibody/
22.	or/14-21
23.	serology/ or serodiagnosis/
24.	hypercalcemia/
25.	hyperlipidemia/
26.	((test* or analysis) adj3 (hypercalc?emia or hyperlipid?emia or serolog* or blood)).ti,ab.
27.	or/23-26
28.	genetic predisposition/ or disease predisposition/
29.	genetic marker/
30.	genetic screening/
31.	(genetic* adj3 (marker* or test* or predisposition*)).ti,ab.
32.	trypsin/ or trypsin inhibitor/
33.	trypsinogen/
34.	(trypsinogen or trypsin or prss1).ti,ab.
35.	(tati or psti).ti,ab.
36.	chymotrypsin/ or chymotrypsin inhibitor/
37.	(chymotrypsin* or ctrc or cldn2).ti,ab.
38.	cystic fibrosis transmembrane conductance regulator/
39.	(cystic fibrosis transmembrane conductance regulator or cftr).ti,ab.
40.	(serine protease inhibitor kazal-type 1 or spink1).ti,ab.
41.	or/8-40
42.	endoscopic ultrasonography/
43.	endoscopic retrograde cholangiopancreatography/
44.	42 or 43
45.	bile duct/
46.	gallbladder/
47.	common bile duct/
48.	or/45-47
49.	44 and 48

50.	((endoscopic retrograde cholangiopancreatograph* or ercp or endoscopic ultraso* or eus or echo-endoscop* or endosonograph*) adj3 (gall bladder or gallbladder or bil* duct* or gallstone* or biliary or cbd or choledoch*)).ti,ab.
51.	duodenoscopy/
52.	((endoscopic ultraso* or eus or echo-endoscop* or endosonograph*) adj3 ((endoscop* adj3 duodenum) or duodenoscop*)).ti,ab.
53.	or/49-52
54.	endoscopic retrograde cholangiopancreatography/
55.	secretin/
56.	54 and 55
57.	(magnetic resonance cholangiopancreatograph* or mrcp or secretin-mrcp).ti,ab.
58.	smrcp.ti,ab.
59.	or/56-58
60.	acute pancreatitis/et (etiology)
61.	(pancrea* adj3 ?etiology).ti,ab.
62.	4 and (7 or 13 or 22 or 27 or 41 or 53 or 59 or 60 or 61)
63.	Study filters RCT (G.3.2) or SR (G.3.3) or OBS (G.3.7)
64.	62 and 63
	Date parameters: see **Table 1**

1 **Cochrane search terms**

#1.	Standard population (G.2.1)
#2.	((medic* or drug* or clinical or patient*) near/3 (history or record* or antecedent*)):ti,ab
#3.	MeSH descriptor: (medical history taking) this term only
#4.	#2 or #3
#5.	MeSH descriptor: (sphincter of oddi) this term only
#6.	((sphincter of oddi or hepatopancreatic sphincter or glisson's sphincter) near/3 (dysfunction* or failure* or disorder*)):ti,ab
#7.	MeSH descriptor: (cholangiopancreatography, endoscopic retrograde) this term only
#8.	(endoscopic retrograde cholangiopancreatograph* or ercp):ti,ab
#9.	#7 or #8
#10.	#5 and #9
#11.	#6 or #10
#12.	MeSH descriptor: (immunoglobulins) explode all trees
#13.	immunoglobulin*:ti,ab
#14.	igg*:ti,ab
#15.	MeSH descriptor: (antibodies, antinuclear) explode all trees
#16.	(autoantibod* or auto-antibod*):ti,ab
#17.	(anti-nuclear antibod* or antinuclear antibod* or ana):ti,ab
#18.	(antinuclear factor* or anti-nuclear factor* or anf):ti,ab
#19.	(or #12-#18)
#20.	MeSH descriptor: (serologic tests) this term only
#21.	MeSH descriptor: (hypercalcemia) this term only
#22.	MeSH descriptor: (hyperlipidemias) this term only
#23.	((test* or analysis) near/3 (hypercalc?emia or hyperlipid?emia or serolog* or blood)):ti,ab
#24.	(or #20-#23)

#25.	MeSH descriptor: (genetic markers) this term only
#26.	MeSH descriptor: (genetic testing) this term only
#27.	MeSH descriptor: (genetic predisposition to disease) this term only
#28.	(genetic* near/3 (marker* or test* or predisposition*)):ti,ab
#29.	MeSH descriptor: (trypsin) this term only
#30.	MeSH descriptor: (trypsinogen) this term only
#31.	(trypsinogen or trypsin or prss1):ti,ab
#32.	(tati or psti):ti,ab
#33.	MeSH descriptor: (chymotrypsin) this term only
#34.	(chymotrypsin* or ctrc or cldn2):ti,ab
#35.	MeSH descriptor: (cystic fibrosis transmembrane conductance regulator) this term only
#36.	(cystic fibrosis transmembrane conductance regulator or cftr):ti,ab
#37.	MeSH descriptor: (trypsin inhibitor, kazal pancreatic) this term only
#38.	(serine protease inhibitor kazal-type 1 or spink1):ti,ab
#39.	(or #25-#38)
#40.	MeSH descriptor: (endosonography) this term only
#41.	MeSH descriptor: (cholangiopancreatography, endoscopic retrograde) explode all trees
#42.	(or #40-#41)
#43.	MeSH descriptor: (biliary tract) explode all trees
#44.	#42 and #43
#45.	((endoscopic retrograde cholangiopancreatograph* or ercp or endoscopic ultraso* or eus or echo-endoscop* or endosonograph*) near/3 (gall bladder or gallbladder or bil* duct* or gallstone* or cbd or choledoch* or biliary)):ti,ab
#46.	MeSH descriptor: (duodenoscopy) this term only
#47.	((endoscopic retrograde cholangiopancreatograph* or ercp or endoscopic ultraso* or eus or echo-endoscop* or endosonograph*) near/3 ((endoscop* near/3 duodenum) or duodenoscop*)):ti,ab
#48.	(or #44-#47)
#49.	MeSH descriptor: (cholangiopancreatography, magnetic resonance) this term only
#50.	MeSH descriptor: (secretin) this term only
#51.	#49 and #50
#52.	(magnetic resonance cholangiopancreatograph* or mrcp or secretin-mrcp):ti,ab
#53.	smrcp:ti,ab
#54.	(or #51-#53)
#55.	(pancrea* near/3 ?etiology):ti,ab
#56.	(or #4, #11, #19, #24, #39, #48, #54-#58)
#57.	#1 and #56
	Date parameters: see **Table 1**

PsycINFO search terms

1.	Standard population (A.2.1)
2.	Excluded study designs and publication types (A.3.1)
3.	1 not 2
4.	Limit 3 to English language
	Date parameters: see **Table 1**

G.4.3 Chronic aetiology

- What is the clinical and cost effectiveness of performing genetic markers and autoantibodies tests for identifying the aetiology of chronic pancreatitis in people with no known family history of pancreatitis, no significant alcohol history, and normal serum calcium and lipids?

Medline search terms

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	exp immunoglobulins/
6.	immunoglobulin*.ti,ab.
7.	igg*.ti,ab.
8.	exp antibodies, antinuclear/
9.	(autoantibod* or auto-antibod*).ti,ab.
10.	(anti-nuclear antibod* or antinuclear antibod* or ana).ti,ab.
11.	(antinuclear factor* or anti-nuclear factor* or anf).ti,ab.
12.	pancreatitis, chronic/et (etiology)
13.	genetic predisposition to disease/
14.	genetic markers/ or genetic testing/
15.	(genetic* adj3 (marker* or test* or predisposition*)).ti,ab.
16.	trypsin/
17.	trypsinogen/
18.	(trypsinogen or trypsin or prss1).ti,ab.
19.	(tati or psti).ti,ab.
20.	chymotrypsin/
21.	(chymotrypsin* or ctrc or cldn2).ti,ab.
22.	cystic fibrosis transmembrane conductance regulator/
23.	(cystic fibrosis transmembrane conductance regulator or cftr).ti,ab.
24.	trypsin inhibitor, kazal pancreatic/
25.	(serine protease inhibitor kazal-type 1 or spink1).ti,ab.
26.	or/5-25
27.	4 and 26
	Date parameters: see **Table 1**

Embase search terms

1.	Chronic pancreatitis population (G.2.2)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	exp immunoglobulin/
6.	immunoglobulin*.ti,ab.
7.	igg*.ti,ab.
8.	exp antinuclear antibody/
9.	(anti-nuclear antibod* or antinuclear antibod* or ana).ti,ab.
10.	(antinuclear factor* or anti-nuclear factor* or anf).ti,ab.

11.	(autoantibod* or auto-antibod*).ti,ab.
12.	autoantibody/
13.	chronic pancreatitis/et (etiology)
14.	autoimmune pancreatitis/et (etiology)
15.	genetic predisposition/ or disease predisposition/
16.	genetic marker/
17.	genetic screening/
18.	(genetic* adj3 (marker* or test* or predisposition*)).ti,ab.
19.	trypsin/ or trypsin inhibitor/
20.	trypsinogen/
21.	(trypsinogen or trypsin or prss1).ti,ab.
22.	(tati or psti).ti,ab.
23.	chymotrypsin/ or chymotrypsin inhibitor/
24.	(chymotrypsin* or ctrc or cldn2).ti,ab.
25.	cystic fibrosis transmembrane conductance regulator/
26.	(cystic fibrosis transmembrane conductance regulator or cftr).ti,ab.
27.	(serine protease inhibitor kazal-type 1 or spink1).ti,ab.
28.	or/5-27
29.	4 and 28
	Date parameters: see **Table 1**

1 **Cochrane search terms**

#1.	Chronic pancreatitis population (G.2.2)
#2.	MeSH descriptor: (immunoglobulins) explode all trees
#3.	immunoglobulin*:ti,ab
#4.	igg*:ti,ab
#5.	MeSH descriptor: (antibodies, antinuclear) explode all trees
#6.	(autoantibod* or auto-antibod*):ti,ab
#7.	(anti-nuclear antibod* or antinuclear antibod* or ana):ti,ab
#8.	(antinuclear factor* or anti-nuclear factor* or anf):ti,ab
#9.	MeSH descriptor: (genetic predisposition to disease) this term only
#10.	MeSH descriptor: (genetic markers) this term only
#11.	MeSH descriptor: (genetic testing) this term only
#12.	(genetic* near/3 (marker* or test* or predisposition*)):ti,ab
#13.	MeSH descriptor: (trypsin) this term only
#14.	MeSH descriptor: (trypsinogen) this term only
#15.	(trypsinogen or trypsin or prss1):ti,ab
#16.	(tati or psti):ti,ab
#17.	MeSH descriptor: (chymotrypsin) this term only
#18.	(chymotrypsin* or ctrc or cldn2):ti,ab
#19.	MeSH descriptor: (cystic fibrosis transmembrane conductance regulator) this term only
#20.	(cystic fibrosis transmembrane conductance regulator or cftr):ti,ab
#21.	MeSH descriptor: (trypsin inhibitor, kazal pancreatic) this term only
#22.	(serine protease inhibitor kazal-type 1 or spink1):ti,ab
#23.	(or #2-#22)

#24.	#1 and #23
	Date parameters: see **Table 1**

PsycINFO search terms

1.	Standard population (A.2.1)
2.	Excluded study designs and publication types (A.3.1)
3.	1 not 2
4.	Limit 3 to English language
	Date parameters: see **Table 1**

G.4.4 Chronic diagnosis

Searches for the following two questions were run as one search:

- In people with suspected (or under investigation for) chronic pancreatitis, in whom other causes have not been excluded by the use of CT scan, US scan and/or upper GI endoscopy, what is the most accurate diagnostic test to identify whether chronic pancreatitis is present (as indicated by the reference standards biopsy, clinical follow-up or subsequent CT scan)?
- In people with suspected (or under investigation for) chronic pancreatitis in whom other causes have not been excluded by the use of CT scan, US scan and/or upper GI endoscopy, what is the most clinically and cost effective test to identify whether chronic pancreatitis is present, when each is followed by the appropriate treatment, in order to improve patient outcomes?
- **Medline search terms**

1.	Chronic pancreatitis population (G.2.2)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	breath tests/
6.	breath test*.ti,ab.
7.	(triglyceride* adj3 test*).ti,ab.
8.	pancreatic function tests/
9.	(pancrea* adj3 function adj3 test*).ti,ab.
10.	feces/di (diagnosis)
11.	((f?ecal or stool* or f?ece* or monoclonal or polyclonal or chymotrypsin or fat) adj3 test*).ti,ab.
12.	((f?ecal or stool* or f?ece*) adj3 (fat or elast*)).ti,ab.
13.	magnetic resonance imaging/
14.	(mri* or magnetic resonance imag* or mr imag*).ti,ab.
15.	cholangiopancreatography, magnetic resonance/
16.	cholangiopancreatography, endoscopic retrograde/
17.	(cholangiopancreatograph* or mrcp or ercp).ti,ab.
18.	endoscopic ultrasound-guided fine needle aspiration/
19.	ultrasonography/ or elasticity imaging techniques/
20.	endoscopy, digestive system/ or endoscopy, gastrointestinal/
21.	(endoscop* adj3 (ultrasound or elastograph* or imag* or eus)).ti,ab.
22.	(secretin-cholecystokinin or secretin-cck or cck).ti,ab.
23.	(secretin adj3 (stimulation or test*)).ti,ab.
24.	or/5-23

25.	Study filters RCT (G.3.2) or SR (G.3.3) or DIAG (G.3.6) or OBS (G.3.7)
26.	4 and 24 and 25
	Date parameters: see **Table 1**

1 **Embase search terms**

1.	Chronic pancreatitis population (G.2.2)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	breath analysis/
6.	breath test*.ti,ab.
7.	(triglyceride* adj3 test*).ti,ab.
8.	(pancrea* adj3 function test*).ti,ab.
9.	pancreas examination/ or pancreas function test/ or pancreatography/
10.	feces analysis/
11.	((f?ecal or stool* or f?ece* or monoclonal or polyclonal or Chymotrypsin or fat) adj3 test*).ti,ab.
12.	((f?ecal or stool* or f?ece*) adj3 (fat or elast*)).ti,ab.
13.	nuclear magnetic resonance imaging/ or magnetic resonance cholangiopancreatography/
14.	(MRI* or magnetic resonance imag* or MR imag*).ti,ab.
15.	endoscopic retrograde cholangiopancreatography/
16.	(cholangiopancreatograph* or MRCP or ERCP).ti,ab.
17.	endoscopic ultrasound guided fine needle biopsy/
18.	elastography/
19.	digestive tract endoscopy/
20.	(endoscop* adj3 (ultrasound or elastograph* or imag* or EUS)).ti,ab.
21.	(secretin-cholecystokinin or Secretin-CCK or CCK).ti,ab.
22.	(secretin adj3 (stimulation or test*)).ti,ab.
23.	or/5-22
24.	Study filters RCT (A.3.2) or SR (A.3.3) or DIAG (A.3.6) or OBS (A.3.7)
25.	4 and 23 and 24
	Date parameters: see **Table 1**

2 **Cochrane search terms**

#1.	Chronic pancreatitis population (G.2.2)
#2.	MeSH descriptor: (breath tests) this term only
#3.	breath test*:ti,ab
#4.	(triglyceride* near/3 test*):ti,ab
#5.	MeSH descriptor: (pancreatic function tests) this term only
#6.	(pancrea* near/3 function near/3 test*):ti,ab
#7.	((f?ecal or stool* or f?ece* or monoclonal or polyclonal or chymotrypsin or fat) near/3 test*):ti,ab
#8.	((f?ecal or stool* or f?ece*) near/3 (fat or elast*)):ti,ab
#9.	MeSH descriptor: (magnetic resonance imaging) this term only
#10.	(mri* or magnetic resonance imag* or mr imag*):ti,ab
#11.	MeSH descriptor: (cholangiopancreatography, magnetic resonance) this term only

#12.	MeSH descriptor: (cholangiopancreatography, endoscopic retrograde) this term only
#13.	MeSH descriptor: (endoscopic ultrasound-guided fine needle aspiration) this term only
#14.	MeSH descriptor: (ultrasonography) this term only
#15.	MeSH descriptor: (elasticity imaging techniques) this term only
#16.	MeSH descriptor: (endoscopy, gastrointestinal) this term only
#17.	MeSH descriptor: (endoscopy, digestive system) this term only
#18.	(endoscop* near/3 (ultrasound or elastograph* or imag* or eus)):ti,ab
#19.	(secretin-cholecystokinin or secretin-cck or cck):ti,ab
#20.	(secretin near/3 (stimulation or test*)):ti,ab
#21.	(or #2-#20)
#22.	#1 and #21
	Date parameters: see **Table 1**

PsycINFO search terms

1.	Standard population (A.2.1)
2.	Excluded study designs and publication types (A.3.1)
3.	1 not 2
4.	Limit 3 to English language
	Date parameters: 1806-28 September 2017

G.4.5 Lifestyle: alcohol

- What is the effectiveness of stopping or reducing alcohol consumption in reducing recurrent episodes of acute pancreatitis and improving quality of life in people with both chronic and acute pancreatitis?

Medline search terms

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	temperance/ or alcohol abstinence/
6.	(alcohol* adj3 (cessat* or ceas* or reduc* or restrict* or avoid* or abstem* or control* or stop* or quit* or giv* up or withdraw* or low* or drop* or fall* or decreas* or less* or moderat* or cut* or regulat* or abstin* or abstain* or discontinu* or chang* or alter* or modif* or adjust* or amend*)).ti,ab.
7.	(alcohol* adj6 (program* or interven* or prevent* or help* or manag* or motivat* or educat* or mentor* or inform* or support* or advice or advis* or counsel* or therap* or strateg* or policy or policies)).ti,ab.
8.	(temperate or temper or tempers or teetotal* or sober* or sobriety).ti,ab.
9.	or/5-8
10.	drinking behavior/ or alcohol drinking/ or alcoholic beverages/
11.	alcohol-related disorders/ or alcohol-induced disorders/ or alcoholic intoxication/ or alcoholism/ or binge drinking/
12.	(alcohol* adj3 "use").ti,ab.
13.	(alcohol* adj3 (addict* or abus* or depend* or overdos* or disorder* or misus* or using or user or drink* or consume* or consumption or risk* or intak* or exposure or excess* or problem* or unit*)).ti,ab.
14.	(intoxicat* or drunken*).ti,ab.

15.	(drink* adj3 (behaviour* or behavior* or binge* or problem* or excess*)).ti,ab.
16.	or/10-15
17.	4 and (9 or 16)
	Date parameters: see **Table 1**

1 **Embase search terms**

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	temperance/ or alcohol abstinence/
6.	(alcohol* adj3 (cessat* or ceas* or reduc* or restrict* or avoid* or abstem* or control* or stop* or quit* or giv* up or withdraw* or low* or drop* or fall* or decreas* or less* or moderat* or cut* or regulat* or abstin* or abstain* or discontinu* or chang* or alter* or modif* or adjust* or amend*)).ti,ab.
7.	(alcohol* adj6 (program* or interven* or prevent* or help* or manag* or motivat* or educat* or mentor* or inform* or support* or advice or advis* or counsel* or therap* or strateg* or policy or policies)).ti,ab.
8.	(temperate or temper or tempers or teetotal* or sober* or sobriety).ti,ab.
9.	or/5-8
10.	drinking behavior/ or alcohol drinking/ or alcoholic beverages/
11.	alcohol-related disorders/ or alcohol-induced disorders/ or alcoholic intoxication/ or alcoholism/ or binge drinking/
12.	(alcohol* adj3 "use").ti,ab.
13.	(alcohol* adj3 (addict* or abus* or depend* or overdos* or disorder* or misus* or using or user or drink* or consume* or consumption or risk* or intak* or exposure or excess* or problem* or unit*)).ti,ab.
14.	(intoxicat* or drunken*).ti,ab.
15.	(drink* adj3 (behaviour* or behavior* or binge* or problem* or excess*)).ti,ab.
16.	or/10-15
17.	4 and (9 or 16)
	Date parameters: see **Table 1**

2 **Cochrane search terms**

#1.	Standard population (G.2.1)
#2.	MeSH descriptor: (temperance) this term only
#3.	MeSH descriptor: (alcohol abstinence) this term only
#4.	(alcohol* near/3 (cessat* or ceas* or reduc* or restrict* or avoid* or abstem* or control* or stop* or quit* or giv* next up or withdraw* or low* or drop* or fall* or decreas* or less* or moderat* or cut* or regulat* or abstin* or abstain* or discontinu* or chang* or alter* or modif* or adjust* or amend*)):ti,ab
#5.	(alcohol* near/6 (program* or interven* or prevent* or help or support* or advice or advise* or counsel* or therap* or strateg* or policy or policies)):ti,ab
#6.	(temperate or temper or tempers or teetotal* or sober* or sobriety):ti,ab
#7.	#2 or #3or #4 or #5 or #6
#8.	MeSH descriptor: (drinking behavior) this term only
#9.	MeSH descriptor: (alcohol drinking) this term only
#10.	MeSH descriptor: (alcoholic beverages) this term only
#11.	MeSH descriptor: (alcohol-related disorders) this term only

#12.	MeSH descriptor: (alcohol-induced disorders) this term only
#13.	MeSH descriptor: (alcoholic intoxication) this term only
#14.	MeSH descriptor: (alcoholism) this term only
#15.	MeSH descriptor: (binge drinking) this term only
#16.	alcohol* near/3 use:ti,ab
#17.	(alcohol* near/3 (addict* or abus* or depend* or overdos* or disorder* or misus* or using or user or drink* or consume* or consumption or risk* or intak* or exposure or excess* or problem* or unit*)):ti,ab
#18.	(intoxicat* or drunken*):ti,ab
#19.	(drink* near/3 (behaviour* or behavior* or binge* or problem* or excess*)):ti,ab
#20.	#8 or #9 or #10or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19
#21.	#7or #20
#22.	#1 and #21
	Date parameters: see **Table 1**

PsycINFO search terms

1.	Standard population (A.2.1)
2.	Excluded study designs and publication types (A.3.1)
3.	1 not 2
4.	Limit 3 to English language
	Date parameters: see **Table 1**

G.4.6 IV fluid management

Searches for the following two questions were run as one search:

- What is the most clinically and cost-effective type of intravenous fluid for resuscitation in people with acute pancreatitis?
- What is the most clinically and cost-effective speed of administration of intravenous fluid for resuscitation in people with acute pancreatitis?

Medline search terms

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	exp fluid therapy/
6.	((fluid* or volum*) adj3 (restor* or resuscita* or replac* or deplet* or deficien*)).ti,ab.
7.	(fluid* adj3 (challenge or bolus)).ti,ab.
8.	colloids/
9.	exp plasma substitutes/
10.	albumins/ or exp serum albumin/
11.	dextrans/
12.	hydroxyethyl starch derivatives/
13.	exp hypertonic solutions/ or isotonic solutions/
14.	gelatin/
15.	(crystalloid* or colloid* or isotonic).ti,ab.
16.	(albumin* or albumex or albunorm or octalbin or zenalb or flexbumin).ti,ab.

17.	(dextran or rescueflow).ti,ab.
18.	(gelatin or gelospan or gelofusine or geloplasma or isoplex or volplex).ti,ab.
19.	(starch* or hetastarch* or pentastarch* or pentaspan* or haemaccel or haes-steril or hemohes or tetrastarch* or tetraspan or venofundin or volulyte or voluven).ti,ab.
20.	(hypertonic or hyperhaes or hypotonic).ti,ab.
21.	potassium chloride/ or sodium chloride/ or sodium bicarbonate/
22.	(sodium or salin* or hartman* or ringer* or glucose or lactate* or acetate*).ti,ab.
23.	(dextrose or potassium or bicarbonate).ti,ab.
24.	(goal adj1 (direct* or orient*) adj1 therap*).ti,ab.
25.	(plasmalyte or plasma-lyte).ti,ab.
26.	or/5-25
27.	4 and 26
	Date parameters: see **Table 1**

1 **Embase search terms**

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	exp fluid therapy/
6.	fluid resuscitation/
7.	fluid balance/
8.	((fluid* or volum*) adj3 (restor* or resuscita* or replac* or deplet* or deficien*)).ti,ab.
9.	(fluid* adj3 (challenge or bolus)).ti,ab.
10.	colloid/
11.	plasma substitute/
12.	albumin/
13.	serum albumin/
14.	hypertonic solution/
15.	isotonic solution/
16.	dextran/
17.	hetastarch derivative/
18.	gelatin/
19.	(crystalloid* or colloid* or isotonic).ti,ab.
20.	(albumin* or albumex or albunorm or octalbin or zenalb or flexbumin).ti,ab.
21.	human serum albumin/
22.	human albumin/
23.	(dextran or rescueflow).ti,ab.
24.	dextran 70/
25.	(gelatin or gelospan or gelofusine or geloplasma or isoplex or volplex).ti,ab.
26.	gelatin succinate/
27.	crystalloid/
28.	(starch* or hetastarch* or pentastarch* or pentaspan* or haemaccel or haes-steril or hemohes or tetrastarch* or tetraspan or venofundin or volulyte or voluven).ti,ab.
29.	polygeline/
30.	(hypertonic or hyperhaes or hypotonic).ti,ab.

31.	potassium chloride/
32.	sodium chloride/
33.	bicarbonate/
34.	(sodium or salin* or hartman* or ringer* or glucose or lactate* or acetate*).ti,ab.
35.	hartmann solution/
36.	ringer lactate solution/ or ringer solution/
37.	(dextrose or potassium or bicarbonate).ti,ab.
38.	(goal adj1 (direct* or orient*) adj1 therap*).ti,ab.
39.	acetic acid plus gluconate sodium plus magnesium chloride plus potassium chloride plus sodium chloride/
40.	(plasmalyte or plasma-lyte).ti,ab.
41.	or/5-41
42.	4 and 42
	Date parameters: see **Table 1**

1 **Cochrane search terms**

#1.	Standard population (G.2.1)
#2.	MeSH descriptor: (fluid therapy) explode all trees
#3.	((fluid* or volum*) near/3 (restor* or resuscita* or replac* or deplet* or deficien*)):ti,ab
#4.	(fluid* near/3 (challenge or bolus)):ti,ab
#5.	MeSH descriptor: (colloids) explode all trees
#6.	MeSH descriptor: (plasma substitutes) explode all trees
#7.	MeSH descriptor: (albumins) explode all trees
#8.	MeSH descriptor: (serum albumin) explode all trees
#9.	MeSH descriptor: (dextrans) explode all trees
#10.	MeSH descriptor: (hydroxyethyl starch derivatives) explode all trees
#11.	(mh "hypertonic solutions")
#12.	(mh "isotonic solutions")
#13.	(mh gelatin)
#14.	(crystalloid* or colloid* or isotonic):ti,ab
#15.	(albumin* or albumex or albunorm or octalbin or zenalb or flexbumin):ti,ab
#16.	(dextran or rescueflow):ti,ab
#17.	(gelatin or gelospan or gelofusine or geloplasma or isoplex or volplex):ti,ab
#18.	(starch* or hetastarch* or pentastarch* or pentaspan* or haemaccel or haes-steril or hemohes or tetrastarch* or tetraspan or venofundin or volulyte or voluven):ti,ab
#19.	(hypertonic or hyperhaes or hypotonic):ti,ab
#20.	(mh "potassium chloride")
#21.	(mh "sodium chloride")
#22.	(mh "sodium bicarbonate")
#23.	(sodium or salin* or hartman* or ringer* or glucose or lactate* or acetate*):ti,ab
#24.	(dextrose or potassium or bicarbonate):ti,ab
#25.	(goal next (direct* or orient*) next therap*):ti,ab
#26.	(plasmalyte or plasma-lyte):ti,ab
#27.	(or #4-#26)
#28.	#1 and #27
	Date parameters: see **Table 1**

PsycINFO search terms

1.	Standard population (A.2.1)
2.	Excluded study designs and publication types (A.3.1)
3.	1 not 2
4.	Limit 3 to English language
	Date parameters: see **Table 1**

G.4.7 Nutrition support

Searches for the following two questions were run as one search:

- What is the clinical and cost effectiveness of early versus late nutritional intervention (for example, food supplements, enzyme supplements) in people with chronic pancreatitis and signs of malnutrition or malabsorption?
- What is the most clinically and cost-effective route of feeding at time of admission to the hospital in people with acute pancreatitis?

Medline search terms

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	exp nutrition therapy/ or nutrition assessment/ or diet therapy/ or exp nutritional support/
6.	dietary supplements/ or exp enzyme therapy/
7.	feeding methods/ or enteral nutrition/ or parenteral nutrition/
8.	((diet* or nutrition* or nutrient* or food or feed*) adj4 (support* or assess* or advice or advise* or counsel* or therap* or intervention* or strateg* or protocol* or manage* or treat* or absorb* or absorption or supplement* or intak* or replace*)).ti,ab.
9.	((enteral or parenteral or gastric or nasogastric or nasojejunal or jejunal or duodenal or nasoduodenal or nasoenteric) adj4 (feed* or fed or food or nutrition* or nutrient* or diet*)).ti,ab.
10.	((enzyme* or calorie* or vitamin* or glutamine or probiotic* or omega-3) adj4 (supplement* or treat* or intervention* or therap* or replace* or absorb* or absorption)).ti,ab.
11.	(ert or pert or pancrease or pancrex or creon or kreon or pancreaze or pancreatin or nutrizym or pankreon or pankreatin).ti,ab.
12.	(pancreatic adj enzyme*).ti,ab.
13.	(tube adj3 (feed* or fed)).ti,ab.
14.	(oral* adj3 (fed or feed* or diet* or supplement*)).ti,ab.
15.	((liquid or soft) adj2 diet*).ti,ab.
16.	immunonutrition.ti,ab.
17.	(route adj2 feed*).ti,ab.
18.	or/5-18
19.	4 and 19
20.	malnutrition/ or malabsorption syndromes/ or nutritional status/
21.	(malnutrition or malabsorption or malnourish* or maldigestion or under-nutrition or undernutrition or under-nourish* or undernourish*).ti,ab.
22.	(nutrition* adj3 (status or deficien* or impair* or deplet* or risk*)).ti,ab.
23.	((micronutrient* or vitamin*) adj3 (deficien* or impair* or deplet*)).ti,ab.
24.	(weight adj2 (lost or loss*)).ti,ab.

25.	(skinfold* or skin fold*).ti,ab.
26.	body mass index/ or skinfold thickness/
27.	weight loss/
28.	or/20-27
29.	4 and 28
30.	Study filters RCT (G.3.2) or SR (G.3.3) or OBS (G.3.7)
31.	30 and (19 or 29)
	Date parameters: see **Table 1**

1 **Embase search terms**

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	diet therapy/ or nutritional assessment/ or nutritional support/
6.	dietary supplement/ or vitamin supplementation/ or diet supplementation/
7.	food intake/ or enteric feeding/ or exp parenteral nutrition/
8.	exp enzyme therapy/
9.	((diet* or nutrition* or nutrient* or food or feed*) adj4 (support* or assess* or advice or advise* or counsel* or therap* or intervention* or strateg* or protocol* or manage* or treat* or absorb* or absorption or supplement* or intak* or replace*)).ti,ab.
10.	((enteral or parenteral or gastric or nasogastric or nasojejunal or jejunal or duodenal or nasoduodenal or nasoenteric) adj4 (feed* or fed or food or nutrition* or nutrient* or diet*)).ti,ab.
11.	((enzyme* or calorie* or vitamin* or glutamine or probiotic* or omega-3) adj4 (supplement* or treat* or intervention* or therap* or replace* or absorb* or absorption)).ti,ab.
12.	(ert or pert or pancrease or pancrex or creon or kreon or pancreaze or pancreatin or nutrizym or pankreon or pankreatin).ti,ab.
13.	(pancreatic adj enzyme*).ti,ab.
14.	(tube adj3 (feed* or fed)).ti,ab.
15.	(oral* adj3 (fed or feed* or diet* or supplement*)).ti,ab.
16.	((liquid or soft) adj2 diet*).ti,ab.
17.	(route adj2 feed*).ti,ab.
18.	immunonutrition.ti,ab.
19.	or/5-18
20.	nutritional status/
21.	(nutrition* adj3 (status or deficien* or impair* or deplet* or risk*)).ti,ab.
22.	malnutrition/ or malabsorption/
23.	(malnutrition or malabsorption or malnourish* or maldigestion or under-nutrition or undernutrition or under-nourish* or undernourish*).ti,ab.
24.	vitamin deficiency/ or nutritional deficiency/
25.	((micronutrient* or vitamin*) adj3 (deficien* or impair* or deplet*)).ti,ab.
26.	weight reduction/ or body mass/ or skinfold thickness/
27.	(weight adj2 (lost or loss*)).ti,ab.
28.	(skinfold* or skin fold*).ti,ab.
29.	or/20-28
30.	4 and (19 or 29)

31.	Study filters RCT (G.3.2) or SR (G.3.3) or OBS (G.3.7)
32.	30 and 31
	Date parameters: see **Table 1**

1 **Cochrane search terms**

#1.	Standard population (G.2.1)
#2.	(mh "nutrition therapy")
#3.	(mh ^"nutrition assessment")
#4.	(mh ^"diet therapy")
#5.	(mh "nutritional support")
#6.	(mh ^"dietary supplements")
#7.	(mh "enzyme therapy")
#8.	(mh ^"feeding methods")
#9.	((diet* or nutrition* or nutrient* or food or feed*) near/4 (support* or assess* or advice or advise* or counsel* or therap* or intervention* or strateg* or protocol* or manage* or treat* or absorb* or absorption or supplement* or intak* or replace*)):ti,ab
#10.	((enteral or parenteral or gastric or nasogastric or nasojejunal or jejunal or duodenal or nasoduodenal or nasoenteric) near/4 (feed* or fed or food or nutrition* or nutrient* or diet*)):ti,ab
#11.	((enzyme* or calorie* or vitamin* or glutamine or probiotic* or omega-3) near/4 (supplement* or treat* or intervention* or therap* or replace* or absorb* or absorption)):ti,ab
#12.	(ert or pert or pancrease or pancrex or creon or kreon or pancreaze or pancreatin or nutrizym or pankreon or pankreatin):ti,ab
#13.	(pancreatic next enzyme*):ti,ab
#14.	(tube near/3 (feed* or fed)):ti,ab
#15.	(oral* near/3 (fed or feed* or diet* or supplement*)):ti,ab
#16.	((liquid or soft) near/2 diet*):ti,ab
#17.	immunonutrition:ti,ab
#18.	(route near/2 feed*):ti,ab
#19.	(or #2-#18)
#20.	#1and #19
#21.	(mh ^malnutrition)
#22.	(mh ^"malabsorption syndromes")
#23.	(mh ^"nutritional status")
#24.	(malnutrition or malabsorption or malnourish* or maldigestion or under-nutrition or undernutrition or under-nourish* or undernourish*):ti,ab
#25.	(nutrition* near/3 (status or deficien* or impair* or deplet* or risk*)):ti,ab
#26.	((micronutrient* or vitamin*) near/3 (deficien* or impair* or deplet*)):ti,ab
#27.	(weight near/2 (lost or loss*)):ti,ab
#28.	(skinfold* or skin fold*):ti,ab
#29.	(mh ^"body mass index")
#30.	(mh ^"skinfold thickness")
#31.	(mh ^"weight loss")
#32.	(or #21-#31)
#33.	#1 and #32
#34.	#19 or #33

	Date parameters: see **Table 1**

PsycINFO search terms

1.	Standard population (A.2.1)
2.	Excluded study designs and publication types (A.3.1)
3.	1 not 2
4.	Limit 3 to English language
	Date parameters: see **Table 1**

G.4.8 Antimicrobial prophylaxis

- What is the clinical and cost-effectiveness of prophylactic antimicrobial agents to prevent infection in people with acute pancreatitis?

Medline search terms

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	exp anti-infective agents/ or superinfection/ or exp bacterial infections/
6.	exp aminoglycosides/
7.	exp beta-lactams/
8.	exp glycopeptides/
9.	exp lincosamides/
10.	exp macrolides/
11.	exp nitroimidazoles/
12.	exp polymyxins/
13.	exp quinolones/
14.	exp sulfonamides/
15.	exp trimethoprim/
16.	exp tetracyclines/
17.	exp chloramphenicol/
18.	fusidic acid/
19.	daptomycin/
20.	linezolid/
21.	exp rifamycins/
22.	nitrofurantoin/
23.	methenamine/
24.	exp triazoles/ or exp imidazoles/
25.	exp polyenes/
26.	echinocandins/
27.	flucytosine/
28.	griseofulvin/
29.	(microb* or antimicrob* or anti-microb* or antiinfect* or anti-infect* or bacter* or antibacter* or anti-bacter* or antibiot* or anti-biot* or fung* or antifung* or anti-fung* or superbug* or super-bug*).ti,ab.
30.	beta-lactam*.mp,hw.

31.	(aminoglycoside* or amikacin or amikin or gentamicin or cidomycingenticin or neomycin or sulphate or nivemycin or streptomycin or tobramycin or nebcin or tobi or podhaler or tobi or tymbrineb or bramitob or tobravisc).mp,hw.
32.	(carbapen#m* or ertapenem or invanz or imipenem or cilastatin or primaxin or meropenem or meronem).mp,hw.
33.	(cephalosporin* or cefadroxil or cefalexin or ceporex or keflex or cefradine or nicef or cefaclor or distaclor or keftid or cefuroxime or zinnat or aprokam or zinacef or cefixime or suprax or cefotaxime or ceftazidime or fortum or kefadim or ceftriaxone or rocephin or ceftaroline or fosamil or zinforo).mp,hw.
34.	(glycopeptide* or teicoplanin or targocid or telavancin or vibativ or vancomycin or vancocin).mp,hw.
35.	(lincosamide* or clindamycin or dalacin or zindaclin).mp,hw.
36.	(macrolide* or azithromycin or zithromax or zedbac or ayter or clarithromycin or clarie or klaricid or erythromycin or erythrocin or erythrolar or erythroped or erymax or primacine or tiloryth or oftalmolosa cusi eritromicina or telithromycin or ketek).mp,hw.
37.	(monobactam* or aztreonam or azactam or cayston).mp,hw.
38.	(nitroimidazole* or metronidazole or flagyl or vaginyl or norzol or metrolyl or tinidazole or fasigyn).mp,hw.
39.	(penicillin* or piperacillin or tazobactam or tazocin or ticarcillin or clavulanic acid or timentin or benzylpenicillin or crystapen or phenoxymethylpenicillin or amoxicillin or amoxil or amix or amoram or amoxient or galenamox or rimoxallin or ampicillin or penbritin or rimacillin or co-fluampicil or flu-amp or magnapen or co-amoxiclav or augmentin or pivmecillinam or selexid or flucloxacillin or floxapen or flucomix or ladropen or temocillin or negaban).mp,hw.
40.	(polymyxin* or colistimethate or colistin or sulfomethate or colomycin or promixin or colobreathe).mp,hw.
41.	(quinolone* or ciprofloxacin or ciproxin or levofloxacin or evoxil or tavanic or moxifloxacin or avelox or nalidixic acid or norfloxacin or ofloxacin or tarivid or perfloxacin).mp,hw.
42.	(sulfonamide* or co-trimoxazole or fectrim or septrin or sulfadiazine or trimethoprim or trimopan).mp,hw.
43.	(tetracycline* or demeclocycline or doxycycline or vibramycin-d or efracea or lymecycline or tetralysal or minocycline or aknemin or acnamino or minocin or sebomin or oxytetracycline or oxymycin or tigecycline or tygacil).mp,hw.
44.	(chloramphenicol or kemicetine or brochlor or brolene or chloromycetin or golden eye or optrex or klorafect or fosfomycin or fomicyt or fusidic acid or sodium fusidate or fucidin or daptomycin or cubicin or linezolid or zyvox or rifaximin or targaxan or xifaxanta or fidaxomicin or dificlir or tedizolid or sivextro).mp,hw.
45.	(nitrofurantoin or macrobid or methenamine hippurate or hexamine hippurate or hiprex).mp,hw.
46.	(triazole* or fluconazole or diflucan or itraconazole or sporanox or posaconazole or noxafil or voriconazole or vfend or omoconazole or epoxiconazole).mp,hw.
47.	(imidazole* or clotrimazole or econazole or tioconazole or ketoconazole or miconazole).mp,hw.
48.	(polyene* or amphotericin or fungizone or abelcet or ambisome).mp,hw.
49.	(echinocandin* or anidulafungin or ecalta or caspofungin or cancidas or micafungin or mycamine).mp,hw.
50.	(flucytosine or ancotil or griseofulvin or terbinafine or lamisil).mp,hw.
51.	or/5-50
52.	4 and 51
	Date parameters: see **Table 1**

Embase search terms

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	exp antiinfective agent/
6.	exp bacterial infection/ or exp superinfection/
7.	exp *aminoglycoside antibiotic agent/
8.	*amikacin/ or *gentamicin/ or *neomycin/ or *streptomycin/ or *tobramycin/
9.	exp *beta lactam antibiotic/
10.	*carbapenem derivative/ or *carbapenem/ or *ertapenem/ or *cilastatin with imipenem/ or *imipenem/ or *meropenem/
11.	exp *cephalosporin derivative/ or exp *cephalosporin/
12.	*cefadroxil/ or *cefalexin/ or *cefradine/ or *cefaclor/ or *cefuroxime/ or *cefixime/ or *cefotaxime/ or *ceftazidime/ or *ceftriaxone/ or *ceftaroline fosamil/
13.	*glycopeptide/
14.	*teicoplanin/ or *telavancin/ or *vancomycin/
15.	*lincosamide/
16.	*clindamycin/
17.	exp *macrolide/
18.	*azithromycin/ or *clarithromycin/ or *erythromycin/ or *telithromycin/
19.	exp *monobactam derivative/
20.	*aztreonam/
21.	exp *nitroimidazole derivative/ or exp *nitroimidazole/
22.	*metronidazole/ or *tinidazole/
23.	exp *penicillin derivative/
24.	*piperacillin plus tazobactam/ or *ticarcillin/ or *clavulanic acid/ or *penicillin g/ or *penicillin v/ or *amoxicillin/ or *ampicillin/ or *ampicillin plus flucloxacillin/ or *amoxicillin plus clavulanic acid/ or *pivmecillinam/ or *flucloxacillin/
25.	*polymyxin/
26.	*colistin/ or *colistimethate/
27.	exp *quinolone derivative/ or exp *quinolone/
28.	*ciprofloxacin/ or *levofloxacin/ or *moxifloxacin/ or *nalidixic acid/ or *norfloxacin/ or *ofloxacin/ or *perfloxacin/
29.	exp *sulfonamide/ or exp *trimethoprim/ or exp *trimethoprim derivative/
30.	*cotrimoxazole/ or *sulfadiazine/
31.	exp *tetracycline derivative/ or exp *tetracycline/
32.	*demeclocycline/ or *doxycycline/ or *lymecycline/ or *minocycline/ or *oxytetracycline/ or *tigecycline/
33.	*chloramphenicol derivative/ or *chloramphenicol/
34.	*fosfomycin/
35.	*fusidic acid/
36.	*daptomycin/
37.	*linezolid/
38.	*rifaximin/
39.	*fidaxomicin/
40.	*tedizolid/

41.	exp *triazole derivative/
42.	*fluconazole/ or *itraconazole/ or *posaconazole/ or *voriconazole/ or *omoconazole/ or *epoxiconazole/
43.	exp *imidazole derivative/
44.	*clotrimazole/ or *econazole/ or *tioconazole/ or *ketoconazole/ or *miconazole/
45.	exp *polyene antibiotic agent/
46.	*amphotericin/
47.	exp *echinocandin/
48.	*anidulafungin/ or *caspofungin/ or *micafungin/
49.	*flucytosine/ or *griseofulvin/ or *terbinafine/
50.	(microb* or antimicrob* or anti-microb* or antiinfect* or anti-infect* or bacter* or antibacter* or anti-bacter* or antibiot* or anti-biot* or fung* or antifung* or anti-fung* or superbug* or super-bug*).ti,ab.
51.	beta-lactam*.mp,hw.
52.	(aminoglycoside* or amikacin or amikin or gentamicin or cidomycingenticin or neomycin or sulphate or nivemycin or streptomycin or tobramycin or nebcin or tobi or podhaler or tobi or tymbrineb or bramitob or tobravisc).mp,hw.
53.	(carbapen#m* or ertapenem or invanz or imipenem or cilastatin or primaxin or meropenem or meronem).mp,hw.
54.	(cephalosporin* or cefadroxil or cefalexin or ceporex or keflex or cefradine or nicef or cefaclor or distaclor or keftid or cefuroxime or zinnat or aprokam or zinacef or cefixime or suprax or cefotaxime or ceftazidime or fortum or kefadim or ceftriaxone or rocephin or ceftaroline or fosamil or zinforo).mp,hw.
55.	(glycopeptide* or teicoplanin or targocid or telavancin or vibativ or vancomycin or vancocin).mp,hw.
56.	(lincosamide* or clindamycin or dalacin or zindaclin).mp,hw.
57.	(macrolide* or azithromycin or zithromax or zedbac or ayter or clarithromycin or clarie or klaricid or erythromycin or erythrocin or erythrolar or erythroped or erymax or primacine or tiloryth or oftalmolosa cusi eritromicina or telithromycin or ketek).mp,hw.
58.	(monobactam* or aztreonam or azactam or cayston).mp,hw.
59.	(nitroimidazole* or metronidazole or flagyl or vaginyl or norzol or metrolyl or tinidazole or fasigyn).mp,hw.
60.	(penicillin* or piperacillin or tazobactam or tazocin or ticarcillin or clavulanic or timentin or benzylpenicillin or crystapen or phenoxymethylpenicillin or amoxicillin or amoxil or amix or amoram or amoxient or galenamox or rimoxallin or ampicillin or penbritin or rimacillin or co-fluampicil or flu-amp or magnapen or co-amoxiclav or augmentin or pivmecillinam or selexid or flucloxacillin or floxapen or flucomix or ladropen or temocillin or negaban).mp,hw.
61.	(polymyxin* or colistimethate or colistin or sulfomethate or colomycin or promixin or colobreathe).mp,hw.
62.	(quinolone* or ciprofloxacin or ciproxin or levofloxacin or evoxil or tavanic or moxifloxacin or avelox or nalidixic acid or norfloxacin or ofloxacin or tarivid or perfloxacin).mp,hw.
63.	(sulfonamide* or co-trimoxazole or cotrimoxazole or fectrim or septrin or sulfadiazine or trimethoprim or trimopan).mp,hw.
64.	(tetracycline* or demeclocycline or doxycycline or vibramycin-d or efracea or lymecycline or tetralysal or minocycline or aknemin or acnamino or minocin or sebomin or oxytetracycline or oxymycin or tigecycline or tygacil).mp,hw.
65.	(chloramphenicol or kemicetine or brochlor or brolene or chloromycetin or golden eye or optrex or klorafect or fosfomycin or fomicyt or fusidic acid or sodium fusidate or fucidin or daptomycin or cubicin or linezolid or zyvox or rifaximin or targaxan or xifaxanta or fidaxomicin or dificlir or tedizolid or sivextro).mp,hw.
66.	(nitrofurantoin or macrobid or methenamine hippurate or hexamine hippurate or

	hiprex).mp,hw.
67.	(triazole* or fluconazole or diflucan or itraconazole or sporanox or posaconazole or noxafil or voriconazole or vfend or omoconazole or epoxiconazole).mp,hw.
68.	(imidazole* or clotrimazole or econazole or tioconazole or ketoconazole or miconazole).mp,hw.
69.	(polyene* or amphotericin or fungizone or abelcet or ambisome).mp,hw.
70.	(echinocandin* or anidulafungin or ecalta or caspofungin or cancidas or micafungin or mycamine).mp,hw.
71.	(flucytosine or ancotil or griseofulvin or terbinafine or lamisil).mp,hw.
72.	or/5-71
73.	4 and 72
	Date parameters: see **Table 1**

1 **Cochrane search terms**

#1.	Standard population (G.2.1)
#2.	MeSH descriptor: (anti-infective agents) explode all trees
#3.	MeSH descriptor: (superinfection) explode all trees
#4.	MeSH descriptor: (bacterial infections) explode all trees
#5.	MeSH descriptor: (aminoglycosides) explode all trees
#6.	MeSH descriptor: (beta-lactams) explode all trees
#7.	MeSH descriptor: (glycopeptides) explode all trees
#8.	MeSH descriptor: (lincosamides) explode all trees
#9.	MeSH descriptor: (macrolides) explode all trees
#10.	MeSH descriptor: (nitroimidazoles) explode all trees
#11.	MeSH descriptor: (polymyxins) explode all trees
#12.	MeSH descriptor: (quinolones) explode all trees
#13.	MeSH descriptor: (sulfonamides) explode all trees
#14.	MeSH descriptor: (trimethoprim) explode all trees
#15.	MeSH descriptor: (tetracyclines) explode all trees
#16.	MeSH descriptor: (chloramphenicol) explode all trees
#17.	MeSH descriptor: (fusidic acid) explode all trees
#18.	MeSH descriptor: (daptomycin) explode all trees
#19.	MeSH descriptor: (linezolid) explode all trees
#20.	MeSH descriptor: (rifamycins) explode all trees
#21.	MeSH descriptor: (nitrofurantoin) explode all trees
#22.	MeSH descriptor: (methenamine) explode all trees
#23.	MeSH descriptor: (azoles) explode all trees
#24.	MeSH descriptor: (polyenes) explode all trees
#25.	MeSH descriptor: (echinocandins) explode all trees
#26.	MeSH descriptor: (flucytosine) explode all trees
#27.	MeSH descriptor: (fosfomycin) explode all trees
#28.	MeSH descriptor: (griseofulvin) explode all trees
#29.	(microb* or antimicrob* or anti-microb* or (anti next microb*) or antiinfect* or anti-infect* or (anti next infect*) or bacter* or antibacter* or anti-bacter* or (anti next bacter*) or antibiot* or anti-biot* or (anti next biot*) or fung* or antifung* or anti-fung* or (anti next fung*) or superbug* or super-bug* or (super next bug*)):ti,ab,kw
#30.	(beta-lactam* or (beta next lactam*)):ti,ab,kw

#31.	(aminoglycoside* or amikacin or amikin or gentamicin or cidomycingenticin or neomycin or sulphate or nivemycin or streptomycin or tobramycin or nebcin or tobi or podhaler or tobi or tymbrineb or bramitob or tobravisc):ti,ab,kw
#32.	(carbapenem* or carbepenam* or ertapenem or invanz or imipenem or cilastatin or primaxin or meropenem or meronem):ti,ab,kw
#33.	(cephalosporin* or cefadroxil or cefalexin or ceporex or keflex or cefradine or nicef or cefaclor or distaclor or keftid or cefuroxime or zinnat or aprokam or zinacef or cefixime or suprax or cefotaxime or ceftazidime or fortum or kefadim or ceftriaxone or rocephin or ceftaroline or fosamil or zinforo):ti,ab,kw
#34.	(glycopeptide* or teicoplanin or targocid or telavancin or vibativ or vancomycin or vancocin):ti,ab,kw
#35.	(lincosamide* or clindamycin or dalacin or zindaclin):ti,ab,kw
#36.	(macrolide* or azithromycin or zithromax or zedbac or ayter or clarithromycin or clarie or klaricid or erythromycin or erythrocin or erythrolar or erythroped or erymax or primacine or tiloryth or oftalmolosa or telithromycin or ketek):ti,ab,kw
#37.	(monobactam* or aztreonam or azactam or cayston):ti,ab,kw
#38.	(nitroimidazole* or metronidazole or flagyl or vaginyl or norzol or metrolyl or tinidazole or fasigyn):ti,ab,kw
#39.	(penicillin* or piperacillin or tazobactam or tazocin or ticarcillin or clavulanic or timentin or benzylpenicillin or crystapen or phenoxymethylpenicillin or amoxicillin or amoxil or amix or amoram or amoxient or galenamox or rimoxallin or ampicillin or penbritin or rimacillin or co-fluampicil or flu-amp or magnapen or co-amoxiclav or augmentin or pivmecillinam or selexid or flucloxacillin or floxapen or flucomix or ladropen or temocillin or negaban):ti,ab,kw
#40.	(polymyxin* or colistimethate or colistin or sulfomethate or colomycin or promixin or colobreathe):ti,ab,kw
#41.	(quinolone* or ciprofloxacin or ciproxin or levofloxacin or evoxil or tavanic or moxifloxacin or avelox or nalidixic acid or norfloxacin or ofloxacin or tarivid or perfloxacin):ti,ab,kw
#42.	(sulfonamide* or co-trimoxazole or fectrim or septrin or sulfadiazine or trimethoprim or trimopan):ti,ab,kw
#43.	(tetracycline* or demeclocycline or doxycycline or vibramycin-d or efracea or lymecycline or tetralysal or minocycline or aknemin or acnamino or minocin or sebomin or oxytetracycline or oxymycin or tigecycline or tygacil):ti,ab,kw
#44.	(chloramphenicol or kemicetine or brochlor or brolene or chloromycetin or golden eye or optrex or klorafect or fosfomycin or fomicyt or fusidic acid or sodium fusidate or fucidin or daptomycin or cubicin or linezolid or zyvox or rifaximin or targaxan or xifaxanta or fidaxomicin or dificlir or tedizolid or sivextro):ti,ab,kw
#45.	(nitrofurantoin or macrobid or methenamine hippurate or hexamine hippurate or hiprex):ti,ab,kw
#46.	(triazole* or fluconazole or diflucan or itraconazole or sporanox or posaconazole or noxafil or voriconazole or vfend or omoconazole or epoxiconazole):ti,ab,kw
#47.	(imidazole* or clotrimazole or econazole or tioconazole or ketoconazole or miconazole):ti,ab,kw
#48.	(polyene* or amphotericin or fungizone or abelcet or ambisome):ti,ab,kw
#49.	(echinocandin* or anidulafungin or ecalta or caspofungin or cancidas or micafungin or mycamine):ti,ab,kw
#50.	(flucytosine or ancotil or griseofulvin or terbinafine or lamisil):ti,ab,kw
#51.	(or #2-#50)
#52.	#1 and #51
	Date parameters: see **Table 1**

PsycINFO search terms

1.	Standard population (A.2.1)
2.	Excluded study designs and publication types (A.3.1)
3.	1 not 2
4.	Limit 3 to English language
	Date parameters: see **Table 1**

G.4.9 Necrosis

Searches for the following two questions were run as one search:

- What is the most clinical and cost-effective method for managing (suspected) infected necrosis in people with acute pancreatitis?
- What is the most clinically and cost-effective timing of intervention for managing infected necrosis in people with acute pancreatitis?

Medline search terms

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	pancreatitis, acute necrotizing/
6.	5 not 22
7.	Limit 6 to English language
8.	necrosis/
9.	necro*.ti,ab.
10.	or/8-9
11.	4 and 10
12.	7 or 11
13.	surgical procedures, operative/ or minimally invasive surgical procedures/ or endoscopy/ or exp endoscopy, digestive system/ or exp laparoscopy/ or laparotomy/ or drainage/
14.	(surgery or surgical or drainage or endoscop* or laparotom* or laparoscop*).ti,ab.
15.	13 or 14
16.	exp anti-infective agents/ or superinfection/ or exp bacterial infections/
17.	exp aminoglycosides/
18.	exp beta-lactams/
19.	exp glycopeptides/
20.	exp lincosamides/
21.	exp macrolides/
22.	exp nitroimidazoles/
23.	exp polymyxins/
24.	exp quinolones/
25.	exp sulfonamides/
26.	exp trimethoprim/
27.	exp tetracyclines/
28.	exp chloramphenicol/
29.	fusidic acid/
30.	daptomycin/

31.	linezolid/
32.	exp rifamycins/
33.	nitrofurantoin/
34.	methenamine/
35.	exp triazoles/ or exp imidazoles/
36.	exp polyenes/
37.	echinocandins/
38.	flucytosine/
39.	griseofulvin/
40.	(microb* or antimicrob* or anti-microb* or antiinfect* or anti-infect* or bacter* or antibacter* or anti-bacter* or antibiot* or anti-biot* or fung* or antifung* or anti-fung* or superbug* or super-bug*).ti,ab.
41.	beta-lactam*.mp,hw.
42.	(aminoglycoside* or amikacin or amikin or gentamicin or cidomycingenticin or neomycin or sulphate or nivemycin or streptomycin or tobramycin or nebcin or tobi or podhaler or tobi or tymbrineb or bramitob or tobravisc).mp,hw.
43.	(carbapen#m* or ertapenem or invanz or imipenem or cilastatin or primaxin or meropenem or meronem).mp,hw.
44.	(cephalosporin* or cefadroxil or cefalexin or ceporex or keflex or cefradine or nicef or cefaclor or distaclor or keftid or cefuroxime or zinnat or aprokam or zinacef or cefixime or suprax or cefotaxime or ceftazidime or fortum or kefadim or ceftriaxone or rocephin or ceftaroline or fosamil or zinforo).mp,hw.
45.	(glycopeptide* or teicoplanin or targocid or telavancin or vibativ or vancomycin or vancocin).mp,hw.
46.	(lincosamide* or clindamycin or dalacin or zindaclin).mp,hw.
47.	(macrolide* or azithromycin or zithromax or zedbac or ayter or clarithromycin or clarie or klaricid or erythromycin or erythrocin or erythrolar or erythroped or erymax or primacine or tiloryth or oftalmolosa cusi eritromicina or telithromycin or ketek).mp,hw.
48.	(monobactam* or aztreonam or azactam or cayston).mp,hw.
49.	(nitroimidazole* or metronidazole or flagyl or vaginyl or norzol or metrolyl or tinidazole or fasigyn).mp,hw.
50.	(penicillin* or piperacillin or tazobactam or tazocin or ticarcillin or clavulanic acid or timentin or benzylpenicillin or crystapen or phenoxymethylpenicillin or amoxicillin or amoxil or amix or amoram or amoxient or galenamox or rimoxallin or ampicillin or penbritin or rimacillin or co-fluampicil or flu-amp or magnapen or co-amoxiclav or augmentin or pivmecillinam or selexid or flucloxacillin or floxapen or flucomix or ladropen or temocillin or negaban).mp,hw.
51.	(polymyxin* or colistimethate or colistin or sulfomethate or colomycin or promixin or colobreathe).mp,hw.
52.	(quinolone* or ciprofloxacin or ciproxin or levofloxacin or evoxil or tavanic or moxifloxacin or avelox or nalidixic acid or norfloxacin or ofloxacin or tarivid or perfloxacin).mp,hw.
53.	(sulfonamide* or co-trimoxazole or fectrim or septrin or sulfadiazine or trimethoprim or trimopan).mp,hw.
54.	(tetracycline* or demeclocycline or doxycycline or vibramycin-d or efracea or lymecycline or tetralysal or minocycline or aknemin or acnamino or minocin or sebomin or oxytetracycline or oxymycin or tigecycline or tygacil).mp,hw.
55.	(chloramphenicol or kemicetine or brochlor or brolene or chloromycetin or golden eye or optrex or klorafect or fosfomycin or fomicyt or fusidic acid or sodium fusidate or fucidin or daptomycin or cubicin or linezolid or zyvox or rifaximin or targaxan or xifaxanta or fidaxomicin or dificlir or tedizolid or sivextro).mp,hw.
56.	(nitrofurantoin or macrobid or methenamine hippurate or hexamine hippurate or hiprex).mp,hw.

57.	(triazole* or fluconazole or diflucan or itraconazole or sporanox or posaconazole or noxafil or voriconazole or vfend or omoconazole or epoxiconazole).mp,hw.
58.	(imidazole* or clotrimazole or econazole or tioconazole or ketoconazole or miconazole).mp,hw.
59.	(polyene* or amphotericin or fungizone or abelcet or ambisome).mp,hw.
60.	(echinocandin* or anidulafungin or ecalta or caspofungin or cancidas or micafungin or mycamine).mp,hw.
61.	(flucytosine or ancotil or griseofulvin or terbinafine or lamisil).mp,hw.
62.	or/16-61
63.	15 or 62
64.	Study filters RCT (G.3.2) or SR (G.3.3) or OBS (G.3.7)
65.	12 and 63 and 64
	Date parameters: see **Table 1**

1 **Embase search terms**

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	acute hemorrhagic pancreatitis/
6.	5 not 2
7.	Limit 6 to English language
8.	necrosis/
9.	necro*.ti,ab.
10.	or/8-9
11.	4 and 10
12.	7 or 11
13.	*surgery/
14.	minimally invasive surgery/
15.	endoscopy/
16.	exp digestive tract endoscopy/
17.	exp laparoscopy/
18.	laparotomy/
19.	exp surgical drainage/
20.	(surgery or surgical or drainage or endoscop* or laparotom* or laparoscop*).ti,ab.
21.	or/13-20
22.	exp antiinfective agent/
23.	exp bacterial infection/ or exp superinfection/
24.	exp *aminoglycoside antibiotic agent/
25.	*amikacin/ or *gentamicin/ or *neomycin/ or *streptomycin/ or *tobramycin/
26.	exp *beta lactam antibiotic/
27.	*carbapenem derivative/ or *carbapenem/ or *ertapenem/ or *cilastatin with imipenem/ or *imipenem/ or *meropenem/
28.	exp *cephalosporin derivative/ or exp *cephalosporin/
29.	*cefadroxil/ or *cefalexin/ or *cefradine/ or *cefaclor/ or *cefuroxime/ or *cefixime/ or *cefotaxime/ or *ceftazidime/ or *ceftriaxone/ or *ceftaroline fosamil/
30.	*glycopeptide/

31.	*teicoplanin/ or *telavancin/ or *vancomycin/
32.	*lincosamide/
33.	*clindamycin/
34.	exp *macrolide/
35.	*azithromycin/ or *clarithromycin/ or *erythromycin/ or *telithromycin/
36.	exp *monobactam derivative/
37.	*aztreonam/
38.	exp *nitroimidazole derivative/ or exp *nitroimidazole/
39.	*metronidazole/ or *tinidazole/
40.	exp *penicillin derivative/
41.	*piperacillin plus tazobactam/ or *ticarcillin/ or *clavulanic acid/ or *penicillin g/ or *penicillin v/ or *amoxicillin/ or *ampicillin/ or *ampicillin plus flucloxacillin/ or *amoxicillin plus clavulanic acid/ or *pivmecillinam/ or *flucloxacillin/
42.	*polymyxin/
43.	*colistin/ or *colistimethate/
44.	exp *quinolone derivative/ or exp *quinolone/
45.	*ciprofloxacin/ or *levofloxacin/ or *moxifloxacin/ or *nalidixic acid/ or *norfloxacin/ or *ofloxacin/ or *perfloxacin/
46.	exp *sulfonamide/ or exp *trimethoprim/ or exp *trimethoprim derivative/
47.	*cotrimoxazole/ or *sulfadiazine/
48.	exp *tetracycline derivative/ or exp *tetracycline/
49.	*demeclocycline/ or *doxycycline/ or *lymecycline/ or *minocycline/ or *oxytetracycline/ or *tigecycline/
50.	*chloramphenicol derivative/ or *chloramphenicol/
51.	*fosfomycin/
52.	*fusidic acid/
53.	*daptomycin/
54.	*linezolid/
55.	*rifaximin/
56.	*fidaxomicin/
57.	*tedizolid/
58.	exp *triazole derivative/
59.	*fluconazole/ or *itraconazole/ or *posaconazole/ or *voriconazole/ or *omoconazole/ or *epoxiconazole/
60.	exp *imidazole derivative/
61.	*clotrimazole/ or *econazole/ or *tioconazole/ or *ketoconazole/ or *miconazole/
62.	exp *polyene antibiotic agent/
63.	*amphotericin/
64.	exp *echinocandin/
65.	*anidulafungin/ or *caspofungin/ or *micafungin/
66.	*flucytosine/ or *griseofulvin/ or *terbinafine/
67.	(microb* or antimicrob* or anti-microb* or antiinfect* or anti-infect* or bacter* or antibacter* or anti-bacter* or antibiot* or anti-biot* or fung* or antifung* or anti-fung* or superbug* or super-bug*).ti,ab.
68.	beta-lactam*.mp,hw.
69.	(aminoglycoside* or amikacin or amikin or gentamicin or cidomycingenticin or neomycin or sulphate or nivemycin or streptomycin or tobramycin or nebcin or tobi or podhaler or tobi or

	tymbrineb or bramitob or tobravisc).mp,hw.
70.	(carbapen#m* or ertapenem or invanz or imipenem or cilastatin or primaxin or meropenem or meronem).mp,hw.
71.	(cephalosporin* or cefadroxil or cefalexin or ceporex or keflex or cefradine or nicef or cefaclor or distaclor or keftid or cefuroxime or zinnat or aprokam or zinacef or cefixime or suprax or cefotaxime or ceftazidime or fortum or kefadim or ceftriaxone or rocephin or ceftaroline or fosamil or zinforo).mp,hw.
72.	(glycopeptide* or teicoplanin or targocid or telavancin or vibativ or vancomycin or vancocin).mp,hw.
73.	(lincosamide* or clindamycin or dalacin or zindaclin).mp,hw.
74.	(macrolide* or azithromycin or zithromax or zedbac or ayter or clarithromycin or clarie or klaricid or erythromycin or erythrocin or erythrolar or erythroped or erymax or primacine or tiloryth or oftalmolosa cusi eritromicina or telithromycin or ketek).mp,hw.
75.	(monobactam* or aztreonam or azactam or cayston).mp,hw.
76.	(nitroimidazole* or metronidazole or flagyl or vaginyl or norzol or metrolyl or tinidazole or fasigyn).mp,hw.
77.	(penicillin* or piperacillin or tazobactam or tazocin or ticarcillin or clavulanic or timentin or benzylpenicillin or crystapen or phenoxymethylpenicillin or amoxicillin or amoxil or amix or amoram or amoxient or galenamox or rimoxallin or ampicillin or penbritin or rimacillin or co-fluampicil or flu-amp or magnapen or co-amoxiclav or augmentin or pivmecillinam or selexid or flucloxacillin or floxapen or flucomix or ladropen or temocillin or negaban).mp,hw.
78.	(polymyxin* or colistimethate or colistin or sulfomethate or colomycin or promixin or colobreathe).mp,hw.
79.	(quinolone* or ciprofloxacin or ciproxin or levofloxacin or evoxil or tavanic or moxifloxacin or avelox or nalidixic acid or norfloxacin or ofloxacin or tarivid or perfloxacin).mp,hw.
80.	(sulfonamide* or co-trimoxazole or cotrimoxazole or fectrim or septrin or sulfadiazine or trimethoprim or trimopan).mp,hw.
81.	(tetracycline* or demeclocycline or doxycycline or vibramycin-d or efracea or lymecycline or tetralysal or minocycline or aknemin or acnamino or minocin or sebomin or oxytetracycline or oxymycin or tigecycline or tygacil).mp,hw.
82.	(chloramphenicol or kemicetine or brochlor or brolene or chloromycetin or golden eye or optrex or klorafect or fosfomycin or fomicyt or fusidic acid or sodium fusidate or fucidin or daptomycin or cubicin or linezolid or zyvox or rifaximin or targaxan or xifaxanta or fidaxomicin or dificlir or tedizolid or sivextro).mp,hw.
83.	(nitrofurantoin or macrobid or methenamine hippurate or hexamine hippurate or hiprex).mp,hw.
84.	(triazole* or fluconazole or diflucan or itraconazole or sporanox or posaconazole or noxafil or voriconazole or vfend or omoconazole or epoxiconazole).mp,hw.
85.	(imidazole* or clotrimazole or econazole or tioconazole or ketoconazole or miconazole).mp,hw.
86.	(polyene* or amphotericin or fungizone or abelcet or ambisome).mp,hw.
87.	(echinocandin* or anidulafungin or ecalta or caspofungin or cancidas or micafungin or mycamine).mp,hw.
88.	(flucytosine or ancotil or griseofulvin or terbinafine or lamisil).mp,hw.
89.	or/22-88
90.	21 or 89
91.	Study filters RCT (G.3.2) or SR (G.3.3) or OBS (G.3.7)
92.	4 and 90 and 91
	Date parameters: see **Table 1**

Cochrane search terms

#1.	Standard population (G.2.1)
#2.	MeSH descriptor: (pancreatitis, acute necrotizing) explode all trees
#3.	MeSH descriptor: (necrosis) explode all trees
#4.	necro*:ti,ab
#5.	#3 or #4
#6.	#1 and #6
#7.	#2 or #6
#8.	MeSH descriptor: (surgical procedures, operative) explode all trees
#9.	MeSH descriptor: (minimally invasive surgical procedures) explode all trees
#10.	MeSH descriptor: (endoscopy) explode all trees
#11.	MeSH descriptor: (endoscopy, digestive system) explode all trees
#12.	MeSH descriptor: (laparoscopy) explode all trees
#13.	MeSH descriptor: (laparotomy) explode all trees
#14.	MeSH descriptor: (drainage) explode all trees
#15.	(surgery or surgical or drainage or endoscop* or laparotom* or laparoscop*):ti,ab
#16.	#8 or #9 or #10 or #11 or #12 or #13 or #14 or #15
#17.	MeSH descriptor: (anti-infective agents) explode all trees
#18.	MeSH descriptor: (superinfection) explode all trees
#19.	MeSH descriptor: (bacterial infections) explode all trees
#20.	MeSH descriptor: (aminoglycosides) explode all trees
#21.	MeSH descriptor: (beta-lactams) explode all trees
#22.	MeSH descriptor: (glycopeptides) explode all trees
#23.	MeSH descriptor: (lincosamides) explode all trees
#24.	MeSH descriptor: (macrolides) explode all trees
#25.	MeSH descriptor: (nitroimidazoles) explode all trees
#26.	MeSH descriptor: (polymyxins) explode all trees
#27.	MeSH descriptor: (quinolones) explode all trees
#28.	MeSH descriptor: (sulfonamides) explode all trees
#29.	MeSH descriptor: (trimethoprim) explode all trees
#30.	MeSH descriptor: (tetracyclines) explode all trees
#31.	MeSH descriptor: (chloramphenicol) explode all trees
#32.	MeSH descriptor: (fusidic acid) explode all trees
#33.	MeSH descriptor: (daptomycin) explode all trees
#34.	MeSH descriptor: (linezolid) explode all trees
#35.	MeSH descriptor: (rifamycins) explode all trees
#36.	MeSH descriptor: (nitrofurantoin) explode all trees
#37.	MeSH descriptor: (methenamine) explode all trees
#38.	MeSH descriptor: (azoles) explode all trees
#39.	MeSH descriptor: (polyenes) explode all trees
#40.	MeSH descriptor: (echinocandins) explode all trees
#41.	MeSH descriptor: (flucytosine) explode all trees
#42.	MeSH descriptor: (fosfomycin) explode all trees
#43.	MeSH descriptor: (griseofulvin) explode all trees
#44.	(microb* or antimicrob* or anti-microb* or (anti next microb*) or antiinfect* or anti-infect* or (anti next infect*) or bacter* or antibacter* or anti-bacter* or (anti next bacter*) or antibiot*

	or anti-biot* or (anti next biot*) or fung* or antifung* or anti-fung* or (anti next fung*) or superbug* or super-bug* or (super next bug*)):ti,ab,kw
#45.	(beta-lactam* or (beta next lactam*)):ti,ab,kw
#46.	(aminoglycoside* or amikacin or amikin or gentamicin or cidomycingenticin or neomycin or sulphate or nivemycin or streptomycin or tobramycin or nebcin or tobi or podhaler or tobi or tymbrineb or bramitob or tobravisc):ti,ab,kw
#47.	(carbapenem* or carbepenam* or ertapenem or invanz or imipenem or cilastatin or primaxin or meropenem or meronem):ti,ab,kw
#48.	(cephalosporin* or cefadroxil or cefalexin or ceporex or keflex or cefradine or nicef or cefaclor or distaclor or keftid or cefuroxime or zinnat or aprokam or zinacef or cefixime or suprax or cefotaxime or ceftazidime or fortum or kefadim or ceftriaxone or rocephin or ceftaroline or fosamil or zinforo):ti,ab,kw
#49.	(glycopeptide* or teicoplanin or targocid or telavancin or vibativ or vancomycin or vancocin):ti,ab,kw
#50.	(lincosamide* or clindamycin or dalacin or zindaclin):ti,ab,kw
#51.	(macrolide* or azithromycin or zithromax or zedbac or ayter or clarithromycin or clarie or klaricid or erythromycin or erythrocin or erythrolar or erythroped or erymax or primacine or tiloryth or oftalmolosa or telithromycin or ketek):ti,ab,kw
#52.	(monobactam* or aztreonam or azactam or cayston):ti,ab,kw
#53.	(nitroimidazole* or metronidazole or flagyl or vaginyl or norzol or metrolyl or tinidazole or fasigyn):ti,ab,kw
#54.	(penicillin* or piperacillin or tazobactam or tazocin or ticarcillin or clavulanic or timentin or benzylpenicillin or crystapen or phenoxymethylpenicillin or amoxicillin or amoxil or amix or amoram or amoxient or galenamox or rimoxallin or ampicillin or penbritin or rimacillin or co-fluampicil or flu-amp or magnapen or co-amoxiclav or augmentin or pivmecillinam or selexid or flucloxacillin or floxapen or flucomix or ladropen or temocillin or negaban):ti,ab,kw
#55.	(polymyxin* or colistimethate or colistin or sulfomethate or colomycin or promixin or colobreathe):ti,ab,kw
#56.	(quinolone* or ciprofloxacin or ciproxin or levofloxacin or evoxil or tavanic or moxifloxacin or avelox or nalidixic acid or norfloxacin or ofloxacin or tarivid or perfloxacin):ti,ab,kw
#57.	(sulfonamide* or co-trimoxazole or fectrim or septrin or sulfadiazine or trimethoprim or trimopan):ti,ab,kw
#58.	(tetracycline* or demeclocycline or doxycycline or vibramycin-d or efracea or lymecycline or tetralysal or minocycline or aknemin or acnamino or minocin or sebomin or oxytetracycline or oxymycin or tigecycline or tygacil):ti,ab,kw
#59.	(chloramphenicol or kemicetine or brochlor or brolene or chloromycetin or golden eye or optrex or klorafect or fosfomycin or fomicyt or fusidic acid or sodium fusidate or fucidin or daptomycin or cubicin or linezolid or zyvox or rifaximin or targaxan or xifaxanta or fidaxomicin or dificlir or tedizolid or sivextro):ti,ab,kw
#60.	(nitrofurantoin or macrobid or methenamine hippurate or hexamine hippurate or hiprex):ti,ab,kw
#61.	(triazole* or fluconazole or diflucan or itraconazole or sporanox or posaconazole or noxafil or voriconazole or vfend or omoconazole or epoxiconazole):ti,ab,kw
#62.	(imidazole* or clotrimazole or econazole or tioconazole or ketoconazole or miconazole):ti,ab,kw
#63.	(polyene* or amphotericin or fungizone or abelcet or ambisome):ti,ab,kw
#64.	(echinocandin* or anidulafungin or ecalta or caspofungin or cancidas or micafungin or mycamine):ti,ab,kw
#65.	(flucytosine or ancotil or griseofulvin or terbinafine or lamisil):ti,ab,kw
#66.	(or #17-#65)
#67.	#16 or #66

#68.	#7 and #67
	Date parameters: see **Table 1**

PsycINFO search terms

1.	Standard population (A.2.1)
2.	Excluded study designs and publication types (A.3.1)
3.	1 not 2
4.	Limit 3 to English language
	Date parameters: see **Table 1**

G.4.10 Pain management

Searches for the following four questions were run as one search:

- What is the most clinically and cost-effective intervention for managing pain in people with chronic pancreatitis?
- What is the most clinically and cost-effective intervention for managing pancreatic duct obstruction, with or without an inflammatory mass, in people with chronic pancreatitis presenting with pain?
- What is the most clinically and cost-effective intervention for managing pseudocysts in people with pancreatitis presenting with or without pain?
- What is the most clinically and cost-effective intervention for managing small-duct disease (in the absence of pancreatic duct obstruction, inflammatory mass or pseudocyst) in people with chronic pancreatitis presenting with pain?

Medline search terms

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	exp narcotics/
6.	(opioid* or opiate* or narcotic*).ti,ab.
7.	morphine/
8.	(morphine or astramorph or avinza or depodur or duramorph or embeda or infumorph or kadian or m-eslon or morcap or morphia or ms contin or msir or mst or nepenthe or oramorph or rescudose or rms or roxanol or sevredol or statex or zomorph).ti,ab.
9.	opium/
10.	(opium or omnopon or pantopon or papaveretum).ti,ab.
11.	hydromorphone/
12.	(hydromorphone or dihydromorphinone or dilaudid or dimorphone or exalgo or hydmrphn or hydromorph* or hydrostat or hymorphan or laudicon or novolauden or palladone).ti,ab.
13.	nicomorphine.ti,ab.
14.	exp oxycodone/
15.	(oxycodone or dazidox or dihydrohydroxycodeinone or dihydrone or dinarkon or endocodone or eth-oxydose or eucodal or hydroxycodeinon or m-oxy or oxiconum or oxycdn or oxycone or oxycontin or oxyfast or oxyir or pancodine or percocet or percolone or remoxy or roxicodone or theocodin).ti,ab.
16.	(dihydrocodeine or contugesic or dhc mundipharma or dicodin or dihydcdn or paracodin or paramol or parzone or rikodeine or tiamon or tosidrin or tuscodin).ti,ab.
17.	(diamorphine or acetomorphine or diacetylmorphine or diagesil or diamorf or heroin or min-i-

	jet morphine sulfate or skag).ti,ab.
18.	exp codeine/
19.	(codeine or ardinex or galcodine or isocodeine or methyl morphine or rx 336m or stanley-linctus or stanley-syrup).ti,ab.
20.	ketobemidone.ti,ab.
21.	exp meperidine/
22.	(pethidine or demerol or dolantin or dolargan or dolcontral or dolosal or dolsin or isonipecain or isonipecaine hydrochloride or lydol or meperidine or operidine epj or pethilorfan).ti,ab.
23.	exp fentanyl/
24.	(fentanyl or abstral or actiq or duragesic or fentanest or fentora or fentyl or ionsys or matrifen or nasalfent or onsolis or oralet or phentanyl or sublimaze).ti,ab.
25.	exp dextromoramide/
26.	dextromoramide.ti,ab.
27.	(piritramide or dipidolor or dipydolor or piridolan or pirium).ti,ab.
28.	exp dextropropoxyphene/
29.	(dextropropoxyphene or darvon or dolene or doloxene or levopropoxyphene or pp-cap or propoxyphene or proxyphen).ti,ab.
30.	(bezitramide or burgodin).ti,ab.
31.	exp methadone/
32.	(methadone or adanon or althose or amidines or amidone or biodone or diskets or dolophine or heptadon or metadol or metasedin or methaddict or metharose or methadose or methdn or methex or phy or phymet or physeptone or pinadone or symoron).ti,ab.
33.	exp benzomorphans/
34.	exp pentazocine/
35.	(pentazocine or fortral or fortwin or lexir or talacen or talwin).ti,ab.
36.	exp phenazocine/
37.	(phenazocine or prinadol or narphen).ti,ab.
38.	oripavine.ti,ab.
39.	exp buprenorphine/
40.	(buprenorphine or '6029-m' or buprenex or buprex or prefin or suboxone or subutex or temgesic).ti,ab.
41.	exp etorphine/
42.	(etorphine or immobilon or m99).ti,ab.
43.	exp morphinans/
44.	exp butorphanol/
45.	(butorphanol or 'bc2627' or beforal or dolorex or moradol or stadol or torbugesic).ti,ab.
46.	exp tilidine/
47.	(tilidine or tilidate or valoron or valtran or tilidin).ti,ab.
48.	exp tramadol/
49.	(tramadol or 'k-315' or ralivia or ryzolt or tramahexal or tramake insts or tramal* or tramedo or ultram or zamadol or zydol).ti,ab.
50.	(dezocine or dalgan or 'wy-16225').ti,ab.
51.	exp meptazinol/
52.	(meptazinol or meptid).ti,ab.
53.	(tapentadol or cg5503 or nucynta).ti,ab.
54.	(remifentanil or 'gi 87084b' or remifentanyl or ultiva).ti,ab.
55.	exp procaine/

56.	(procaine or allocaine or anuject or gerokit or mericaine or novocaine or procaina serra).ti,ab.
57.	alfentanil.ti,ab.
58.	(alfenta or alfentanyl or fanaxal or limifen or rapifen).ti,ab.
59.	(dipipanone or co-dydramol or co-codamaol).ti,ab.
60.	analgesics/ or analgesics, non-narcotic/
61.	(non-steroid* or non-narcotic* or analgesic* or pharmacolog*).ti,ab.
62.	somatostatin/
63.	octreotide/
64.	(somatostatin* or octreotide or sandostatin or lanreotide or somatuline).ti,ab.
65.	acetaminophen/
66.	(aspirin or acetaminophen or paracetamol or panadol or perfalgan or nefopam or acupan).ti,ab.
67.	anti-inflammatory agents, non-steroidal/ or aspirin/ or diclofenac/ or flurbiprofen/ or ibuprofen/ or ketoprofen/ or ketorolac/ or ketorolac tromethamine/ or meclofenamic acid/ or mefenamic acid/ or naproxen/ or phenylbutazone/ or piroxicam/ or sulindac/
68.	ziconotide.ti,ab.
69.	(nsaid* or ibuprofen or aspirin or naproxen or fenoprofen or flurbiprofen or ketoprofen or dexketoprofen or dexibuprofen or tiaprofenic acid or diclofenac or aceclofenac or indometacin or mefenamic acid or meloxicam or nabumetone or phenylbutazone or piroxicam or sulindac or tenoxicam or tolfenamic acid or ketorolac or celecoxib or etoricoxib or aceclofenac or acemetacin or diclofenac or etodolac).ti,ab.
70.	nerve block/
71.	((nerve or percutaneous or splanchnic or subarachnoid or celiac or coeliac* or solar) adj1 block*).ti,ab.
72.	((celiac or coeliac* or solar) adj1 plexus).ti,ab.
73.	celiac plexus/
74.	splanchnic nerves/
75.	spinal cord stimulation/
76.	((spinal cord* or dorsal column) adj2 stimulation*).ti,ab.
77.	splanchnicectom*.ti,ab.
78.	neurolysis/
79.	(neurolys* or neurolytic*).ti,ab.
80.	cholangiopancreatography, endoscopic retrograde/
81.	(endoscopic retrograde cholangiopancreatograph* or ercp).ti,ab.
82.	endoscopy, gastrointestinal/ or endoscopy, digestive system/
83.	(balloon adj dilatation*).ti,ab.
84.	dilatation/
85.	stents/ or self expandable metallic stents/
86.	(stent* or endoprosthes* or wallstent*).ti,ab.
87.	sphincterotomy, endoscopic/
88.	sphincterotom*.ti,ab.
89.	drainage/
90.	lithotripsy/
91.	(extracorporeal shock wave lithotrips* or eswl).ti,ab.
92.	(stone adj (extract* or remov*)).ti,ab.
93.	(endoscop* or endotherap* or minimally invasive).ti,ab.
94.	endoscopy/

95.	(pancreaticojejunostom* or pancreatico-jejunostom* or puestow).ti,ab.
96.	anastomosis, roux-en-y/ or pancreaticojejunostomy/
97.	roux-en-y.ti,ab.
98.	anastomos*.ti,ab.
99.	frey*.ti,ab.
100.	(partington adj rochelle).ti,ab.
101.	beger.ti,ab.
102.	pancreaticoduodenectomy/
103.	(pancreaticoduodenectom* or pancreatico-duodenectom* or pancreatoduodenectom* or pancreato-duodenectom*or whipple).ti,ab.
104.	surgical procedures, operative/
105.	pancreatectomy/
106.	(pancreatectom* or resect* or operat* or drain* or denervat* or decompress* or surg*).ti,ab.
107.	decompression, surgical/
108.	(cystogastrostom* or cysto gastrostom* or cyst-gastrostom*).ti,ab.
109.	(cystojejunostom* or cysto jejunostom* or cyst-jejunostom*).ti,ab.
110.	(cystoduodenostom* or cysto duodenostom* or cyst-duodenostom*).ti,ab.
111.	(pseudocystogastrostom* or pseudo cystogastrostom* or pseudocyst-gastrostom*).ti,ab.
112.	(pseudocystojejunostom* or pseudo cystojejunostom* or pseudocyst-jejunostom*).ti,ab.
113.	(pseudocystoduodenostom* or pseudo cystoduodenostom* or pseudocyst-duodenostom*).ti,ab.
114.	(hepatico-jejunostom* or hepaticojejunostom* or hepatojejunostom* or hepato-jejunostom* or hepat* jejunostom*).ti,ab.
115.	(pylorus preserving pancreatoduodectom* or pppd).ti,ab.
116.	v-shaped excision.ti,ab.
117.	sphincteroplast*.ti,ab.
118.	exp psychotherapy/
119.	biofeedback, psychology/
120.	(behavio?r* adj therap*).ti,ab.
121.	(cognitive adj2 therap*).ti,ab.
122.	(relax* adj2 (therap* or technique*)).ti,ab.
123.	(meditat* or psychotherap*).ti,ab.
124.	(psychological adj (treatment* or therap*)).ti,ab.
125.	(group* adj therap*).ti,ab.
126.	(self-regulat* adj train*).ti,ab.
127.	(coping adj skill*).ti,ab.
128.	(pain-related adj thought*).ti,ab.
129.	(behavio?r* adj2 rehabilitat*).ti,ab.
130.	((psychoeducation or psycho-education) adj1 group*).ti,ab.
131.	exp mind-body therapies/
132.	((mind and body) adj (relaxation or therap*)).ti,ab.
133.	enzyme replacement therapy/
134.	exp pancreatic extracts/
135.	exp enzymes/tu (therapeutic use)
136.	(digest* adj2 enzyme*).ti,ab.
137.	(enzyme adj2 (replacement or therap*)).ti,ab.

138.	ert.ti,ab.
139.	(creon or nutrizym or pancrease or pancrex or pankreon or viokase).ti,ab.
140.	(pancreatin or pancrelipase).ti,ab.
141.	exp antioxidants/
142.	beta carotene/ or curcumin/ or methionine/ or allopurinol/ or glutathione/ or sodium selenite/ or acetylcysteine/ or flavonoids/ or riboflavin/ or zinc/ or magnesium/
143.	exp oxidation-reduction/
144.	exp free radical scavengers/
145.	(antioxidant* or anti-oxidant* or micronutrient* or micro-nutrient*).ti,ab.
146.	(ascorbic acid or bilirubin or butylated hydroxyanisole or butylated hydroxytoluene or butylcresol or canthaxanthin or canthaxanthine or carotenoid* or catalase or ergothioneine or thioneine or grape seed extract or melatonin or nordihydroguaiaretic acid or masoprocol or probucol or superlipid or propyl gallate or pyrogallol or pyrogallic acid or gallic acid or quercetin or dikvertin or selenium or silymarin or milk thistle or silimarin or thioctic acid or lipoic acid or tocopherol* or tocotrienol* or uric acid or trioxopurine or urate or vitamin e or vitamin c or vitamin a or retinol or carotene* or curcumin or methionine or allopurin* or glutathione or sodium selenite or acetylcysteine or zinc or magnesium or riboflavin or flavone* or flavonoid*).ti,ab.
147.	(free radical adj2 scaveng*).ti,ab.
148.	(reduct* adj2 oxidat*).ti,ab.
149.	or/5-148
150.	Study filters RCT (A.3.2) or SR (A.3.3) or OBS (A.7)
151.	4 and 149 and 150
	Date parameters: see **Table 1**

1 **Embase search terms**

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	exp *narcotic agent/
6.	(opioid* or opiate* or narcotic*).ti,ab.
7.	(morphine or astramorph or avinza or depodur or duramorph or embeda or infumorph or kadian or m-eslon or morcap or morphia or ms contin or msir or mst or nepenthe or oramorph or rescudose or rms or roxanol or sevredol or statex or zomorph).ti,ab.
8.	*opiate/
9.	(opium or omnopon or pantopon or papaveretum).ti,ab.
10.	(hydromorphone or dihydromorphinone or dilaudid or dimorphone or exalgo or hydmrphn or hydromorph* or hydrostat or hymorphan or laudicon or novolauden or palladone).ti,ab.
11.	nicomorphine.ti,ab.
12.	(oxycodone or dazidox or dihydrohydroxycodeinone or dihydrone or dinarkon or endocodone or eth-oxydose or eucodal or hydroxycodeinon or m-oxy or oxiconum or oxycdn or oxycone or oxycontin or oxyfast or oxyir or pancodine or percocet or percolone or remoxy or roxicodone or theocodin).ti,ab.
13.	(dihydrocodeine or contugesic or dhc mundipharma or dicodin or dihydcdn or paracodin or paramol or parzone or rikodeine or tiamon or tosidrin or tuscodin).ti,ab.
14.	(diamorphine or acetomorphine or diacetylmorphine or diagesil or diamorf or heroin or min-i-jet morphine sulfate or skag).ti,ab.
15.	(codeine or ardinex or galcodine or isocodeine or methyl morphine or rx 336m or stanley-

	linctus or stanley-syrup).ti,ab.
16.	ketobemidone.ti,ab.
17.	(pethidine or demerol or dolantin or dolargan or dolcontral or dolosal or dolsin or isonipecain or isonipecaine hydrochloride or lydol or meperidine or operidine epj or pethilorfan).ti,ab.
18.	(fentanyl or abstral or actiq or duragesic or fentanest or fentora or fentyl or ionsys or matrifen or nasalfent or onsolis or oralet or phentanyl or sublimaze).ti,ab.
19.	dextromoramide.ti,ab.
20.	(piritramide or dipidolor or dipydolor or piridolan or pirium).ti,ab.
21.	(dextropropoxyphene or darvon or dolene or doloxene or levopropoxyphene or pp-cap or propoxyphene or proxyphen).ti,ab.
22.	(bezitramide or burgodin).ti,ab.
23.	(methadone or adanon or althose or amidines or amidone or biodone or diskets or dolophine or heptadon or metadol or metasedin or methaddict or metharose or methadose or methdn or methex or phy or phymet or physeptone or pinadone or symoron).ti,ab.
24.	exp *benzomorphan derivative/
25.	exp *pentazocine lactate/ or exp *pentazocine/ or exp *paracetamol plus pentazocine/ or exp *naloxone plus pentazocine/
26.	(pentazocine or fortral or fortwin or lexir or talacen or talwin).ti,ab.
27.	exp *phenazocine/
28.	(phenazocine or prinadol or narphen).ti,ab.
29.	oripavine.ti,ab.
30.	(buprenorphine or '6029-m' or buprenex or buprex or prefin or suboxone or subutex or temgesic).ti,ab.
31.	(etorphine or immobilon or m99).ti,ab.
32.	exp *morphinan derivative/
33.	exp *butorphanol tartrate/ or exp *butorphanol/
34.	(butorphanol or 'bc2627' or beforal or dolorex or moradol or stadol or torbugesic).ti,ab.
35.	(tilidine or tilidate or valoron or valtran or tilidin).ti,ab.
36.	exp *tramadol/ or exp *paracetamol plus tramadol/
37.	(tramadol or 'k-315' or ralivia or ryzolt or tramahexal or tramake insts or tramal* or tramedo or ultram or zamadol or zydol).ti,ab.
38.	(dezocine or dalgan or 'wy-16225').ti,ab.
39.	exp *meptazinol/
40.	(meptazinol or meptid).ti,ab.
41.	(tapentadol or cg5503 or nucynta).ti,ab.
42.	(remifentanil or 'gi 87084b' or remifentanyl or ultiva).ti,ab.
43.	exp *penicillin g sodium plus procaine penicillin/ or exp *procaine/ or exp *adrenalin plus procaine/ or exp *penicillin g sodium plus procaine penicillin plus streptomycin sulfate/ or exp *penicillin g potassium plus procaine penicillin plus streptomycin sulfate/ or exp *procaine penicillin/ or exp *penicillin g potassium plus procaine penicillin/ or exp *benzathine penicillin plus procaine penicillin/ or exp *procaine penicillin plus streptomycin sulfate/
44.	(procaine or allocaine or anuject or gerokit or mericaine or novocaine or procaina serra).ti,ab.
45.	exp *cocodamol/
46.	alfentanil.ti,ab.
47.	(alfenta or alfentanyl or fanaxal or limifen or rapifen).ti,ab.
48.	(dipipanone or co-dydramol or co-codamaol).ti,ab.
49.	exp *paracetamol/ or exp *nonsteroid antiinflammatory agent/ or exp *analgesic agent/
50.	(non-steroid* or non-narcotic* or analgesic* or pharmacolog*).ti,ab.

51.	exp *somatostatin/
52.	exp *octreotide/
53.	(somatostatin* or octreotide or sandostatin or lanreotide or somatuline).ti,ab.
54.	(aspirin or acetaminophen or paracetamol or panadol or perfalgan or nefopam or acupan).ti,ab.
55.	ziconotide.ti,ab.
56.	(nsaid* or ibuprofen or aspirin or naproxen or fenoprofen or flurbiprofen or ketoprofen or dexketoprofen or dexibuprofen or tiaprofenic acid or diclofenac or aceclofenac or indometacin or mefenamic acid or meloxicam or nabumetone or phenylbutazone or piroxicam or sulindac or tenoxicam or tolfenamic acid or ketorolac or celecoxib or etoricoxib or aceclofenac or acemetacin or diclofenac or etodolac).ti,ab.
57.	exp nerve block/
58.	celiac plexus/
59.	splanchnic nerve/
60.	spinal cord stimulation/
61.	neurolysis/
62.	((nerve or percutaneous or splanchnic or subarachnoid or celiac or coeliac* or solar) adj1 block*).ti,ab.
63.	((celiac or coeliac* or solar) adj1 plexus).ti,ab.
64.	((spinal cord* or dorsal column) adj2 stimulation*).ti,ab.
65.	splanchnicectom*.ti,ab.
66.	(neurolys* or neurolytic*).ti,ab.
67.	endoscopic retrograde cholangiopancreatography/
68.	(endoscopic retrograde cholangiopancreatograph* or ercp).ti,ab.
69.	digestive tract endoscopy/ or gastrointestinal endoscopy/
70.	(balloon adj dilatation*).ti,ab.
71.	dilatation/
72.	stent/
73.	self expandable metallic stent/
74.	(stent* or endoprosthes* or wallstent*).ti,ab.
75.	endoscopic sphincterotomy/
76.	sphincterotom*.ti,ab.
77.	exp surgical drainage/
78.	exp lithotripsy/
79.	(extracorporeal shock wave lithotrips* or eswl).ti,ab.
80.	(stone adj (extract* or remov*)).ti,ab.
81.	(endoscop* or endotherap* or minimally invasive).ti,ab.
82.	endoscopy/
83.	(pancreaticojejunostom* or pancreatico-jejunostom* or puestow).ti,ab.
84.	pancreas surgery/ or pancreaticojejunostomy/
85.	roux y anastomosis/
86.	roux-en-y.ti,ab.
87.	anastomos*.ti,ab.
88.	frey*.ti,ab.
89.	(partington adj rochelle).ti,ab.
90.	beger.ti,ab.

91.	pancreaticoduodenectomy/
92.	(pancreaticoduodenectom* or pancreatico-duodenectom* or pancreatoduodenectom* or pancreato-duodenectom*or whipple).ti,ab.
93.	surgical technique/
94.	pancreas resection/
95.	(pancreatectom* or resect* or operat* or drain* or denervat* or decompress* or surg*).ti,ab.
96.	decompression surgery/
97.	(cystogastrostom* or cysto gastrostom* or cyst-gastrostom*).ti,ab.
98.	(cystojejunostom* or cysto jejunostom* or cyst-jejunostom*).ti,ab.
99.	(cystoduodenostom* or cysto duodenostom* or cyst-duodenostom*).ti,ab.
100.	(pseudocystogastrostom* or pseudo cystogastrostom* or pseudocyst-gastrostom*).ti,ab.
101.	(pseudocystojejunostom* or pseudo cystojejunostom* or pseudocyst-jejunostom*).ti,ab.
102.	(pseudocystoduodenostom* or pseudo cystoduodenostom* or pseudocyst-duodenostom*).ti,ab.
103.	(hepatico-jejunostom* or hepaticojejunostom* or hepatojejunostom* or hepato-jejunostom* or hepatic jejunostom*).ti,ab.
104.	(pylorus preserving pancreatoduodectom* or pppd).ti,ab.
105.	v-shaped excision.ti,ab.
106.	sphincteroplast*.ti,ab.
107.	exp psychotherapy/
108.	psychophysiology/
109.	(behavio?r* adj therap*).ti,ab.
110.	(cognitive adj2 therap*).ti,ab.
111.	(relax* adj2 (therap* or technique*)).ti,ab.
112.	(meditat* or psychotherap*).ti,ab.
113.	(psychological adj (treatment* or therap*)).ti,ab.
114.	(group* adj therap*).ti,ab.
115.	(self-regulat* adj train*).ti,ab.
116.	(coping adj skill*).ti,ab.
117.	(pain-related adj thought*).ti,ab.
118.	(behavio?r* adj2 rehabilitat*).ti,ab.
119.	((psychoeducation or psycho-education) adj1 group*).ti,ab.
120.	alternative medicine/
121.	((mind and body) adj (relaxation or therap*)).ti,ab.
122.	enzyme replacement/
123.	pancreas extract/
124.	exp enzyme/th (therapy)
125.	(digest* adj2 enzyme*).ti,ab.
126.	(enzyme adj2 (replacement or therap*)).ti,ab.
127.	ert.ti,ab.
128.	(creon or nutrizym or pancrease or pancrex or pankreon or viokase).ti,ab.
129.	(pancreatin or pancrelipase).ti,ab.
130.	oxidation reduction reaction/
131.	antioxidant activity/
132.	scavenger/
133.	ascorbic acid/ or bilirubin/ or butylated hydroxyanisole/ or butylcresol/ or canthaxanthin/ or

	carotenoid/ or catalase/ or thioneine/ or grape seed extract/ or melatonin/ or nordihydroguaiaretic acid/ or probucol/ or gallic acid propyl ester/ or pyrogallol/ or quercetin/ or flavonoid/ or selenium/ or silymarin/ or thioctic acid/ or tocopherol/ or alpha tocotrienol/ or uric acid/ or urate/ or retinol/ or carotene/ or curcumin/ or methionine/ or flavone/ or beta carotene/ or allopurinol/ or glutathione/ or sodium selenite/ or acetylcysteine/ or riboflavin/ or zinc/ or magnesium/
134.	(antioxidant* or anti-oxidant* or micronutrient* or micro-nutrient*).ti,ab.
135.	(ascorbic acid or bilirubin or butylated hydroxyanisole or butylated hydroxytoluene or butylcresol or canthaxanthin or canthaxanthine or carotenoid* or catalase or ergothioneine or thioneine or grape seed extract or melatonin or nordihydroguaiaretic acid or masoprocol or probucol or superlipid or propyl gallate or pyrogallol or pyrogallic acid or gallic acid or quercetin or dikvertin or selenium or silymarin or milk thistle or silimarin or thioctic acid or lipoic acid or tocopherol* or tocotrienol* or uric acid or trioxopurine or urate or vitamin e or vitamin c or vitamin a or retinol or carotene* or curcumin or methionine or allopurin* or glutathione or sodium selenite or acetylcysteine or zinc or magnesium or riboflavin or flavone* or flavonoid*).ti,ab.
136.	(free radical adj2 scaveng*).ti,ab.
137.	(reduct* adj2 oxidat*).ti,ab.
138.	or/5-137
139.	Study filters RCT (A.3.2) or SR (A.3.3) or OBS (A.3.7)
140.	4 and 138 and 139
	Date parameters: see **Table 1**

1 **Cochrane search terms**

#1.	Standard population (G.2.1)
#2.	(mh narcotics)
#3.	(opioid* or opiate* or narcotic*):ti,ab
#4.	(mh ^morphine)
#5.	(morphine or astramorph or avinza or depodur or duramorph or embeda or infumorph or kadian or m-eslon or morcap or morphia or ms contin or msir or mst or nepenthe or oramorph or rescudose or rms or roxanol or sevredol or statex or zomorph):ti,ab
#6.	(mh ^opium)
#7.	(opium or omnopon or pantopon or papaveretum):ti,ab
#8.	(mh ^hydromorphone)
#9.	(hydromorphone or dihydromorphinone or dilaudid or dimorphone or exalgo or hydmrphn or hydromorph* or hydrostat or hymorphan or laudicon or novolauden or palladone):ti,ab
#10.	nicomorphine:ti,ab
#11.	(mh oxycodone)
#12.	(oxycodone or dazidox or dihydrohydroxycodeinone or dihydrone or dinarkon or endocodone or eth-oxydose or eucodal or hydroxycodeinon or m-oxy or oxiconum or oxycdn or oxycone or oxycontin or oxyfast or oxyir or pancodine or percocet or percolone or remoxy or roxicodone or theocodin):ti,ab
#13.	(dihydrocodeine or contugesic or dhc mundipharma or dicodin or dihydcdn or paracodin or paramol or parzone or rikodeine or tiamon or tosidrin or tuscodin):ti,ab
#14.	(diamorphine or acetomorphine or diacetylmorphine or diagesil or diamorf or heroin or min-i-jet morphine sulfate or skag):ti,ab
#15.	(mh codeine)
#16.	(codeine or ardinex or galcodine or isocodeine or methyl morphine or rx 336m or stanley-linctus or stanley-syrup):ti,ab
#17.	ketobemidone:ti,ab

#18.	(mh meperidine)
#19.	(pethidine or demerol or dolantin or dolargan or dolcontral or dolosal or dolsin or isonipecain or isonipecaine hydrochloride or lydol or meperidine or operidine epj or pethilorfan):ti,ab
#20.	(mh fentanyl)
#21.	(fentanyl or abstral or actiq or duragesic or fentanest or fentora or fentyl or ionsys or matrifen or nasalfent or onsolis or oralet or phentanyl or sublimaze):ti,ab
#22.	(mh dextromoramide)
#23.	dextromoramide:ti,ab
#24.	(piritramide or dipidolor or dipydolor or piridolan or pirium):ti,ab
#25.	(mh dextropropoxyphene)
#26.	(dextropropoxyphene or darvon or dolene or doloxene or levopropoxyphene or pp-cap or propoxyphene or proxyphen):ti,ab
#27.	(bezitramide or burgodin):ti,ab
#28.	(mh methadone)
#29.	(methadone or adanon or althose or amidines or amidone or biodone or diskets or dolophine or heptadon or metadol or metasedin or methaddict or metharose or methadose or methdn or methex or phy or phymet or physeptone or pinadone or symoron):ti,ab
#30.	(mh benzomorphans)
#31.	(mh pentazocine)
#32.	(pentazocine or fortral or fortwin or lexir or talacen or talwin):ti,ab
#33.	(mh phenazocine)
#34.	(phenazocine or prinadol or narphen):ti,ab
#35.	oripavine:ti,ab
#36.	(mh buprenorphine)
#37.	(buprenorphine or '6029-m' or buprenex or buprex or prefin or suboxone or subutex or temgesic):ti,ab
#38.	(mh etorphine)
#39.	(etorphine or immobilon or m99):ti,ab
#40.	(mh morphinans)
#41.	(mh butorphanol)
#42.	(butorphanol or 'bc2627' or beforal or dolorex or moradol or stadol or torbugesic):ti,ab
#43.	(mh tilidine)
#44.	(tilidine or tilidate or valoron or valtran or tilidin):ti,ab
#45.	(mh tramadol)
#46.	(tramadol or 'k-315' or ralivia or ryzolt or tramahexal or tramake insts or tramal* or tramedo or ultram or zamadol or zydol):ti,ab
#47.	(dezocine or dalgan or 'wy-16225'):ti,ab
#48.	(mh meptazinol)
#49.	(meptazinol or meptid):ti,ab
#50.	(tapentadol or cg5503 or nucynta):ti,ab
#51.	(remifentanil or 'gi 87084b' or remifentanyl or ultiva):ti,ab
#52.	(mh procaine)
#53.	(procaine or allocaine or anuject or gerokit or mericaine or novocaine or procaina serra):ti,ab
#54.	(alfenta or alfentanyl or fanaxal or limifen or rapifen):ti,ab
#55.	(dipipanone or co-dydramol or co-codamaol):ti,ab
#56.	(mh ^analgesics)
#57.	(mh ^"analgesics, non-narcotic")

#58.	(non-steroid* or non-narcotic* or analgesic* or pharmacolog*):ti,ab
#59.	(mh ^somatostatin)
#60.	(mh ^octreotide)
#61.	(somatostatin* or octreotide or sandostatin or lanreotide or somatuline):ti,ab
#62.	(mh acetaminophen)
#63.	(aspirin or acetaminophen or paracetamol or panadol or perfalgan or nefopam or acupan):ti,ab
#64.	(mh ^"anti-inflammatory agents, non-steroidal")
#65.	(mh ^aspirin)
#66.	(mh ^diclofenac)
#67.	(mh ^flurbiprofen)
#68.	(mh ^ibuprofen)
#69.	(mh ^ketoprofen)
#70.	(mh ^ketorolac)
#71.	(mh ^"ketorolac tromethamine")
#72.	(mh ^"meclofenamic acid")
#73.	(mh ^"mefenamic acid")
#74.	(mh ^naproxen)
#75.	(mh ^phenylbutazone)
#76.	(mh ^piroxicam)
#77.	(mh ^sulindac)
#78.	ziconotide:ti,ab
#79.	(nsaid* or ibuprofen or aspirin or naproxen or fenoprofen or flurbiprofen or ketoprofen or dexketoprofen or dexibuprofen or tiaprofenic acid or diclofenac or aceclofenac or indometacin or mefenamic acid or meloxicam or nabumetone or phenylbutazone or piroxicam or sulindac or tenoxicam or tolfenamic acid or ketorolac or celecoxib or etoricoxib or aceclofenac or acemetacin or diclofenac or etodolac):ti,ab
#80.	(mh ^"nerve block")
#81.	((nerve or percutaneous or splanchnic or subarachnoid or celiac or coeliac* or solar) near/1 block*):ti,ab
#82.	((celiac or coeliac* or solar) near/1 plexus):ti,ab
#83.	(mh ^"celiac plexus")
#84.	(mh ^"splanchnic nerves")
#85.	(mh ^"spinal cord stimulation")
#86.	((spinal cord* or dorsal column) near/2 stimulation*):ti,ab
#87.	splanchnicectom*:ti,ab
#88.	(mh ^neurolysis)
#89.	(neurolys* or neurolytic*):ti,ab
#90.	(mh ^"cholangiopancreatography, endoscopic retrograde")
#91.	(endoscopic retrograde cholangiopancreatograph* or ercp):ti,ab
#92.	(mh ^"endoscopy, gastrointestinal")
#93.	(mh ^"endoscopy, digestive system")
#94.	balloon next dilatation*:ti,ab
#95.	(mh ^dilatation)
#96.	(mh ^stents)
#97.	(mh ^"self expandable metallic stents")

#98.	(stent* or endoprosthes* or wallstent*):ti,ab
#99.	(mh ^"sphincterotomy, endoscopic")
#100.	sphincterotom*:ti,ab
#101.	(mh ^drainage)
#102.	(mh ^lithotripsy)
#103.	(extracorporeal shock wave lithotrips* or eswl):ti,ab
#104.	(stone next (extract* or remov*)):ti,ab
#105.	(endoscop* or endotherap* or minimally invasive):ti,ab
#106.	(mh ^endoscopy)
#107.	(pancreaticojejunostom* or pancreatico-jejunostom* or puestow):ti,ab
#108.	(mh ^"anastomosis, roux-en-y")
#109.	(mh ^pancreaticojejunostomy)
#110.	roux-en-y:ti,ab
#111.	anastomos*:ti,ab
#112.	frey*:ti,ab
#113.	(partington next rochelle):ti,ab
#114.	beger:ti,ab
#115.	(mh ^pancreaticoduodenectomy)
#116.	(pancreaticoduodenectom* or pancreatico-duodenectom* or pancreatoduodenectom* or pancreato-duodenectom*or whipple):ti,ab
#117.	(mh ^"surgical procedures, operative")
#118.	(mh ^pancreatectomy)
#119.	(pancreatectom* or resect* or operat* or drain* or denervat* or decompress* or surg*):ti,ab
#120.	(mh ^"decompression, surgical")
#121.	(cystogastrostom* or cysto next gastrostom* or cyst-gastrostom*):ti,ab
#122.	(cystojejunostom* or cysto next jejunostom* or cyst-jejunostom*):ti,ab
#123.	(cystoduodenostom* or cysto next duodenostom* or cyst-duodenostom*):ti,ab
#124.	(pseudocystogastrostom* or pseudo next cystogastrostom* or pseudocyst-gastrostom*):ti,ab
#125.	(pseudocystojejunostom* or pseudo next cystojejunostom* or pseudocyst-jejunostom*):ti,ab
#126.	(pseudocystoduodenostom* or pseudo next cystoduodenostom* or pseudocyst-duodenostom*):ti,ab
#127.	(hepatico-jejunostom* or hepaticojejunostom* or hepatojejunostom* or hepato-jejunostom* or hepat* next jejunostom*):ti,ab
#128.	(pylorus next preserving next pancreatoduodectom* or pppd):ti,ab
#129.	"v-shaped excision":ti,ab
#130.	sphincteroplast*:ti,ab
#131.	(mh psychotherapy)
#132.	(mh ^"biofeedback, psychology")
#133.	(cognitive near/2 therap*):ti,ab
#134.	(relax* near/2 (therap* or technique*)):ti,ab
#135.	(meditat* or psychotherap*):ti,ab
#136.	(psychological next (treatment* or therap*)):ti,ab
#137.	(group* next therap*):ti,ab
#138.	(self-regulat* next train*):ti,ab
#139.	(coping next skill*):ti,ab
#140.	(pain-related next thought*):ti,ab

#141.	(behavio?r* near/2 rehabilitat*):ti,ab
#142.	((psychoeducation or psycho-education) near/1 group*):ti,ab
#143.	(mh "mind-body therapies")
#144.	((mind and body) next (relaxation or therap*)):ti,ab
#145.	(mh ^"enzyme replacement therapy")
#146.	(mh "pancreatic extracts")
#147.	MeSH descriptor: (enzymes) explode all trees and with qualifier(s): (therapeutic use - tu)
#148.	(digest* near/2 enzyme*):ti,ab
#149.	(enzyme near/2 (replacement or therap*)):ti,ab
#150.	ert:ti,ab
#151.	(creon or nutrizym or pancrease or pancrex or pankreon or viokase):ti,ab
#152.	(pancreatin or pancrelipase):ti,ab
#153.	(mh antioxidants)
#154.	(mh ^"beta carotene")
#155.	(mh ^curcumin)
#156.	(mh ^methionine)
#157.	(mh ^allopurinol)
#158.	(mh ^glutathione)
#159.	(mh ^"sodium selenite")
#160.	(mh ^acetylcysteine)
#161.	(mh ^flavonoids)
#162.	(mh ^riboflavin)
#163.	(mh ^zinc)
#164.	(mh magnesium)
#165.	(mh oxidation-reduction)
#166.	(mh "free radical scavengers")
#167.	(antioxidant* or anti-oxidant* or anti next oxidant* or micronutrient* or micro-nutrient* or micro next nutrient*):ti,ab
#168.	(ascorbic next acid or bilirubin or butylated next hydroxyanisole or butylated next hydroxytoluene or butylcresol or canthaxanthin or canthaxanthine or carotenoid* or catalase or ergothioneine or thioneine or grape next seed next extract or melatonin or nordihydroguaiaretic next acid or masoprocol or probucol or superlipid or propyl next gallate or pyrogallol or pyrogallic next acid or gallic next acid or quercetin or dikvertin or selenium or silymarin or milk next thistle or silimarin or thioctic next acid or lipoic next acid or tocopherol* or tocotrienol* or uric next acid or trioxopurine or urate or vitamin next e or vitamin next c or vitamin next a or retinol or carotene* or curcumin or methionine or allopurin* or glutathione or sodium next selenite or acetylcysteine or zinc or magnesium or riboflavin or flavone* or flavonoid*):ti,ab
#169.	(free radical near/2 scaveng*):ti,ab
#170.	(reduct* near/2 oxidat*):ti,ab
#171.	(or #2-#170)
#172.	#1 and #171
	Date parameters: see **Table 1**

1 **PsycINFO search terms**

1.	Standard population (A.2.1)
2.	Excluded study designs and publication types (A.3.1)
3.	1 not 2

4.	Limit 3 to English language
	Date parameters: see **Table 1**

G.4.11 Pancreatic ascites and pleural effusion

- What are the most clinically and cost-effective interventions for treating pancreatic ascites and pleural effusion secondary to acute or chronic pancreatitis?

Medline search terms

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	ascites/ or ascitic fluid/
6.	ascit*.ti,ab.
7.	(peritoneal adj2 fluid*).ti,ab.
8.	exp pleural effusion/
9.	((intrapleura* or intra-pleura* or pleura*) adj2 (effusion* or fluid*)).ti,ab.
10.	pancreatic fistula/ or fistula/
11.	((pancrea* or pleura*) adj6 fistula*).ti,ab.
12.	(pancrea* adj3 leak*).ti,ab.
13.	(duct* adj3 disrupt*).ti,ab.
14.	((intra-abdominal or intraabdominal or intrapleura* or intra-pleura* or pleura*) adj2 collection*).ti,ab.
15.	or/5-14
16.	4 and 15
	Date parameters: see **Table 1**

Embase search terms

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	ascites fluid/
6.	ascites/
7.	ascit*.ti,ab.
8.	(peritoneal adj2 fluid*).ti,ab.
9.	pleura effusion/
10.	((intrapleura* or intra-pleura* or pleura*) adj2 (effusion* or fluid*)).ti,ab.
11.	fistula/ or pancreas fistula/
12.	((pancrea* or pleura*) adj6 fistula*).ti,ab.
13.	(pancrea* adj3 leak*).ti,ab.
14.	(duct* adj3 disrupt*).ti,ab.
15.	((intra-abdominal or intraabdominal or intrapleura* or intra-pleura* or pleura*) adj2 collection*).ti,ab.
16.	or/5-15
17.	4 and 16

	Date parameters: see **Table 1**

Cochrane search terms

#1.	Standard population (G.2.1)
#2.	MeSH descriptor: (ascites) this term only
#3.	MeSH descriptor: (ascitic fluid) this term only
#4.	ascit*:ti,ab
#5.	(peritoneal near/2 fluid*):ti,ab
#6.	MeSH descriptor: (pleural effusion) explode all trees
#7.	((intrapleura* or intra-pleura* or pleura*) near/2 (effusion* or fluid*)):ti,ab
#8.	MeSH descriptor: (fistula) this term only
#9.	MeSH descriptor: (pancreatic fistula) this term only
#10.	((pancrea* or pleura*) near/6 fistula*):ti,ab
#11.	(pancrea* near/3 leak*):ti,ab
#12.	(duct* near/3 disrupt*):ti,ab
#13.	((intra-abdominal or intraabdominal or intrapleura* or intra-pleura* or pleura*) near/2 collection*):ti,ab
#14.	#2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13
#15.	#1 and #14
	Date parameters: see **Table 1**

PsycINFO search terms

1.	Standard population (A.2.1)
2.	Excluded study designs and publication types (A.3.1)
3.	1 not 2
4.	Limit 3 to English language
	Date parameters: see **Table 1**

G.4.12 Biliary obstruction

- What is the most clinically and cost-effective intervention for treating biliary obstruction in people with chronic pancreatitis?

Medline search terms

1.	Standard population (G.2.1)
2.	Chronic pancreatitis population (G.2.2)
3.	Excluded study designs and publication types (G.3.1)
4.	1 not 3
5.	2 not 3
6.	Limit 4 to English language
7.	Limit 5 to English language
8.	bile ducts/ or bile ducts, extrahepatic/ or bile ducts, intrahepatic/
9.	common bile duct/ or cystic duct/ or hepatic duct, common/
10.	biliary tract diseases/ or bile duct diseases/
11.	(biliary or bile or cbd or choledoch*).ti,ab.
12.	((cystic or hepatic) adj2 duct*).ti,ab.
13.	cholestasis/ or cholestasis, extrahepatic/ or cholestasis, intrahepatic/
14.	cholestasis.ti,ab.

15.	cholelithiasis/ or choledocholithiasis/
16.	(cholelithiasis or choledocholithiasis).ti,ab.
17.	gallstones/
18.	gallstone*.ti,ab.
19.	jaundice, obstructive/
20.	(jaundice* adj3 (obstruc* or block* or stricture*)).ti,ab.
21.	cholangitis/
22.	cholangitis.ti,ab.
23.	or/8-22
24.	(surger* or operation* or procedure* or bypass* or drain* or resect*).ti,ab.
25.	drainage/
26.	surgical procedures, operative/
27.	endoscopy, gastrointestinal/ or endoscopy, digestive system/
28.	biliary tract surgical procedures/
29.	anastomosis, roux-en-y/
30.	roux-en-y.ti,ab.
31.	biliary-enteric anastomos?s.ti,ab.
32.	choledochostomy/
33.	(choledochoduodenostom* or choledocho-duodenostom*).ti,ab.
34.	(choledocho-jejunostom* or choledochojejunostom*).ti,ab.
35.	(hepatico-jejunostom* or hepaticojejunostom* or hepatojejunostom* or hepato-jejunostom* or hepatic jejunostom*).ti,ab.
36.	cholangiopancreatography, endoscopic retrograde/
37.	(endoscopic retrograde cholangiopancreatograph* or ercp).ti,ab.
38.	stents/ or self expandable metallic stents/
39.	(stent* or wallstent).ti,ab.
40.	or/24-39
41.	Study filters RCT (A.3.2) or SR (A.3.3)
42.	exp clinical trial/
43.	exp clinical trials as topic/
44.	exp evaluation studies/ or follow-up studies/ or prospective studies/
45.	exp epidemiological studies/
46.	cohort stud*.ti,ab.
47.	case control stud*.ti,ab.
48.	((crossover or cross-over or cross over) adj2 (design* or stud* or procedure* or trial*)).ti,ab.
49.	or/41-48
50.	41 or 49
51.	7 and 23
52.	6 and 23 and 40 and 50
53.	51 or 52
	Date parameters: see **Table 1**

1 **Embase search terms**

1.	Standard population (G.2.1)
2.	Chronic pancreatitis population (G.2.2)
3.	Excluded study designs and publication types (G.3.1)

4.	1 not 3
5.	2 not 3
6.	Limit 4 to English language
7.	Limit 5 to English language
8.	(biliary or bile or cbd or choledoch*).ti,ab.
9.	bile duct/ or extrahepatic bile duct/ or intrahepatic bile duct/
10.	common bile duct/ or common hepatic duct/ or cystic duct/
11.	biliary tract disease/ or bile duct disease/
12.	((cystic or hepatic) adj2 duct*).ti,ab.
13.	cholestasis/ or obstructive bile duct disease/
14.	cholestasis.ti,ab.
15.	cholelithiasis/
16.	bile duct stone/ or common bile duct stone/
17.	(cholelithiasis or choledocholithiasis).ti,ab.
18.	gallstone/
19.	obstructive jaundice/
20.	gallstone*.ti,ab.
21.	(jaundice* adj3 (obstruc* or block* or stricture*)).ti,ab.
22.	cholangitis/
23.	cholangitis.ti,ab.
24.	or/8-23
25.	(surger* or operation* or procedure* or bypass* or drain* or resect*).ti,ab.
26.	biliary tract drainage/ or biliary tract surgery/ or surgical drainage/
27.	surgery/
28.	gastrointestinal endoscopy/ or digestive tract endoscopy/
29.	roux y anastomosis/
30.	roux-en-y.ti,ab.
31.	biliary-enteric anastomos?s.ti,ab.
32.	bile duct bypass/ or choledochojejunostomy/ or hepatojejunostomy/
33.	(choledochoduodenostom* or choledocho-duodenostom*).ti,ab.
34.	(choledocho-jejunostom* or choledochojejunostom*).ti,ab.
35.	(hepatico-jejunostom* or hepaticojejunostom* or hepatojejunostom* or hepato-jejunostom* or hepatic jejunostom*).ti,ab.
36.	endoscopic retrograde cholangiopancreatography/
37.	(endoscopic retrograde cholangiopancreatograph* or ercp).ti,ab.
38.	stent/ or metal stent/ or self expanding stent/
39.	(stent* or wallstent).ti,ab.
40.	or/25-39
41.	Study filters RCT (A.3.2) or SR (A.3.3) or OBS (A.3.7)
42.	7 and 24
43.	6 and 24 and 40 and 41
44.	42 or 43
	Date parameters: see **Table 1**

1 **Cochrane search terms**

#1.	Standard population (G.2.1)

#2.	Chronic pancreatitis population (G.2.2)
#3.	(biliary or bile or cbd or choledoch*):ti,ab
#4.	MeSH descriptor: (bile ducts) this term only
#5.	MeSH descriptor: (bile ducts, extrahepatic) this term only
#6.	MeSH descriptor: (bile ducts, intrahepatic) this term only
#7.	MeSH descriptor: (common bile duct) this term only
#8.	MeSH descriptor: (cystic duct) this term only
#9.	MeSH descriptor: (hepatic duct, common) this term only
#10.	MeSH descriptor: (biliary tract diseases) this term only
#11.	MeSH descriptor: (bile duct diseases) this term only
#12.	MeSH descriptor: (cholestasis) this term only
#13.	MeSH descriptor: (cholestasis, extrahepatic) this term only
#14.	MeSH descriptor: (cholestasis, intrahepatic) this term only
#15.	cholestasis:ti,ab
#16.	MeSH descriptor: (cholelithiasis) this term only
#17.	MeSH descriptor: (choledocholithiasis) this term only
#18.	(cholelithiasis or choledocholithiasis):ti,ab
#19.	MeSH descriptor: (gallstones) this term only
#20.	gallstone*:ti,ab
#21.	MeSH descriptor: (jaundice, obstructive) this term only
#22.	(jaundice* near/3 (obstruc* or block* or stricture*)):ti,ab
#23.	MeSH descriptor: (cholangitis) this term only
#24.	cholangitis:ti,ab
#25.	(or #3-#25)
#26.	(surger* or operation* or procedure* or bypass* or drain* or resect*):ti,ab
#27.	(mh ^drainage)
#28.	(mh ^"surgical procedures, operative")
#29.	(mh ^"endoscopy, gastrointestinal")
#30.	(mh ^"biliary tract surgical procedures")
#31.	(mh ^"anastomosis, roux-en-y")
#32.	roux-en-y:ti,ab
#33.	biliary-enteric anastomos?s:ti,ab
#34.	(mh ^choledochostomy)
#35.	(choledochoduodenostom* or choledocho-duodenostom*):ti,ab
#36.	(choledocho-jejunostom* or choledochojejunostom*):ti,ab
#37.	(hepatico-jejunostom* or hepaticojejunostom* or hepatojejunostom* or hepato-jejunostom* or hepatic jejunostom*):ti,ab
#38.	(mh ^"cholangiopancreatography, endoscopic retrograde")
#39.	(endoscopic retrograde cholangiopancreatograph* or ercp):ti,ab
#40.	(mh ^stents)
#41.	(mh ^"self expandable metallic stents")
#42.	(stent* or wallstent):ti,ab
#43.	(or #26-#42)
#44.	#1 and #25 and #43
#45.	#2 and #25

#46.	#44 or #45
	Date parameters: see **Table 1**

PsycINFO search terms

1.	Standard population (A.2.1)
2.	Excluded study designs and publication types (A.3.1)
3.	1 not 2
4.	Limit 3 to English language
	Date parameters: see **Table 1**

G.4.13 Diabetes

Searches for the following two questions were run as one search:

- How often should follow-up to identify the development of diabetes be carried out in people with chronic pancreatitis?
- What is the most clinically and cost-effective insulin regimen strategy specifically for type 3c diabetes secondary to pancreatitis?

Medline search terms

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	diabetes mellitus/
6.	diabet*.ti,ab.
7.	or/5-6
8.	4 and 7
9.	t3cdm.ti,ab.
10.	(diabet* and pancreatogenic).ti,ab.
11.	or/9-10
12.	8 or 11
13.	Study filters RCT (A.3.2) or SR (A.3.3) or OBS (A.3.7)
14.	12 and 13
	Date parameters: see **Table 1**

Embase search terms

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	diabetes mellitus/
6.	diabet*.ti,ab.
7.	or/5-6
8.	4 and 7
9.	t3cdm.ti,ab.
10.	(diabet* and pancreatogenic).ti,ab.
11.	or/9-10

12.	7 or 11
13.	Study filters RCT (A.3.2) or SR (A.3.3) or OBS (A.3.7)
14.	12 and 13
	Date parameters: see **Table 1**

Cochrane search terms

#1.	Standard population (G.2.1)
#2.	MeSH descriptor: (diabetes mellitus) this term only
#3.	diabet*:ti,ab
#4.	#2 or #3
#5.	#1 and #4
#6.	(diabet* and pancreatogenic):ti,ab
#7.	"t3cdm":ti,ab
#8.	#5 or #6 or #7
	Date parameters: see **Table 1**

PsycINFO search terms

1.	Standard population (A.2.1)
2.	Excluded study designs and publication types (A.3.1)
3.	1 not 2
4.	Limit 3 to English language
	Date parameters: see **Table 1**

G.4.14 Specialist assessment

Searches for the following two questions were run as one search:

- What is the clinical and cost effectiveness of receiving specialist input in people with acute pancreatitis?
- What is the clinical and cost effectiveness of a specialist nutritional assessment compared to a non-specialist assessment for managing malabsorption or malnutrition in people with chronic pancreatitis?

Medline search terms

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	tertiary care centers/
6.	(tertiary adj3 (unit* or center* or centre* or facilit* or team* or service*)).ti,ab.
7.	(specialis* or specializ* or expert* or consultant*).ti,ab.
8.	consultants/
9.	((pancreatitis or pancreas) adj4 (clinic* or unit* or centre* or center* or facilit* or team* or service*)).ti,ab.
10.	exp "referral and consultation"/
11.	decision making/
12.	((multidisciplin* or team* or interdisciplin* or mdt or idt or interprofessional* or multiprofessional* or inter-disciplin* or multi-disciplin* or inter-professional or multi-professional or multicenter* or multicentre* or multi-center* or multi-centre*) adj3 (support

	or liais* or co-operat* or cooperat* or contact* or relationship* or convers* or dialog* or talk* or exchange* or discuss* or advice or advis* or input or approach* or consult*)).ti,ab.
13.	((surgeon* or surgical or surgery or endoscop* or gastroenterol* or diet* or nutrition* or radiolog*) adj3 (support or liais* or co-operat* or cooperat* or contact* or relationship* or convers* or dialog* or talk* or exchange* or discuss* or advice or advis* or input or consult*)).ti,ab.
14.	telemedicine/
15.	remote consultation/
16.	(telemedicine or tele?consult*).ti,ab.
17.	nutrition therapy/ or diet therapy/ or nutritional support/ or nutrition assessment/
18.	((virtual or tele* or "face to face" or "in person" or remote) adj3 (consult* or refer* or refers or referral* or referring or centre* or center* or service* or input or meeting* or support* or advice or advis* or liais* or contact* or relationship* or convers* or dialog* or talk* or exchange* or discuss*)).ti,ab.
19.	or/5-18
20.	Study filters RCT (A.3.2) or SR (A.3.3) or OBS (G.3.7)
21.	4 and 19 and 20
	Date parameters: see **Table 1**

1 **Embase search terms**

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	tertiary care center/
6.	(tertiary adj3 (unit* or center* or centre* or facilit* or team* or service*)).ti,ab.
7.	(Specialis* or specializ* or expert* or consultant*).ti,ab.
8.	consultation/ or teleconsultation/
9.	((pancreatitis or pancreas) adj4 (clinic* or unit* or centre* or center* or facilit* or team* or service*)).ti,ab.
10.	patient referral/
11.	decision making/
12.	((multidisciplin* or team* or interdisciplin* or MDT or IDT or interprofessional* or multiprofessional* or inter-disciplin* or multi-disciplin* or inter-professional or multi-professional or multicenter* or multicentre* or multi-center* or multi-centre*) adj3 (support or liais* or co-operat* or cooperat* or contact* or relationship* or convers* or dialog* or talk* or exchange* or discuss* or advice or advis* or input or approach* or consult*)).ti,ab.
13.	((surgeon* or surgical or surgery or endoscop* or gastroenterol* or diet* or nutrition* or radiolog*) adj3 (support or liais* or co-operat* or cooperat* or contact* or relationship* or convers* or dialog* or talk* or exchange* or discuss* or advice or advis* or input or consult*)).ti,ab.
14.	telemedicine/
15.	(telemedicine or tele?consult*).ti,ab.
16.	diet therapy/ or nutritional support/
17.	((virtual or tele* or "face to face" or "in person" or remote) adj3 (consult* or refer* or refers or referral* or referring or centre* or center* or service* or input or meeting* or support* or advice or advis* or liais* or contact* or relationship* or convers* or dialog* or talk* or exchange* or discuss*)).ti,ab.
18.	or/5-17
19.	Study filters RCT (A.3.2) or SR (A.3.3) or OBS (G.3.7)

20.	4 and 18 and 19
	Date parameters: see **Table 1**

Cochrane search terms

#1.	Standard population (G.2.1)
#2.	(mh ^"tertiary care centers")
#3.	(tertiary near/3 (unit* or center* or centre* or facilit* or team* or service*)):ti,ab
#4.	(specialis* or specializ* or expert* or consultant*):ti,ab
#5.	(mh ^consultants)
#6.	((pancreatitis or pancreas) near/4 (clinic* or unit* or centre* or center* or facilit* or team* or service*)):ti,ab
#7.	(mh "referral and consultation")
#8.	(mh ^"decision making")
#9.	((multidisciplin* or team* or interdisciplin* or mdt or idt or interprofessional* or multiprofessional* or inter-disciplin* or multi-disciplin* or inter-professional or multi-professional or multicenter* or multicentre* or multi-center* or multi-centre*) near/3 (support or liais* or co-operat* or cooperat* or contact* or relationship* or convers* or dialog* or talk* or exchange* or discuss* or advice or advis* or input or approach* or consult*)):ti,ab
#10.	((surgeon* or surgical or surgery or endoscop* or gastroenterol* or diet* or nutrition* or radiolog*) near/3 (support or liais* or co-operat* or cooperat* or contact* or relationship* or convers* or dialog* or talk* or exchange* or discuss* or advice or advis* or input or consult*)):ti,ab
#11.	(mh ^telemedicine)
#12.	(mh ^"remote consultation")
#13.	(telemedicine or tele?consult*):ti,ab
#14.	(mh ^"nutrition therapy")
#15.	(mh ^"diet therapy")
#16.	(mh ^"nutritional support")
#17.	(mh ^"nutrition assessment")
#18.	((virtual or tele* or remote) near/3 (consult* or refer* or refers or referral* or referring or centre* or center* or service* or input or meeting* or support* or advice or advis* or liais* or contact* or relationship* or convers* or dialog* or talk* or exchange* or discuss*)):ti,ab
#19.	((face next to next face) near/3 (consult* or refer* or refers or referral* or referring or centre* or center* or service* or input or meeting* or support* or advice or advis* or liais* or contact* or relationship* or convers* or dialog* or talk* or exchange* or discuss*)):ti,ab
#20.	((in next person) near/3 (consult* or refer* or refers or referral* or referring or centre* or center* or service* or input or meeting* or support* or advice or advis* or liais* or contact* or relationship* or convers* or dialog* or talk* or exchange* or discuss*)):ti,ab
#21.	(or #2-#20)
#22.	#1 and #21
	Date parameters: see **Table 1**

PsycINFO search terms

1.	Standard population (A.2.1)
2.	Excluded study designs and publication types (A.3.1)
3.	1 not 2
4.	Limit 3 to English language
	Date parameters: see **Table 1**

G.4.15 Follow up: pancreatic function

- How often should follow-up to assess pancreatic exocrine function and any secondary health issues, if any, be carried out in people with chronic pancreatitis?

Medline search terms

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	pancreatic elastase/
6.	elastase.ti,ab.
7.	nutritional status/
8.	iron/ or iron, dietary/
9.	vitamins/ or vitamin d deficiency/ or vitamin a deficiency/ or vitamin d/ or vitamin a/ or vitamin e/
10.	((nutrition* or nutrient* or micronutrient* or micro-nutrient* or diet* or vitamin* or iron) adj6 (assess* or status or evaluat* or test* or screen* or investigat* or follow-up* or followup* or surveillance* or marker* or biomarker* or indicat* or parameter* or exam* or check-up* or checkup* or monitor* or measure*)).ti,ab.
11.	((vitamin* or iron or nutrition* or nutrient* or micronutrient* or micro-nutrient* or diet* or exocrine) adj3 (deficien* or insuffic*)).ti,ab.
12.	exocrine pancreatic insufficiency/
13.	(pancrea* adj2 (function or insuffic* or deficien*) adj6 (assess* or status or evaluat* or test* or screen* or investigat* or follow-up* or followup* or surveillance* or marker* or biomarker* or indicat* or parameter* or exam* or check-up* or checkup* or monitor* or measure*)).ti,ab.
14.	(exocrine adj6 (assess* or status or evaluat* or test* or screen* or investigat* or follow-up* or followup* or surveillance* or marker* or biomarker* or indicat* or parameter* or exam* or check-up* or checkup* or monitor* or measure*)).ti,ab.
15.	anthropometry/
16.	anthropometr*.ti,ab.
17.	z score*.ti,ab.
18.	bone density/
19.	dexa.ti,ab.
20.	(bone adj2 (density or mineral* or metabolism* or health)).ti,ab.
21.	body weight/ or body mass index/
22.	exp body composition/
23.	((body or muscle* or weight or bmi or metaboli*) adj6 (assess* or status or evaluat* or test* or screen* or investigat* or follow-up* or followup* or surveillance* or marker* or biomarker* or indicat* or parameter* or exam* or check-up* or checkup* or monitor* or measure*)).ti,ab.
24.	(body adj composition*).ti,ab.
25.	(primary hyperparathyroid* or parathyroid hormone* or pth).ti,ab.
26.	(biochemi* adj6 (assess* or status or evaluat* or test* or screen* or investigat* or follow-up* or followup* or surveillance* or marker* or biomarker* or indicat* or parameter* or exam* or check-up* or checkup* or monitor* or measure*)).ti,ab.
27.	(exocrine and ((assess* or evaluat* or test* or screen* or investigat* or follow-up or followup* or surveillance or marker* or biomarker* or monitor* or check-up* or checkup* or measure* or examin*) adj6 (interval* or frequen* or day* or week* or month* or year* or time* or timing* or regular* or ongoing or on-going or continu* or recurr* or repeat*))).ti,ab.

28.	((pancrea* adj2 function*) and ((assess* or evaluat* or test* or screen* or investigat* or follow-up or followup* or surveillance or marker* or biomarker* or monitor* or check-up* or checkup* or measure* or examin*) adj6 (interval* or frequen* or day* or week* or month* or year* or time* or timing* or regular* or ongoing or on-going or continu* or recurr* or repeat*))).ti,ab.
29.	or/5-28
30.	"pancreatic function tests"/
31.	time factors/
32.	30 and 31
33.	29 or 32
34.	Study filters RCT (A.3.2) or SR (A.3.3) or OBS (A.3.7)
35.	4 and 32 and 33
	Date parameters: see **Table 1**

1 **Embase search terms**

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	pancreatic elastase/
6.	elastase.ti,ab.
7.	nutritional status/ or nutritional parameters/
8.	iron/ or iron absorption/ or iron deficiency/
9.	vitamin/ or vitamin D/ or vitamin K group/ or vitamin D deficiency/ or retinol/ or alpha tocopherol/
10.	((nutrition* or nutrient* or micronutrient* or micro-nutrient* or diet* or vitamin* or iron) adj6 (assess* or status or evaluat* or test* or screen* or investigat* or follow-up* or followup* or surveillance* or marker* or biomarker* or indicat* or parameter* or exam* or check-up* or checkup* or monitor* or measure*)).ti,ab.
11.	((vitamin* or iron or nutrition* or nutrient* or micronutrient* or micro-nutrient* or diet* or exocrine) adj3 (deficien* or insuffic*)).ti,ab.
12.	exocrine pancreatic insufficiency/ or pancreatic insufficiency/ or pancreas function/
13.	(pancrea* adj2 (function or insuffic* or deficien*) adj6 (assess* or status or evaluat* or test* or screen* or investigat* or follow-up* or followup* or surveillance* or marker* or biomarker* or indicat* or parameter* or exam* or check-up* or checkup* or monitor* or measure*)).ti,ab.
14.	(exocrine adj6 (assess* or status or evaluat* or test* or screen* or investigat* or follow-up* or followup* or surveillance* or marker* or biomarker* or indicat* or parameter* or exam* or check-up* or checkup* or monitor* or measure*)).ti,ab.
15.	anthropometry/ or anthropometric parameters/
16.	anthropometr*.ti,ab.
17.	z score*.ti,ab.
18.	bone density/
19.	dexa.ti,ab.
20.	(bone adj2 (density or mineral* or metabolism* or health)).ti,ab.
21.	body weight/ or body composition/ or body distribution/ or body fat/ or body fat distribution/ or body mass/
22.	((body or muscle* or weight or BMI or metaboli*) adj6 (assess* or status or evaluat* or test* or screen* or investigat* or follow-up* or followup* or surveillance* or marker* or

	biomarker* or indicat* or parameter* or exam* or check-up* or checkup* or monitor* or measure*)).ti,ab.
23.	(body adj composition*).ti,ab.
24.	(primary hyperparathyroid* or parathyroid hormone* or PTH).ti,ab.
25.	(biochemi* adj6 (assess* or status or evaluat* or test* or screen* or investigat* or follow-up* or followup* or surveillance* or marker* or biomarker* or indicat* or parameter* or exam* or check-up* or checkup* or monitor* or measure*)).ti,ab.
26.	(exocrine and ((assess* or evaluat* or test* or screen* or investigat* or follow-up or followup* or surveillance or marker* or biomarker* or monitor* or check-up* or checkup* or measure* or examin*) adj6 (interval* or frequen* or day* or week* or month* or year* or time* or timing* or regular* or ongoing or on-going or continu* or recurr* or repeat*))).ti,ab.
27.	((pancrea* adj2 function*) and ((assess* or evaluat* or test* or screen* or investigat* or follow-up or followup* or surveillance or marker* or biomarker* or monitor* or check-up* or checkup* or measure* or examin*) adj6 (interval* or frequen* or day* or week* or month* or year* or time* or timing* or regular* or ongoing or on-going or continu* or recurr* or repeat*))).ti,ab.
28.	or/5-27
29.	pancreas function test/
30.	time/ or time factor/
31.	29 and 30
32.	28 or 31
33.	Study filters RCT (A.3.2) or SR (A.3.3) or OBS (A.3.7)
34.	4 and 32 and 33
	Date parameters: see **Table 1**

1 **Cochrane search terms**

#1.	Standard population (G.2.1)
#2.	(mh ^"pancreatic elastase")
#3.	elastase:ti,ab
#4.	(mh ^"nutritional status")
#5.	(mh ^iron)
#6.	(mh ^"iron, dietary")
#7.	(mh ^vitamins)
#8.	MeSH descriptor: (vitamin d deficiency) this term only
#9.	MeSH descriptor: (vitamin a deficiency) this term only
#10.	(mh ^"vitamin d")
#11.	(mh ^"vitamin a")
#12.	(mh ^"vitamin e")
#13.	((nutrition* or nutrient* or micronutrient* or micro next nutrient* or diet* or vitamin* or iron) next/6 (assess* or status or evaluat* or test* or screen* or investigat* or follow next up* or followup* or surveillance* or marker* or biomarker* or indicat* or parameter* or exam* or check next up* or checkup* or monitor* or measure*)):ti,ab
#14.	((vitamin* or iron or nutrition* or nutrient* or micronutrient* or micro next nutrient* or diet* or exocrine) next/3 (deficien* or insuffic*)):ti,ab
#15.	(mh ^"exocrine pancreatic insufficiency")
#16.	(pancrea* next/2 (function or insuffic* or deficien*) next/6 (assess* or status or evaluat* or test* or screen* or investigat* or follow next up* or followup* or surveillance* or marker* or biomarker* or indicat* or parameter* or exam* or check next up* or checkup* or monitor* or measure*)):ti,ab

#17.	(exocrine next/6 (assess* or status or evaluat* or test* or screen* or investigat* or follow-up* or followup* or surveillance* or marker* or biomarker* or indicat* or parameter* or exam* or check-up* or checkup* or monitor* or measure*)):ti,ab
#18.	(mh ^anthropometry)
#19.	anthropometr*:ti,ab
#20.	z score*:ti,ab
#21.	(mh ^"bone density")
#22.	dexa:ti,ab
#23.	(bone next/2 (density or mineral* or metabolism* or health)):ti,ab
#24.	(mh ^"body weight")
#25.	(mh ^"body mass index")
#26.	(mh "body composition")
#27.	((body or muscle* or weight or bmi or metaboli*) next/6 (assess* or status or evaluat* or test* or screen* or investigat* or follow next up* or followup* or surveillance* or marker* or biomarker* or indicat* or parameter* or exam* or check next up* or checkup* or monitor* or measure*)):ti,ab
#28.	body next composition*:ti,ab
#29.	(primary hyperparathyroid* or parathyroid hormone* or pth):ti,ab
#30.	(biochemi* next/6 (assess* or status or evaluat* or test* or screen* or investigat* or follow next up* or followup* or surveillance* or marker* or biomarker* or indicat* or parameter* or exam* or check next up* or checkup* or monitor* or measure*)):ti,ab
#31.	(exocrine and ((assess* or status or evaluat* or test* or screen* or investigat* or follow next up* or followup* or surveillance* or marker* or biomarker* or indicat* or parameter* or exam* or check next up* or checkup* or monitor* or measure*) next/6 (interval* or frequen* or day* or week* or month* or year* or time* or timing* or regular* or ongoing or on-going or continu* or recurr* or repeat*))):ti,ab
#32.	((pancrea* next/2 function*) and ((assess* or status or evaluat* or test* or screen* or investigat* or follow next up* or followup* or surveillance* or marker* or biomarker* or indicat* or parameter* or exam* or check next up* or checkup* or monitor* or measure*) next/6 (interval* or frequen* or day* or week* or month* or year* or time* or timing* or regular* or ongoing or on-going or continu* or recurr* or repeat*))):ti,ab
#33.	(or #2-#32)
#34.	(mh ^"pancreatic function tests")
#35.	(mh ^"time factors")
#36.	#34 and #35
#37.	#33 or #36
#38.	#1 and #37
	Date parameters: see **Table 1**

PsycINFO search terms

1.	Standard population (A.2.1)
2.	Excluded study designs and publication types (A.3.1)
3.	1 not 2
4.	Limit 3 to English language
	Date parameters: see **Table 1**

G.4.16 Follow up: pancreatic cancer

- How often should follow-up to identify development of pancreatic cancer be carried out in people with chronic pancreatitis?

1 **Medline search terms**

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2
4.	Limit 3 to English language
5.	pancreas/
6.	neoplasms/
7.	(carcin* or cancer* or neoplas* or tumour* or tumor* or growth* or adenocarcin* or malig*).ti,ab.
8.	5 and (6 or 7)
9.	(pancrea* adj6 (carcin* or cancer* or neoplas* or tumour* or tumor* or growth* or adenocarcin* or malig*)).ti,ab.
10.	carcinoma, pancreatic ductal/ or pancreatic neoplasms/
11.	or/8-10
12.	((carcin* or cancer* or neoplas* or tumour* or tumor* or growth* or adenocarcin* or malig*) adj6 (assess* or status or evaluat* or test* or screen* or investigat* or follow-up* or followup* or surveillance* or marker* or biomarker* or indicat* or parameter* or exam* or check-up* or checkup* or monitor* or measure*)).ti,ab.
13.	(ca19-9 or ca-19* or muc1 or mucin* or muc* or antigen* or cea or heat shock protein* or hsp or microrna* or mrna* or mirna*).ti,ab.
14.	biomarkers, tumor/ or antigens, tumor-associated, carbohydrate/ or ca-19-9 antigen/ or antigens, neoplasm/
15.	((ercp or cholangiopancreatograph* or cholangio-pancreatograph*) and (carcin* or cancer* or neoplas* or tumour* or tumor* or growth* or adenocarcin* or malig*)).ti,ab.
16.	((eus or ultrasonic endoscop* or endoscopic ultrasonograph* or endosonograph* or ultrasound* or scan* or ct* or tomograph* or mri* or magnetic resonance or mrcp or pet-ct) and (carcin* or cancer* or neoplas* or tumour* or tumor* or growth* or adenocarcin* or malig*)).ti,ab.
17.	(methylat* and (carcin* or cancer* or neoplas* or tumour* or tumor* or growth* or adenocarcin* or malig*)).ti,ab.
18.	or/12-17
19.	biomarkers/
20.	cholangiopancreatography, endoscopic retrograde/
21.	tomography/ or magnetic resonance imaging/ or cholangiopancreatography, magnetic resonance/ or exp tomography, emission-computed/ or ultrasonography/
22.	tomography, x-ray computed/
23.	endosonography/
24.	or/19-23
25.	24 and (6 or 7)
26.	11 or 18 or 25
27.	Study filters RCT (A.3.2) or SR (A.3.3) or OBS (A.3.7)
28.	4 and 26 and 27
	Date parameters: see **Table 1**

2 **Embase search terms**

1.	Standard population (G.2.1)
2.	Excluded study designs and publication types (G.3.1)
3.	1 not 2

4.	Limit 3 to English language
5.	pancreas/
6.	neoplasm/ or malignant neoplasm/
7.	(carcin* or cancer* or neoplas* or tumour* or tumor* or growth* or adenocarcin* or malig*).ti,ab.
8.	5 and (6 or 7)
9.	(pancrea* adj6 (carcin* or cancer* or neoplas* or tumour* or tumor* or growth* or adenocarcin* or malig*)).ti,ab.
10.	pancreas adenoma/ or pancreas tumor/ or pancreas adenocarcinoma/ or pancreas cancer/ or pancreas carcinoma/
11.	or/8-10
12.	((carcin* or cancer* or neoplas* or tumour* or tumor* or growth* or adenocarcin* or malig*) adj6 (assess* or status or evaluat* or test* or screen* or investigat* or follow-up* or followup* or surveillance* or marker* or biomarker* or indicat* or parameter* or exam* or check-up* or checkup* or monitor* or measure*)).ti,ab.
13.	(ca19-9 or ca-19* or muc1 or mucin* or muc* or antigen* or cea or heat shock protein* or hsp or microrna* or mrna* or mirna*).ti,ab.
14.	tumor antigen/ or ca 19-9 antigen/ or carbohydrate antigen/
15.	((ercp or cholangiopancreatograph* or cholangio-pancreatograph*) and (carcin* or cancer* or neoplas* or tumour* or tumor* or growth* or adenocarcin* or malig*)).ti,ab.
16.	((eus or ultrasonic endoscop* or endoscopic ultrasonograph* or endosonograph* or ultrasound* or scan* or ct* or tomograph* or mri* or magnetic resonance or mrcp or pet-ct) and (carcin* or cancer* or neoplas* or tumour* or tumor* or growth* or adenocarcin* or malig*)).ti,ab.
17.	(methylat* and (carcin* or cancer* or neoplas* or tumour* or tumor* or growth* or adenocarcin* or malig*)).ti,ab.
18.	or/12-17
19.	biological marker/
20.	endoscopic retrograde cholangiopancreatography/
21.	x-ray computed tomography/
22.	tomography/
23.	nuclear magnetic resonance/
24.	magnetic resonance cholangiopancreatography/
25.	exp computer assisted emission tomography/
26.	echography/ or endoscopic ultrasonography/
27.	or/19-26
28.	27 and (6 or 7)
29.	(11 or 18 or 28)
30.	Study filters RCT (A.3.2) or SR (A.3.3) or OBS (A.3.7)
31.	4 and 29 and 30
	Date parameters: see **Table 1**

1 **Cochrane search terms**

#1.	Standard population (G.2.1)
#2.	(mh ^pancreas)
#3.	(mh ^neoplasms)
#4.	(carcin* or cancer* or neoplas* or tumour* or tumor* or growth* or adenocarcin* or malig*):ti,ab

#5.	#2 and (#3 or #4)
#6.	(pancrea* next/6 (carcin* or cancer* or neoplas* or tumour* or tumor* or growth* or adenocarcin* or malig*)):ti,ab
#7.	(mh ^"carcinoma, pancreatic ductal")
#8.	(mh ^"pancreatic neoplasms")
#9.	(or #5-#8)
#10.	((carcin* or cancer* or neoplas* or tumour* or tumor* or growth* or adenocarcin* or malig*) next/6 (assess* or status or evaluat* or test* or screen* or investigat* or follow-up* or followup* or surveillance* or marker* or biomarker* or indicat* or parameter* or exam* or check-up* or checkup* or monitor* or measure*)):ti,ab
#11.	(ca19* or ca next 19* or muc1 or mucin* or muc* or antigen* or cea or heat shock protein* or hsp or microrna* or mrna* or mirna*):ti,ab
#12.	(mh ^"biomarkers, tumor")
#13.	(mh ^"antigens, tumor-associated, carbohydrate")
#14.	(mh ^"ca-19-9 antigen")
#15.	(mh ^"antigens, neoplasm")
#16.	((ercp or cholangiopancreatograph* or cholangio next pancreatograph*) and (carcin* or cancer* or neoplas* or tumour* or tumor* or growth* or adenocarcin* or malig*)):ti,ab
#17.	((eus or ultrasonic endoscop* or endoscopic ultrasonograph* or endosonograph* or ultrasound* or scan* or ct* or tomograph* or mri* or magnetic resonance or mrcp or pet-ct) and (carcin* or cancer* or neoplas* or tumour* or tumor* or growth* or adenocarcin* or malig*)):ti,ab
#18.	(methylat* and (carcin* or cancer* or neoplas* or tumour* or tumor* or growth* or adenocarcin* or malig*)):ti,ab
#19.	(or #10-#18)
#20.	(mh ^biomarkers)
#21.	(mh ^"cholangiopancreatography, endoscopic retrograde")
#22.	(mh ^tomography)
#23.	(mh ^"magnetic resonance imaging")
#24.	(mh ^"cholangiopancreatography, magnetic resonance")
#25.	(mh "tomography, emission-computed")
#26.	(mh ^ultrasonography)
#27.	(mh ^"tomography, x-ray computed")
#28.	(mh ^endosonography)
#29.	(or #20-#28)
#30.	#29 and (#3 or #4)
#31.	#1 and (#9 or #19 or #30)
	Date parameters: see **Table 1**

PsycINFO search terms

1.	Standard population (A.2.1)
2.	Excluded study designs and publication types (A.3.1)
3.	1 not 2
4.	Limit 3 to English language
	Date parameters: see **Table 1**

G.5 Health economics search terms

G.5.1 Health economic (HE) reviews

Economic searches were conducted in Medline, Embase and CRD

Medline & Embase search terms

1.	12.	Standard population (G.2.1)
2.	13.	Excluded study designs and publication types (G.3.1)
3.	14.	1 not 2
4.	15.	Limit 3 to English language
5.	16.	Study filter HE (G.3.4)
6.	17.	4 and 5
18.	19.	Date parameters: 2014 – 28 September 2017

CRD search terms

#1.	Standard population (G.2.1)
	Date parameters: Inception – 28 September 2017

G.5.2 Quality of life (QoL) reviews

Quality of life searches were conducted in Medline and Embase only

Medline & Embase search terms

1.	20.	Standard population (G.2.1)
2.	21.	Excluded study designs and publication types (G.3.1)
3.	22.	1 not 2
4.	23.	Limit 3 to English language
5.	24.	Study filter QOL (G.3.5)
6.	25.	4 and 5
26.	27.	Date parameters: 1946– 20 April 2016 (Medline)
28.	29.	Date parameters: 1974 – 20 April 2016 (Embase)

Appendix H: Clinical evidence tables

H.1 Patient information (qualitative evidence tables)

Study	Cronin 2012[257]
Aim	To develop an understanding and construct a meaning of living with chronic pancreatitis and, in so doing, to: illuminate the everyday contextualised and culturally situated lives of the participants, and explicate the meaning of living with chronic pancreatitis as a basis for understanding and interpretation by others.
Population	14 people living with chronic pancreatitis and 5 relatives Characteristics of those with pancreatitis: n= 14 ; male = 10/female = 4; age range 26 - 58 years. 7 participants had been living with chronic pancreatitis for 2 years or less, 4 for 2-5 years and 3 for more than 5 years.
Setting	All participants were under the care of a hospital-based pancreatic specialist in Ireland.
Study design	Qualitative unstructured interviews.
Methods and analysis	Participants recruited through the clinical nurse specialist (CNS) or the pancreas data controller employed for the service. The CNS distributed 14 invitations to patients with a diagnosis of chronic pancreatitis over a period of 8 months. The data controller sent 33 invitations to patients identified from the hospital database as having a primary or secondary diagnosis of chronic pancreatitis. Multiple unstructured audiotaped conversations were conducted with each participant over a period of several months. Biographical and contextual data were also collected. In addition 5 close family members were interviewed. A total of 41 individual or joint interviews took place. Interviews and diary entries were transcribed and returned to the participants for comment. A 4 step data analysis cycle was undertaken including labelling of codes and themes that represented the experiences of the participants: 1. gaining understanding of the whole text 2. Detailed analysis of text and identification of themes 3. Expansion of the unity of the understood sense 4. Representing shared understandings A sample of texts were blind coded, compared and reviewed by 2 researchers.
Findings	Most considered that the **information with which they left the hospital with was inadequate** in facilitating their understanding and management of the condition. It was only through attempting to assimilate chronic pancreatitis into their everyday lives that its implications became evident. Participants described this as 'coming to know' and marked the beginning of their health/illness transition. For example, despite following advice, most found that symptoms either did not resolve or recurred:

Study	Cronin 2012[257]
	" I pretty much thought that if I never drank again, then I'd never feel ill again… then it came around acutely the second time"
	Participants reported **differences** in the **information with which they were provided**. Most sought information from other sources such as the internet, family and friends, books/articles/mass media and fellow patients, but all reported that there was little 'lay' knowledge available about the condition: *"I'm still caught between what I've read and what the specialists have told me"* Although all knew that there was no cure for chronic pancreatitis and that the condition was a life-long one, few grasped fully the meaning of its progressive nature: *"No one has told me exactly why my pancreas had decided to continue the progression of the disease even though I'm not drinking*" Furthermore, most did not appear to have any knowledge of long-term complications associated with chronic pancreatitis
	Relationships with healthcare professionals were important mediators in facilitating or constraining their coping: "You go to casualty, you've got this triage battle… having to fight your case like a barrister for admittance into the hospital" "No matter what I said about he doesn't drink… I always thought they didn't believe me…" Family member (wife)
	All participants made **lifestyle modifications** which included abstaining from alcohol, adjusting diet and 'prioritising demands' and 'struggling to live well'. Continuous 'self-monitoring' provides participants with feedback on their body's response to illness and contributes to how they make decisions: "I've sort of made up my own diet… I've been eliminating anything that caused me to get sick"
	Participants also used **coping strategies** including 'emotional coping' and 'drawing on social resources' such as family, friends and professional agencies: "When I go to [Alcoholics Anonymous] meeting, I don't think I am going because I'm an alcoholic. I'm thinking of them as part and parcel of my daily routine of keeping well" "We're both very much in tune with how each other is feeling… she'll know when something is wrong'.

Study	Cronin 2012[257]
	Participants also kept regular and necessary contact with the healthcare system for the purpose of ongoing monitoring and being treated including strategies for managing what they perceive as shortcomings in the system.
Limitations and applicability of evidence	This paper is applicable to this review question, but also includes other themes on suffering, and adjusting and managing, which do not detail anything on information or support. Unclear as to what exact questions were asked.

H.2 Lifestyle interventions: stopping or reducing alcohol consumption

Study	Nordback 2009[803]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=120)
Countries and setting	Conducted in Finland; Setting: Tampere University Hospital
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 2 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients who had been admitted to the hospital for their first alcohol-associated acute pancreatitis (AP). The diagnosis of first AP was confirmed when the patient reported no previous symptoms, signs or findings of pancreatitis and now needed to be admitted to the hospital because of symptoms and signs consistent with AP together with serum amylase levels more than 3 times the upper normal range and/or AP in the abdominal imaging. Alcohol was considered a probable aetiology because of the association with alcohol consumption that was observed. Each patient or a family member reported heavy alcohol consumption, or heavy consumption was detected by the WHO-recommended Alcohol Use Disorder Identification Test (AUDIT) questionnaire. Lower consumption of alcohol still carries a risk of an association between alcohol consumption and AP, but was not accepted in this study for the association.
Exclusion criteria	Other possible aetiologies for AP were excluded by history, liver, chemistry, US, and serum calcium and lipids measurements

Study	Nordback 2009[803]
Recruitment/selection of patients	People admitted to hospital with first AP
Age, gender and ethnicity	Age - Mean (range): Control group 47 (18-73), intervention group 46 (25-71). Gender (M:F): 101/19. Ethnicity: not reported
Further population details	1. Aetiology of pancreatitis: Alcohol-related 2. Amount of alcohol consumed: High (as defined by national guidelines) (People with heavy consumption). 3. Previous pancreatic surgery: Not stated / Unclear 4. Severity of pancreatitis: Systematic review: mixed (Severe pancreatitis according to Atlanta criteria: control group n=15, intervention group n=18).
Extra comments	Baseline alcohol use in the control and intervention group, respectively: AUDIT scale (0-40) 20 (1-38), 22 (10-38); SADD scale (0-45) 13 (0-36), 15(0-36); self-reported alcohol consumption during past week, g of absolute ethanol 456 (72-2016), 590 (12-2184); calculated daily dose 65 (10-288), 84 (2-312); self-reported alcohol consumption during past 2 months, g of absolute ethanol 2880 (288-15456), 3372 (454-13248); calculated daily dose 48 (5-288), 56 (8-221)
Indirectness of population	No indirectness
Interventions	(n=59) Intervention 1: Structured programme to support people with both chronic and acute pancreatitis in stopping or reducing alcohol consumption. Repeated intervention: initial in-hospital intervention plus repeated similar interventions at 6-months intervals in the gastrointestinal outpatient clinic. The intervention consisted of a 30-minute conversation, which consisted of 3 portions: a) information on the toxic effect of alcohol on the pancreas: the patient should not use any alcohol because that is the only way to guarantee avoidance of recurrent alcoholic pancreatitis, because no other safe limit exists. 2) the need for a change in drinking habits and the patient's responsibility for the change: one feature was to try to go through the situations associated with alcohol use and to offer other kinds of behaviour models for those situations. 3) focus on social problems, which were very common and included unemployment, economic and marital difficulties, etc. Help was searched for depending on the respective need. Duration 2 years. Concurrent medication/care: Not stated Further details: 1. Type of programme: (n=61) Intervention 2: No structured programme/usual care (for example, general advice) . Initial in-hospital intervention. The intervention consisted of a 30-minute conversation, which consisted of 3 portions: a) information on the toxic effect of alcohol on the pancreas: the patient should not use any alcohol because that is the only way to guarantee avoidance of recurrent alcoholic pancreatitis, because no other safe limit exists. 2) the need for a change in drinking habits and the patient's responsibility for the change: one feature was to try to go through the situations associated with alcohol use and to offer other kinds of behaviour models for those situations. 3) focus on social problems, which were very common and included unemployment, economic and marital difficulties, etc. Help was searched for depending on the respective need. Duration 1 initial session plus 2 years follow-up. Concurrent medication/care: Not stated

Study	Nordback 2009[803]
	Further details: 1. Type of program:
Funding	Academic or government funding (The work was supported by the Pirkanmaa Hospital District Research Fund)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: STRUCTURED PROGRAMME TO SUPPORT PEOPLE WITH BOTH CHRONIC AND ACUTE PANCREATITIS IN STOPPING OR REDUCING ALCOHOL CONSUMPTION versus NO STRUCTURED PROGRAMME/USUAL CARE (FOR EXAMPLE, GENERAL ADVICE)

Protocol outcome 1: Admission to hospital at no time cut-off
- Actual outcome: Admissions to hospital (n of patients admitted for abdominal complaints) - ITT at 2 years; Group 1: 7/59, Group 2: 16/61
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - No details on ITT imputation?; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome: Admissions to hospital (n of patients admitted for abdominal complaints fulfilling criteria of recurrent AP) - ITT at 2 years; Group 1: 5/59, Group 2: 13/61
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - No details on ITT imputation?; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome: Admissions to hospital (n of patients admitted for abdominal complaints fulfilling criteria of recurrent AP) - ACA at 2 years; Group 1: 3/39, Group 2: 9/45
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - No details on ITT imputation?; Indirectness of outcome: No indirectness ; Group 1 Number missing: 26, Reason: 1 died; 3 other possible etiology (gallstones) detected, 3 were revealed to have had AP before inclusion, 5 did not attend one or more visits during the 2 year period, 14 did not attend the 2-year visit as scheduled (6 were phone interviewed); Group 2 Number missing: 21, Reason: 3 died; 18 did not attend the 2-year visit as scheduled (5 were phone interviewed)

Protocol outcome 2: Recurrent episodes of pancreatitis at no time cut-off
- Actual outcome: Number of episodes of recurrent AP - ACA at 36 months; Group 1: 7/39, Group 2: 14/45
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - No details on ITT imputation?; Indirectness of outcome: No indirectness ; Group 1 Number missing: 26, Reason: 1 died; 3 other possible etiology (gallstones) detected, 3 were revealed to have had AP before inclusion, 5 did not attend one or more visits during the 2 year period, 14 did not attend the 2-year visit as scheduled (6 were phone interviewed); Group 2 Number missing: 21, Reason: 3 died; 18 did not attend the 2-year visit as scheduled (5 were phone interviewed)
- Actual outcome: Number of episodes of recurrent AP - ITT at 36 months; Group 1: 9/59, Group 2: 20/61
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - No details on ITT imputation?; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Alcohol consumption at no time cut-off
- Actual outcome: Dependency on alcohol (SADD scale, 0-45) at 2 years; Mean; (median (range) for intervention and control group, respectively: 3 (0-28), 5 (0-26)));

Study	Nordback 2009[803]
	Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - No details on ITT imputation?; Indirectness of outcome: No indirectness ; Group 1 Number missing: 26, Reason: 1 died; 3 other possible etiology (gallstones) detected, 3 were revealed to have had AP before inclusion, 5 did not attend one or more visits during the 2 year period, 14 did not attend the 2-year visit as scheduled (6 were phone interviewed); Group 2 Number missing: 21, Reason: 3 died; 18 did not attend the 2-year visit as scheduled (5 were phone interviewed) - Actual outcome: Self-reported alcohol consumption (g of absolute alcohol during past week) at 2 years; Mean; (median (range) for intervention and control group, respectively: 0 (0-1126), 0(0-912))); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - No details on ITT imputation?; Indirectness of outcome: No indirectness ; Group 1 Number missing: 26, Reason: 1 died; 3 other possible etiology (gallstones) detected, 3 were revealed to have had AP before inclusion, 5 did not attend one or more visits during the 2 year period, 14 did not attend the 2-year visit as scheduled (6 were phone interviewed); Group 2 Number missing: 21, Reason: 3 died; 18 did not attend the 2-year visit as scheduled (5 were phone interviewed) - Actual outcome: Self-reported alcohol consumption (g of absolute alcohol during past 2 months) at 2 years; Mean; (median (range) for intervention and control group, respectively: 168(0-9408), 324(0-5880))); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - No details on ITT imputation?; Indirectness of outcome: No indirectness ; Group 1 Number missing: 26, Reason: 1 died; 3 other possible etiology (gallstones) detected, 3 were revealed to have had AP before inclusion, 5 did not attend one or more visits during the 2 year period, 14 did not attend the 2-year visit as scheduled (6 were phone interviewed); Group 2 Number missing: 21, Reason: 3 died; 18 did not attend the 2-year visit as scheduled (5 were phone interviewed) - Actual outcome: Alcohol consumption (AUDIT scale, 0-40) at 2 years; Mean; (median (range) for intervention and control group, respectively: 12(0-35), 11(0-33))); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - No details on ITT imputation?; Indirectness of outcome: No indirectness ; Group 1 Number missing: 26, Reason: 1 died; 3 other possible etiology (gallstones) detected, 3 were revealed to have had AP before inclusion, 5 did not attend one or more visits during the 2 year period, 14 did not attend the 2-year visit as scheduled (6 were phone interviewed); Group 2 Number missing: 21, Reason: 3 died; 18 did not attend the 2-year visit as scheduled (5 were phone interviewed)
Protocol outcomes not reported by the study	Quality of life at no time cut-off; Morbidity (for example, pancreatic function, pain) at no time cut-off; Mortality at no time cut-off; Alcohol consumption at no time cut-off; Nutritional status at no time cut-off; Morbidity at no time cut-off; Nutritional status at no time cut-off

H.3 Aetiology of acute pancreatitis

None

H.4 Aetiology of chronic pancreatitis

None

H.5 Diagnosing chronic pancreatitis

Study	Ketwaroo 2013[591]
Study type	Retrospective cohort
Number of studies (number of participants	1 (n=116)
Country and setting	USA; Beth Israel Deaconess Medical Centre Boston, Massachusetts (tertiary referral centre)
Funding	No financial support
Duration of study	Data relative to 1995-2008 years
Age, gender, ethnicity	Characteristics of SPTF positive and negative groups, respectively: mean age (SD) 45.5 (13.3), 45.5 (11.1) years; males 20%, 32.9%; white ethnicity 70%, 77.1%.
Patient characteristics	Patients with a clinical history highly suggestive of chronic pancreatitis, that is, epigastric pain worse with eating, and radiating to the back, and with prior work-up that usually includes a negative esophagogastroduedonoscopy, gastric emptying study; abdominal ultrasound, and laboratory testing. All patients had normal cross-sectional or endoscopic pancreatic imaging before referral for SPFT. All patients were evaluated by a Pancreas specialist before performing SPFT.
Index test	Secretin pancreatic function test (SPFT): standard esophagogastroduodenoscopy was performed and a guidewire was placed through the endoscope under fluoroscopic guidance beyond the ligament of Treitz. The endoscope was removed keeping the guidewire in place, and a double-lumen gastroduodenal tube or Dreiling tube with gastric and duodenal ports was placed over the wire with the tip of the tube in the third to fourth portion of the duodenum. The guidewire was then removed after placement of the Dreiling tube was confirmed fluoroscopically. IV human secretin was administered to stimulate the secretion of bicarbonate. AN initial test dose of 0.1 ml was given and if there was no evidence of an adverse or allergic reaction, and the full dose of 0/2 mcg/kg was administered over 2 min. In the recovery room, the gastric port was attached to continuous suction and the gastric aspirate was discarded. The duodenal juice was continuously aspirated from the duodenal port of the Dreiling tube with collection representing 15, 30, 45 and 60 minute intervals after the secretin had been administered. Analysis for bicarbonate concentration was performed on all samples using the hospital autoanalyser. A positive test was defined as a peak bicarbonate

Study	Ketwaroo 2013[591]
	level of <75 mEq/L in any of the duodenal fluid collections following administration of IV secretin. A pH of about 7 was required to ensure that the aspirated duodenal fluid was not contaminated by gastric contents.
Reference standard	Patient follow-up: medical records of patients who had undergone SPFT were reviewed for evidence of subsequent development of findings consistent with chronic pancreatitis by imaging or pathology from surgical specimens. In addition, records were also reviewed to determine if chronic pancreatitis had been conclusively ruled out, and if an alternative diagnosis had been made. Patients were contacted by telephone, if there was insufficient data based on medical record review, including outside record if available. All subsequent relevant radiology and endoscopy reports were reviewed for documentation of findings consistent with chronic pancreatitis. Imaging was read by gastrointestinal radiology attendings; positive findings were reviewed and confirmed by an independent gastrointestinal radiologist who was not blinded to the SPFT data. Imaging finding consistent with CP included the following: i) CT: findings of parenchymal and ductal calcifications, parenchymal atrophy, dilated main pancreatic duct, and dilated side branches; atrophy and hypertrophy were evaluated. Patients with only fullness of the pancreatic head were considered negative; ii) ERCP and MRI/MRCP: findings per Cambridge classification; iii)EUS, based on a 9-points based scoring system of pancreatic ductal and parenchymal changes; patients were considered to have CP with at least 5 criteria. Pathology confirmed changes consistent with CP such as periductal fibrosis, duct dilation, intralobular inflammation and atrophy; this was reviewed by a gastrointestinal pathologist who was not blinded to clinical data.
Target condition	Chronic pancreatitis in people presenting with chronic abdominal pain, and normal or uncertain CT or ultrasound scan or upper GI endoscopy

Results: 2x2 table calculated using author-reported sens, spec and study prevalence

Secretin pancreatic function test (SPFT): cut-off peak bicarbonate level of <75 mEq/L

TP: 9

FP: 11

FN: 2

TN: 68

Sensitivity: 0.82

Specificity: 0.86

Number of people analysed: 90

Prevalence 0.12

PPV 0.45

Study	Ketwaroo 2013[591]
NPV 0.97 Positive likelihood ratio 5.88 Negative likelihood ratio 0.21	
General limitations (according to QUADAS-2): patients were enrolled consecutively. It is unclear whether the index test results were interpreted without knowledge of the results of the reference test. The reference standard results were interpreted with knowledge of the results of the index test (non-blinded assessors). Duration of interval between index test and reference standard test is unclear. Not all patients received the same reference standard (clinical follow-up including a number of imaging test). Not all people were included in the final analysis (26 lost to follow-up, no further details).	

H.6 Type of intravenous fluid for resuscitation in people with acute pancreatitis

Study	Aboelsoud 2016 [4]
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=198)
Countries and setting	Conducted in USA; Setting: Not reported
Line of therapy	Adjunctive to current care
Duration of study	Not clear:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis based on the ICD-9 code and confirmed by elevated serum amylase and/or lipase (>three times the upper limit of normal), and/or finding on CT abdomen consistent with AP.
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Diagnosis based on the ICD-9 code and confirmed by elevated serum amylase and/or lipase (>three times the upper limit of normal), and/or finding on CT abdomen consistent with AP.
Exclusion criteria	Patients who received colloids were excluded
Recruitment/selection of patients	Subjects were identified on the Multi-parameter Intelligent Monitoring in Intensive Care research database
Age, gender and ethnicity	Age - Range: 44-74. Gender (M:F): 100:98. Ethnicity: LR group: Caucasian: 78%, African American: 10%, Other: 12% IS group: Caucasian: 76%, African American: 13%, Other: 11%

Further population details	1. Age: <75 years 2. Severity of pancreatitis (as defined by study): Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=68) Intervention 1: Balanced crystalloids. Patients received lactated Ringers solution. If a patient received both LR and IS, they were assigned to the group of predominant fluid amount. Duration 72 hours. Concurrent medication/care: Not reported (n=130) Intervention 2: Saline. Dose/quantity, brand name, extra details. Duration 72 hours. Concurrent medication/care: Not reported
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LACTATED RINGERS SOLUTION versus ISOTONIC SALINE Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year - Actual outcome for Adults (>16 years): Length of stay in CCU at During admission; Group 1: mean 6.2 days (SD 6.9); n=68, Group 2: mean 4.2 days (SD 4.49); n=130; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 2: Mortality at <1 year - Actual outcome for Adults (>16 years): Mortality at During admission; Group 1: 39/68, Group 2: 21/130; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Systemic complications (persistent organ failure; fluid overload) at during admission; Serious adverse events at during admission; Length of stay (in intensive therapy unit or hospital) at <1 year; Local complications (fluid collection; cystic collection; pancreas necrosis; peri-pancreatic necrosis; local infection) at <6 months

Study	De-Madaria 2017[271]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=40)
Countries and setting	Conducted in Spain; Setting: Not reported
Line of therapy	Adjunctive to current care
Duration of study	Not clear
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: AP was defined as two of the following three criteria: (1) characteristic abdominal pain, (2) serum amylase and/or lipase greater than three times the upper limit of normal, and (3) cross-sectional abdominal imaging demonstrating changes consistent with AP
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients aged 18 years or older who initially presented to the emergency room and were subsequently admitted to the center with a first episode of AP
Exclusion criteria	The exclusion criteria were: time from pain onset to randomization >24 hours, known history of renal disease (basal creatinine >2mg/dl, patient under chronic hemodialysis), greater than New York Heart Association class II heart failure, chronic lung disease requiring supplemental home oxygen, active acute infection (including acute cholecystitis and acute cholangitis), hypernatremia (serum sodium>145mEq/l) or hyponatremia (<135mEq/l), rhabdomyolysis, metastatic malignant disease, autoimmune diseases associated with inflammation (including inflammatory bowel disease), chronic infection (e.g. human immunodeficiency virus (HIV) and tuberculosis).
Recruitment/selection of patients	Patients who presented to the emergency room
Age, gender and ethnicity	Age – Mean (SD): Lactaded Ringer's group 63.8 (19.1), saline group 61.4 (15.5). Gender (M:F): 19:21. Ethnicity: Not reported
Further population details	1. Age: <75 years 2. Severity of pancreatitis (as defined by study): Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=68) Intervention 1: Balanced crystalloids. Patients with hematocrit >44% and/or two or more SIRS criteria and/or blood urea nitrogen>20 mg/dl and/or signs of dehydration or hypovolemia received more vigorous resuscitation: 15 ml/kg of the study fluid in 60 minutes immediately after randomization, and then 1.2 ml/kg/hour of the study fluid for three days. All other patients received 10 ml/kg of the study fluid in 60 minutes immediately after randomization, and then 1 ml/kg/hour of the study fluid for three days. In patients with oliguria or hypotension, the attending

	physician could administer boluses of 500 to 1000 ml of the study fluid in 30 to 60 minutes as needed. In case of fluid overload, the attending physician could decrease the study fluid volume rate and use diuretics as needed. Duration 3 days. Concurrent medication/care: All patients received 1000 ml of 10% dextrose solution in addition to the study fluid. (n=130) Intervention 2: Saline. Normal saline. Duration 3 days. Concurrent medication/care: All patients received 1000 ml of 10% dextrose solution in addition to the study fluid.
Funding	The RCT was funded by AIGPA, an association of researchers in gastroenterology from the province of Alicante, Spain. In vitro experiments were supported by a national Spanish public grant from Instituto de Salud Carlos III; L.B. is supported by a predoctoral fellowship from Generalitat de Catalunya (AGAUR, FI DGR 2013).
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LACTATED RINGERS SOLUTION versus ISOTONIC SALINE Protocol outcome 1: Persistent organ failure at <1 year - Actual outcome for Adults (>16 years): Systemic complications (persistent organ failure; fluid overload) at during admission; Group 1: 0/19, Group 2: 1/21 Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 2: Mortality at <1 year - Actual outcome for Adults (>16 years): Mortality at During admission; Group 1: 0/19, Group 2: 1/21; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 3: CCU admission at <1 year - Actual outcome for Adults (>16 years): Serious adverse events at during admission; Group 1: 0/19, Group 2: 1/21 Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 3: (peri) pancreatic necrosis at <1 year - Actual outcome for Adults (>16 years): Local complications (fluid collection; cystic collection; pancreas necrosis; peri-pancreatic necrosis; local infection) at <6 months; Group 1: 0/19, Group 2: 1/21 Risk of bias: Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year

Study	Wu 2011[1040]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=40)
Countries and setting	Conducted in USA; Setting: Brigham and Women's Hospital, Faulkner Hospital and Dartmouth-Hitchcock Medical Center
Line of therapy	Adjunctive to current care
Duration of study	Unclear
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis was confirmed by the presence of 2 or more of the following criteria: epigastric abdominal pain, elevation in serum amylase and/or lipase level greater than 3 times the upper limit of normal, confirmatory findings on cross-sectional imaging.
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Not reported
Exclusion criteria	Patients were excluded from participation if they met any of the following criteria: known history of severe cardiovascular, respiratory, renal, hepatic, hematologic, or immunologic disease defined as greater than New York Heart Association class II heart failure, active myocardial ischaemia or cardiovascular intervention within previous 60 days, history of cirrhosis or chronic kidney disease with creatinine clearance <40 mL/min, or chronic obstructive pulmonary disease with requirement for home oxygen. Individuals were also excluded from participation if they had evidence of a concurrent metabolic or physiological derangement that required specific fluid management including sepsis (presence of suspected or confirmed infection in the setting of SIRS), hypernatremia (serum sodium <135 mEq/L), or rhabdomyolysis. Patients transferred from an outside hospital were excluded from participation. Patients with a history of metastatic malignancy, active inflammatory bowel disease, autoimmune conditions such as systemic lupus erythematosus, autoimmune pancreatitis, giant cell arteritis, rheumatoid arthritis, or chronic infectious disease including human immunodeficiency virus or tuberculosis were excluded because of potential confounding related to markers of systemic inflammation.
Recruitment/selection of patients	Eligible patients were identified in real time by a direct paging system from the clinical laboratory at each institution on the basis of lipase levels. Patients were approached either in the emergency department or on the general medical ward for study participation.
Age, gender and ethnicity	Age - Median (IQR): LR group: 50 (40, 73), NS group: 54 (40, 60). Gender (M:F): 22:18. Ethnicity: Not reported
Further population details	1. Age : <75 years 2. Severity of pancreatitis (as defined by study): Not stated / Unclear
Extra comments	LR group: Etiology - Biliary (42%), Alcohol (11%), Post-ERCP (11%), Other (36%); duration of symptoms (median, h): 8;

	SIRS: (32%), BISAP: (median): 0, APACHE II (median): 3 NS group: Etiology - Biliary (48%), Alcohol (19%), Post-ERCP (5%), Other (28%); duration of symptoms (median, h): 6; SIRS: (19%), BISAP: (median): 1, APACHE II (median): 3
Indirectness of population	No indirectness
Interventions	(n=19) Intervention 1: Balanced crystalloids. Patients received either 20 mL/kg or standard resuscitation of lactated Ringer's solution controlled by their treating physicians. Duration Unclear. Concurrent medication/care: Not reported (n=21) Intervention 2: Saline. Patients received either 20 mL/kg or standard resuscitation of normal saline controlled by their treating physicians. Duration Unclear. Concurrent medication/care: Not reported
Funding	Academic or government funding (Dr Wu is supported by a 2009 Junior Faculty Career Development Award from the American College of Gastroenterology)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: RINGERS LACTATED SOLUTION versus SALINE

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome for Adults (>16 years): Length of stay at Unclear; Risk of bias: ; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality at <1 year
- Actual outcome for Adults (>16 years): Mortality at Unclear; Group 1: 0/19, Group 2: 0/21; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 3: Local complications (fluid collection; cystic collection; pancreas necrosis; peri-pancreatic necrosis; local infection) at <6 months
- Actual outcome for Adults (>16 years): Necrosis at Unclear; Group 1: 0/19, Group 2: 1/21; Risk of bias: Very high; Indirectness of outcome: No indirectness
- Actual outcome for Adults (>16 years): Infection at Unclear; Group 1: 0/19, Group 2: 2/21; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 4: Systemic complications (persistent organ failure; fluid overload) at during admission
- Actual outcome for Adults (>16 years): Respiratory organ failure at Unclear; Group 1: 0/19, Group 2: 1/21; Risk of bias: Very high; Indirectness of outcome: No indirectness
- Actual outcome for Adults (>16 years): Shock at Unclear; Group 1: 0/19, Group 2: 1/21; Risk of bias: Very high; Indirectness of outcome: No indirectness
- Actual outcome for Adults (>16 years): Renal failure at Unclear; Group 1: 1/19, Group 2: 2/21; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 5: Serious adverse events at during admission
- Actual outcome for Adults (>16 years): Transfer to CCU at Unclear; Group 1: 1/19, Group 2: 3/21; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcomes not reported by the study	Quality of life at <1 year; Length of stay (in intensive therapy unit or hospital) at <1 year

H.7 Speed of intravenous fluid for resuscitation in people with acute pancreatitis

Study	Buxbaum 2017[178]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=60)
Countries and setting	Conducted in USA; Setting: Emergency department
Line of therapy	Unclear
Duration of study	Intervention + follow up: 60 hours
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Acute pancreatitis, defined by two of three criteria: epigastric abdominal pain; elevated amylase or lipase >3 times the upper limit of normal; or imaging consistent with acute pancreatitis. Eligible patients were required to be evaluated, consented, and randomised within 4 hours of diagnosis.
Exclusion criteria	Systemic inflammatory response syndrome; New York Heart Associated Class II or greater heart failure; decompensated cirrhosis (Child's Class B or C); hypotension (systolic blood pressure <90mm Hg); renal insufficiency (Cr>2mg/dl at time of randomisation) or dialysis requirement; respiratory insufficiency (oxygen saturation <90% on room air); hyponatremia (sodium <135meq/l); clinical signs of volume overload (peripheral edema, pulmonary rales, and acites); gastrointestinal bleeding; pregnancy; and pancreatitis following an endoscopic, radiographic or surgical procedure. Also patients who had pancreatic abscess or necrosis on imaging
Recruitment/selection of patients	Not reported

Age, gender and ethnicity	Age - Mean (SD): Agressive group: 44.4 (13.7); standard group: 45.3 (12.3). Gender (M:F): 45:15. Ethnicity: Hispanic 75.5%
Further population details	1. Age : <75 years 2. Severity of pancreatitis (as defined by study): Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=27) Intervention 1: 'Aggressive' fluid administration - 'Aggressive' as defined by studies. Aggressive intravenous hydration with Lactated Ringer's solution. Patients received a 20ml/kg bolus followed by infusion at 3ml/kg/h. This aggressive rate was based on a randomised trial of goal directed versus standard fluids for pancreatitis . Duration 12 hours. Concurrent medication/care: At 12 hours after randomisation, the patients were examined by the study team and laboratory testing was performed. This included a complete blood count, BUN, creatinine and electrolytes. If the hematocrit, BUN, or creatinine level had increased above its baseline value, the patient, regardless of study assignment was given a 20ml/kg LR bolus followed by LR at 3ml/kg/h; this was done if any one of the three laboratory tests increased even if the others stayed the same or decreased. If the laboratory tests did not increase and the abdominal pain decreased on the visual analogue scale, a clear liquid diet was also initiated. Patients were reassessed and fluid management was determined in the same way at subsequent checkpoints at 24 and 36 hours. . Indirectness: No indirectness (n=33) Intervention 2: 'Conservative' fluid administration - 'Conservative' as defined by studies. Patients randomised to standard hydration were given a 10ml/kg bolus followed by infusion at 1.5ml/kg/h. This rate was based on a discussion with the authors of a prior trial. . Duration 12 hours. Concurrent medication/care: At 12 hours after randomisation, the patients were examined by the study team and laboratory testing was performed. This included a complete blood count, BUN, creatinine and electrolytes. If the hematocrit, BUN, or creatinine level had increased above its baseline value, the patient, regardless of study assignment was given a 20ml/kg LR bolus followed by LR at 3ml/kg/h; this was done if any one of the three laboratory tests increased even if the others stayed the same or decreased. If the laboratory tests did not increase and the abdominal pain decreased on the visual analogue scale, a clear liquid diet was also initiated. Patients were reassessed and fluid management was determined in the same way at subsequent checkpoints at 24 and 36 hours. . Indirectness: No indirectness
Funding	Academic or government funding (Supported by NIH/NCRR SC CTSI Grant)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 'AGGRESSIVE' AS DEFINED BY STUDIES versus 'CONSERVATIVE' AS DEFINED BY STUDIES Protocol outcome 1: Mortality at <1 year - Actual outcome for Adults (>16 years): Mortality at 3 days; Group 1: 0/27, Group 2: 1/33 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in number of people with white blood cells >12x10^9/l (44% versus 24%); Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Local complications (fluid collection; cystic collection; pancreas necrosis; peri-pancreatic necrosis; local infection) at <6 months - Actual outcome for Adults (>16 years): Hemoconcentration at 36 hours; Group 1: 3/27, Group 2: 12/33 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in number of people with white blood cells >12x10^9/l (44% versus 24%); Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Systemic complications (persistent organ failure; fluid overload) at during admission - Actual outcome for Adults (>16 years): Development of SIRS at 36 hours; Group 1: 4/27, Group 2: 9/33 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in number of people with white blood cells >12x10^9/l (44% versus 24%); Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults (>16 years): Persistent SIRS at 36 hours; Group 1: 2/27, Group 2: 7/33 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in number of people with white blood cells >12x10^9/l (44% versus 24%); Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Serious adverse events at during admission - Actual outcome for Adults (>16 years): Severe pancreatitis at 36 hours; Group 1: 0/27, Group 2: 1/33 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in number of people with white blood cells >12x10^9/l (44% versus 24%); Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life at <1 year; Achievement of pre-specified target for resuscitation (eg target central venous pressure, urine output, lactate levels, PiCCO measurements) at <1 year; Length of stay (in intensive therapy unit or hospital) at <1 year; Length of stay (in intensive therapy unit or hospital) at <1 year

Study	De-Madaria 2011[272]
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=247)
Countries and setting	Conducted in Spain; Setting: The Pancreatic unit of Hospital General Universitario of Alicante
Line of therapy	Adjunctive to current care
Duration of study	Intervention time: 2.5 years
Method of assessment of guideline condition	Unclear method of assessment/diagnosis
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Adult patients (aged 18 and over) with AP admitted to the Pancreatic unit of Hospital General Universitario of Alicante
Exclusion criteria	Not reported
Recruitment/selection of patients	All patients admitted to the unit with AP were enrolled
Age, gender and ethnicity	Age - Range: 50-81. Gender (M:F): 135:112. Ethnicity: Not reported
Further population details	1. Age : Systematic review: mixed 2. Severity of pancreatitis (as defined by study): Systematic review: mixed

Extra comments	Group A: Etiology - Gallstones: 33, Alcohol: 7, Idiopathic: 15, Other: 8, SIRS: 31, APACHE II >8: 25 Group B: Etiology - Gallstones: 71, Alcohol: 19, Idiopathic: 14, Other: 19, SIRS: 31, APACHE II >8: 44 Group C: Etiology - Gallstones: 30, Alcohol: 13, Idiopathic: 9, Other: 8, SIRS: 27, APACHE II >8: 24
Indirectness of population	No indirectness
Interventions	(n=61) Intervention 1: 'Aggressive' fluid administration - 'Aggressive' as defined by studies. Participants were given >4.1 L during the initial 24 hours of admission. Duration During admission. Concurrent medication/care: All other treatment followed the centers protocol for general management of AP. (n=123) Intervention 2: 'Aggressive' fluid administration - 'Aggressive' as defined by studies. Participants were given 3.1-4.1 L during the initial 24 hours of admission. Duration During admission. Concurrent medication/care: All other treatment followed the centers protocol for general management of AP. (n=63) Intervention 3: 'Conservative' fluid administration - 'Conservative' as defined by studies. Participants were given <3.1 L during the initial 24 hours of admission. Duration During admission. Concurrent medication/care: All other treatment followed the centers protocol for general management of AP.
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: >4.1L versus 3.1-4.1 L

Protocol outcome 1: Local complications (fluid collection; cystic collection; pancreas necrosis; peri-pancreatic necrosis; local infection) at <6 months
- Actual outcome for Adults (>16 years): Necrosis at Unclear; Group 1: 12/61, Group 2: 13/123; Risk of bias: Very high ; Indirectness of outcome: No indirectness
- Actual outcome for Adults (>16 years): Acute collections at Unclear; Group 1: 32/61, Group 2: 40/123; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 2: Systemic complications (persistent organ failure; fluid overload) at during admission

- Actual outcome for Adults (>16 years): Persistent organ failure at Unclear; Group 1: 8/61, Group 2: 2/123; Risk of bias: Very high; Indirectness of outcome: No indirectness RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: >4.1L versus <3.1L Protocol outcome 1: Local complications (fluid collection; cystic collection; pancreas necrosis; peri-pancreatic necrosis; local infection) at <6 months - Actual outcome for Adults (>16 years): Necrosis at Unclear; Group 1: 12/61, Group 2: 7/62; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome for Adults (>16 years): Acute collections at Unclear; Group 1: 32/61, Group 2: 14/63; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 2: Systemic complications (persistent organ failure; fluid overload) at during admission - Actual outcome for Adults (>16 years): Persistent organ failure at Unclear; Group 1: 8/61, Group 2: 4/63; Risk of bias: Very high; Indirectness of outcome: No indirectness RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 3.1-4.1 L versus <3.1L Protocol outcome 1: Local complications (fluid collection; cystic collection; pancreas necrosis; peri-pancreatic necrosis; local infection) at <6 months - Actual outcome for Adults (>16 years): Necrosis at Unclear; Group 1: 13/123, Group 2: 7/62; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome for Adults (>16 years): Acute collections at Unclear; Group 1: 40/123, Group 2: 14/63; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 2: Systemic complications (persistent organ failure; fluid overload) at during admission - Actual outcome for Adults (>16 years): Persistent organ failure at Unclear; Group 1: 2/123, Group 2: 8/61; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Mortality at <1 year; Achievement of pre-specified target for resuscitation (eg target central venous pressure, urine output, lactate levels, PiCCO measurements) at <1 year; Serious adverse events at during admission; Length of stay (in intensive therapy unit or hospital) at <1 year; Length of stay (in intensive therapy unit or hospital) at <1 year

Study	Eckerwall 2006[331]
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=99)
Countries and setting	Conducted in Sweden; Setting: Lund University Hospital
Line of therapy	Adjunctive to current care
Duration of study	Other: 9 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Organ failure and/or local complications (necrosis, organ failure or pancreatic abscess) defined according to the Atlanta classification system.
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Organ failure and/or local complications (necrosis, organ failure or pancreatic abscess) defined according to the Atlanta classification system.
Exclusion criteria	Patients with pancreatic fluid collection alone were excluded.
Recruitment/selection of patients	Patients were identified from the hospital records by the aid of a computer search of the patient database.
Age, gender and ethnicity	Age - Mean (SD): 60 (18). Gender (M:F): 64:35. Ethnicity: Not reported
Further population details	1. Age : <75 years 2. Severity of pancreatitis (as defined by study): Severe pancreatitis
Extra comments	Weight - Male: 86 (17), Female: 77 (16) Etiology - Biliary: 31, Alcohol: 30, Other: 38

Indirectness of population	No indirectness
Interventions	(n=32) Intervention 1: 'Aggressive' fluid administration - 'Aggressive' as defined by studies. Patients received 4000 mL or more during the first 24 hours of admission. Duration 24 hours. Concurrent medication/care: 69/95 of the patients received TPN (n=67) Intervention 2: 'Conservative' fluid administration - 'Conservative' as defined by studies. Patients received less than 4000 mL of fluid during the first 24 hours of admission. Duration 24 hours. Concurrent medication/care: 69/95 of the patients received TPN
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 'AGGRESSIVE' AS DEFINED BY STUDIES versus 'CONSERVATIVE' AS DEFINED BY STUDIES Protocol outcome 1: Systemic complications (persistent organ failure; fluid overload) at during admission - Actual outcome for Adults (>16 years): Respiratory complications at During admission; Group 1: 21/32, Group 2: 36/67; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome for Adults (>16 years): Pulmonary oedema at During admission; Group 1: 0/32, Group 2: 0/67; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Mortality at <1 year; Local complications (fluid collection; cystic collection; pancreas necrosis; peri-pancreatic necrosis; local infection) at <6 months; Achievement of pre-specified target for resuscitation (eg target central venous pressure, urine output, lactate levels, PiCCO measurements) at <1 year; Serious adverse events at during admission; Length of stay (in intensive therapy unit or hospital) at <1 year; Length of stay (in intensive therapy unit or hospital) at <1 year

Study	Gardner 2009[389]
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=45)
Countries and setting	Conducted in USA; Setting: Mayo Medical Center (Rochester, Minn., USA)
Line of therapy	Adjunctive to current care
Duration of study	Other: 15 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis was based on at least two of the following: admitting serum amylase and/or lipase activity greater than three times the upper limit of normal, symptoms consistent with acute pancreatitis, or supporting cross-sectional imaging
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Age ≥ 18 years, acute pancreatitis as the primary admitting diagnosis, diagnosis of acute pancreatitis based on at least two of the following: admitting serum amylase and/or lipase activity greater than three times the upper limit of normal, symptoms consistent with acute pancreatitis, or supporting cross-sectional imaging, and diagnosis of severe acute pancreatitis as per the Atlanta Classification.
Exclusion criteria	All patients transferred from other institutions were excluded from the study. Patients in whom documentation of IV fluid volumes was incomplete from the time of presentation to the emergency room were also excluded.
Age, gender and ethnicity	Age - Mean (SD): Early group: 53 (13) Late group: 57 (17). Gender (M:F): 29:16. Ethnicity: Not reported

Further population details	1. Age : <75 years 2. Severity of pancreatitis (as defined by study): Severe pancreatitis
Extra comments	Early group - BMI: 28 (4), Charlson score: 2.2 (2.1), Etiology - Gallstone: 4, Alcoholic: 4, Post-ERCP: 5, Idiopathic: 2, Other: 2, Admission hematocrit: 35% Late group - BMI: 29 (6), Charlson score: 3.3 (2.6), Etiology - Gallstone: 14, Alcoholic: 5, Post-ERCP: 2, Idiopathic: 1, Medication: 2, Other: 4, Admission hematocrit: 39%
Indirectness of population	No indirectness
Interventions	(n=17) Intervention 1: 'Aggressive' fluid administration - 'Aggressive' as defined by studies. Participants received ≥33% of their cumulative 72-hour intravenous fluid within the first 24 hours after presentation to the emergency room. Total volume in the first 72 hours: 12, 190 mL. The mean rate of IV fluid resuscitation in the first 24 hours was 203 mL/h.. Duration 72 hours. Concurrent medication/care: All patients were given crystalloid solutions for their resuscitation fluids; 32 received 0.9% NaCl, 9 received 5% Dextrose with 0.45% NaCl, and 4 received lactated Ringer's solution. (n=28) Intervention 2: 'Conservative' fluid administration - 'Conservative' as defined by studies. Participants received <33% of their cumulative 72-hour intravenous fluid within the first 24 hours after presentation to the emergency room. Total volume in the first 72 hours: 7, 664 mL. The mean rate of IV fluid resuscitation in the first 24 hours was 71 mL/h.. Duration 72 hours. Concurrent medication/care: Participants received ≥33% of their cumulative 72-hour intravenous fluid within the first 24 hours after presentation to the emergency room.
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EARLY RESUSCITATION versus LATE RESUSCITATION

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome for Adults (>16 years): Duration of stay at During admission; Group 1: mean 40 days (SD 66); n=17, Group 2: mean 37 days (SD 70); n=28; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality at <1 year - Actual outcome for Adults (>16 years): Mortality at During admission; Group 1: 0/17, Group 2: 5/28; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 3: Local complications (fluid collection; cystic collection; pancreas necrosis; peri-pancreatic necrosis; local infection) at <6 months - Actual outcome for Adults (>16 years): Necrosis at During admission; Group 1: 8/17, Group 2: 11/28; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome for Adults (>16 years): Development of a pseudocyst or abscess at During admission; Group 1: 11/17, Group 2: 20/28; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 4: Systemic complications (persistent organ failure; fluid overload) at during admission - Actual outcome for Adults (>16 years): Persistent organ failure at During admission; Group 1: 6/17, Group 2: 12/28; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome for Adults (>16 years): SIRS at During admission; Group 1: 15/17, Group 2: 20/28; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Serious adverse events at during admission; Length of stay (in intensive therapy unit or hospital) at <1 year; Achievement of pre-specified target for resuscitation (eg target central venous pressure, urine output, lactate levels, PiCCO measurements) at <1 year

Study	Singh 2017[999]
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=1010)
Countries and setting	Conducted in Spain, USA; Setting: Four institutions
Line of therapy	Adjunctive to current care
Duration of study	Not clear:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Defined according to the revised Atlanta classification
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Only adult (>18 years of age) patients with first or recurrent acute pancreatitis were included
Exclusion criteria	Patients with chronic pancreatitis, with missing or incomplete data regarding fluid administration in the ER, those undergoing chronic hemodialysis, and those transferred from outside institutions were excluded from the analysis
Recruitment/selection of patients	Consecutive patients
Age, gender and ethnicity	Age - Mean (SD): 53.6 (19.6). Gender (M:F): 508:502. Ethnicity: Not reported
Further population details	1. Age : <75 years 2. Severity of pancreatitis (as defined by study): Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=314) Intervention 1: 'Aggressive' fluid administration - 'Aggressive' as defined by studies. Aggressive fluid volume administration in the emergency room, defined as >100ml from the time of arrival at the ER to 4 hours after diagnosis

	of acute pancreatitis. Duration 4 hours. Concurrent medication/care: Not reported. Indirectness: No indirectness (n=427) Intervention 2: 'Conservative' fluid administration - 'Conservative' as defined by studies. Moderate fluid volume administered in emergency room, defined as 500-1000ml. Duration 4 hours. Concurrent medication/care: Not reported. Indirectness: No indirectness (n=269) Intervention 3: 'Conservative' fluid administration - 'Conservative' as defined by studies. Non-aggressive fluid volume administered in emergency room, defined as <500ml. Duration 4 hours. Concurrent medication/care: Not reported. Indirectness: No indirectness
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 'AGGRESSIVE' AS DEFINED BY STUDIES versus 'CONSERVATIVE' AS DEFINED BY STUDIES (MODERATE)

Protocol outcome 1: Mortality at <1 year
- Actual outcome for Adults (>16 years): Mortality at Not reported; Group 1: 8/314, Group 2: 7/427
Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Local complications (fluid collection; cystic collection; pancreas necrosis; peri-pancreatic necrosis; local infection) at <6 months
- Actual outcome for Adults (>16 years): Local complications at Not reported; Group 1: 50/314, Group 2: 19/427
Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Systemic complications (persistent organ failure; fluid overload) at during admission
- Actual outcome for Adults (>16 years): Persistent organ failure at Not reported; Group 1: 15/314, Group 2: 19/427
Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 'AGGRESSIVE' AS DEFINED BY STUDIES versus 'CONSERVATIVE' AS DEFINED BY STUDIES (NON-AGRESSIVE)

Protocol outcome 1: Mortality at <1 year - Actual outcome for Adults (>16 years): Mortality at Not reported; Group 1: 8/314, Group 2: 8/269 Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Local complications (fluid collection; cystic collection; pancreas necrosis; peri-pancreatic necrosis; local infection) at <6 months - Actual outcome for Adults (>16 years): Local complications at Not reported; Group 1: 50/314, Group 2: 51/269 Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Systemic complications (persistent organ failure; fluid overload) at during admission - Actual outcome for Adults (>16 years): Persistent organ failure at Not reported; Group 1: 15/314, Group 2: 19/269 Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life at <1 year; Achievement of pre-specified target for resuscitation (eg target central venous pressure, urine output, lactate levels, PiCCO measurements) at <1 year; Serious adverse events at during admission; Length of stay (in intensive therapy unit or hospital) at <1 year; Length of stay (in intensive therapy unit or hospital) at <1 year

Study	**Szabo 2015[1049]**
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=201)
Countries and setting	Conducted in USA; Setting: Cincinnati Children's Hospital Medical Center
Line of therapy	Adjunctive to current care
Duration of study	Other: 5 years
Method of assessment of guideline condition	Unclear method of assessment/diagnosis
Stratum	Children (<16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients admitted to general paediatrics or the gastroenterology services, mild AP as defined by the Atlanta criteria (meeting 2 or 3 criteria: symptoms of pain, vomiting; elevated lipase and/or amylase at ≥3 times the normal upper limit; imaging findings of AP), or 0-21 years old at time of admission.
Exclusion criteria	Patients with AP and SAP on admission: multisystem organ failure, SIRS, local pancreatic complications (such as necrosis, hemorrhage, pseudocyst formation), or respiratory complications; and patients with pancreatitis related to trauma, gallstone pancreatitis, or postsurgery if they were admitted to the surgical service or CCU.
Recruitment/selection of patients	Identification of cases of AP was based on International Classification of Diseases, 9th Revision codes that started with 577 (AP)
Age, gender and ethnicity	Age - Range: 1-21. Gender (M:F): 94:107. Ethnicity: Not reported

Further population details	1. Age : <75 years 2. Severity of pancreatitis (as defined by study): Mild pancreatitis
Extra comments	NPO + IVF lo: BMI – Mean (SD): 67.7 (28), Etiology – Viral: 0, Drug: 1, Trauma: 0, Gallstone: 4, Idiopathic: 8, Familial: 1, Systemic: 2, Post-ERCP:0, Hypertriglyceridemia: 1, Anatomic: 3, Alcohol: 0; Amylase – Mean (SD): 310 (259), Lipase – Mean (SD): 3139 (2982) NPO + IVF hi: BMI – Mean (SD): 60.9 (37.8), Etiology – Viral: 0, Drug: 5, Trauma: 0, Gallstone: 1, Idiopathic: 9, Familial: 8, Systemic: 2, Post-ERCP:1, Hypertriglyceridemia: 1, Anatomic: 3, Alcohol: 0; Amylase – Mean (SD): 596 (626), Lipase – Mean (SD): 5634 (6045) PO + IVF lo: BMI – Mean (SD): 65 (34.3), Etiology – Viral: 4, Drug: 6, Trauma: 1, Gallstone: 3, Idiopathic: 27, Familial: 0, Systemic: 6, Post-ERCP: 3, Hypertriglyceridemia: 2, Anatomic: 1, Alcohol: 2; Amylase – Mean (SD): 392 (434), Lipase – Mean (SD): 3926 (4963) PO + IVF hi: BMI – Mean (SD): 60.8 (34.4), Etiology – Viral: 3, Drug: 6, Trauma: 1, Gallstone: 8, Idiopathic: 41, Familial: 15, Systemic: 7, Post-ERCP: 7, Hypertriglyceridemia: 1, Anatomic: 7, Alcohol: 0; Amylase – Mean (SD): 594 (814), Lipase – Mean (SD): 5670 (7803)
Indirectness of population	No indirectness
Interventions	(n=126) Intervention 1: 'Aggressive' fluid administration - 'Aggressive' as defined by studies. Intravenous fluid was initiated at 1.5-2 times the maintenance rate of dextrose 5% normal saline on admission. Intravenous fluid was administered within 24 hours of admission.. Duration Unclear. Concurrent medication/care: 30 participants received enteral nutrition and 96 did not. (n=75) Intervention 2: 'Conservative' fluid administration - 'Conservative' as defined by studies. Intravenous fluid was initiated at the normal maintenance rate of dextrose 5% normal saline on admission. Intravenous fluid was administered within 24 hours of admission.. Duration Unclear. Concurrent medication/care: 20 participants received enteral nutrition and 55 did not.
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: IVF HI versus IVF LO

Protocol outcome 1: Serious adverse events at during admission
- Actual outcome for Children (<16 years): Readmission rate at Unclear; Group 1: 5/126, Group 2: 5/75; Risk of bias: Very high; Indirectness of outcome: No indirectness
- Actual outcome for Children (<16 years): CCU transfer rate at Unclear; Group 1: 5/126, Group 2: 14/75; Risk of bias: Very high; Indirectness of outcome: No indirectness
- Actual outcome for Children (<16 years): Severe AP rate at Unclear; Group 1: 12/126, Group 2: 9/75; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 2: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome for Children (<16 years): Length of stay at During admission (NPO group); Group 1 : 5 (0.58), Group 2: 7.1 (1.01) ; Risk of bias: Very high; Indirectness of outcome: No indirectness
- Actual outcome for Children (<16 years): Length of stay at During admission (PO group); Group 1 : 3.2 (0.22), Group 2: 2.8 (0.24) ; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcomes not reported by the study	Quality of life at <1 year; Mortality at <1 year; Local complications (fluid collection; cystic collection; pancreas necrosis; peri-pancreatic necrosis; local infection) at <6 months; Achievement of pre-specified target for resuscitation (eg target central venous pressure, urine output, lactate levels, PiCCO measurements) at <1 year; Systemic complications (persistent organ failure; fluid overload) at during admission; Length of stay (in intensive therapy unit or hospital) at <1 year; Length of stay (in intensive therapy unit or hospital) at <1 year

Study	Outcome	Intervention results	Intervention group (n)	Comparison results	Comparison group (n)	Risk of bias
Szabo 2015	Length of stay (in hospital), days, <1 year (NPO group)	Mean (SE): 5 (0.58)	30	Mean (SE): 7.1 (1.01)	20	Very high
Szabo 2015	Length of stay (in hospital), days, <1 year (PO group)	Mean (SE): 3.2 (0.22)	96	Mean (SE): 2.8 (0.24)	55	Very high

Study	Wall 2011[1126]
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=286)
Countries and setting	Conducted in USA; Setting:
Line of therapy	Adjunctive to current care
Duration of study	Other: 1 year per group
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Two of the following: abdominal pain typical of acute pancreatitis, elevation of amylase and/or lipase more than 3 times the upper normal limit, and/or findings consistent with acute pancreatitis on abdominal cross-sectional imaging.
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Diagnosis of AP based on having two of the following: abdominal pain typical of acute pancreatitis, elevation of amylase and/or lipase more than 3 times the upper normal limit, and/or findings consistent with acute pancreatitis on abdominal cross-sectional imaging.
Exclusion criteria	A known history of severe hepatic dysfunction (albumin <3 mg/dL), cardiovascular insufficiency (>NYHA Class II heart failure), respiratory insufficiency on admission defined by an oxygen saturation of less than 90% on room air, renal insufficiency or hematologic disease. Patients who were transferred after the diagnosis of acute pancreatitis was established were also not included.
Age, gender and ethnicity	Age - Mean (SD): 1998 group: 59.8 (17.1) 2008 group: 57.4 (19.4). Gender (M:F): 121:165. Ethnicity: Not reported

Further population details	1. Age : <75 years 2. Severity of pancreatitis (as defined by study): Not stated / Unclear
Extra comments	1998 group: BMI: 28.1 (3.3), Cause - biliary: 43%, alcohol: 19%, idiopathic: 16%, Post-ERCP: 14%, hypertriglyceridemia: 8% 2008 group: BMI: 28.8 (4.1), Cause - biliary: 43%, alcohol: 26%, idiopathic: 20%, Post-ERCP: 6%, hypertriglyceridemia: 6%
Indirectness of population	No indirectness
Interventions	(n=113) Intervention 1: 'Aggressive' fluid administration - 'Aggressive' as defined by studies. Hydration was provided at 284 mL/h during the first 6 hours and 221 mL/h during the first 12 hours. Duration Unclear. Concurrent medication/care: Not reported (n=173) Intervention 2: 'Conservative' fluid administration - 'Conservative' as defined by studies. Hydration was provided at 113 (80) mL/h during the first 6 hours and 152 (67) mL/h during the first 12 hours . Duration Unclear. Concurrent medication/care: Not reported
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 'AGGRESSIVE' AS DEFINED BY STUDIES versus 'CONSERVATIVE' AS DEFINED BY STUDIES

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome for Adults (>16 years): Length of stay at During admission; Group1: 5.5, Group 2: 7.7; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality at <1 year
- Actual outcome for Adults (>16 years): Mortality at During admission; Group 1: 4/113, Group 2: 16/173; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 3: Local complications (fluid collection; cystic collection; pancreas necrosis; peri-pancreatic necrosis; local infection) at <6 months - Actual outcome for Adults (>16 years): Pancreatic necrosis at During admission; Group 1: 8/113, Group 2: 26/173; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 4: Systemic complications (persistent organ failure; fluid overload) at during admission - Actual outcome for Adults (>16 years): Renal failure at During admission; Group 1: 5/113, Group 2: 9/173; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome for Adults (>16 years): Pulmonary failure at During admission; Group 1: 4/113, Group 2: 9/173; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome for Adults (>16 years): Cardiovascular failure at During admission; Group 1: 4/113, Group 2: 7/173; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome for Adults (>16 years): Multi organ failure at During admission; Group 1: 5/113, Group 2: 18/173; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Serious adverse events at during admission; Length of stay (in intensive therapy unit or hospital) at <1 year; Achievement of pre-specified target for resuscitation (eg target central venous pressure, urine output, lactate levels, PiCCO measurements) at <1 year

Study	Wang 2013[1130]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=200)
Countries and setting	Conducted in China; Setting: The Intensive Care Unit in Wuxi Second People's Hospital
Line of therapy	Adjunctive to current care
Duration of study	Intervention time: 4 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Patients met Atlanta criteria for severe acute pancreatitis
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	People admitted to hospital with severe acute pancreatitis were enrolled within 24 hours after on set of disease
Exclusion criteria	Any of the following: sepsis, less than 18 or more than 70 years of age, pregnant, chronic heart disease, pacemaker installed, chronic renal failure and SAP with unknown etiology
Age, gender and ethnicity	Age - Range: 18-70. Gender (M:F): Not reported. Ethnicity: Not reported
Further population details	1. Age : <75 years 2. Severity of pancreatitis (as defined by study): Severe pancreatitis
Indirectness of population	No indirectness
Interventions	(n=64) Intervention 1: 'Aggressive' fluid administration - 'Aggressive' as defined by studies. during the first six

	hours of resuscitation, the goals of initial resuscitation should include all of the following: central venous pressure 8-12 mmHg, mean arterial pressure ≥65 mmHg, urine output ≥0.5 mL/kg/h and central venous or mixed venous oxygen saturation ≥70%.. Duration Unclear. Concurrent medication/care: All patients were managed and cared for in the same manner according to Practice Guideline in Acute Pancreatitis, including supportive care, enteral feeding, treatment of sterile pancreatic necrosis, treatment of associated pancreatic duct disrupstions, and use of antibiotics. (n=68) Intervention 2: 'Conservative' fluid administration - 'Conservative' as defined by studies. Patients fluid resuscitation was in line with the Practice Guidelines in Acute Pancreatitis. Duration Unclear. Concurrent medication/care: All patients were managed and cared for in the same manner according to Practice Guideline in Acute Pancreatitis, including supportive care, enteral feeding, treatment of sterile pancreatic necrosis, treatment of associated pancreatic duct disrupstions, and use of antibiotics.
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EARLY GOAL-DIRECTED FLUID THERAPY versus 'CONSERVATIVE' AS DEFINED BY STUDIES

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome for Adults (>16 years): Length of time in CCU at During admission; Group 1: mean 18.6 days (SD 6.3); n=64, Group 2: mean 20.6 days (SD 6.8); n=68; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality at <1 year
- Actual outcome for Adults (>16 years): Mortality at During admission; Group 1: 14/64, Group 2: 16/68; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 3: Systemic complications (persistent organ failure; fluid overload) at during admission
- Actual outcome for Adults (>16 years): Abdominal compartment syndrome at During admission; Group 1: 14/64, Group 2: 20/68; Risk of bias: Very high; Indirectness of outcome: No indirectness
- Actual outcome for Adults (>16 years): Multiple organ dysfunction syndrome at During admission; Group 1: 18/64, Group 2: 20/68; Risk of bias: Very

high; Indirectness of outcome: No indirectness Protocol outcome 4: Serious adverse events at during admission - Actual outcome for Adults (>16 years): Days on ventilation at During admission; Group 1: mean 12.3 days (SD 4.2); n=64, Group 2: mean 15.3 days (SD 5.2); n=68; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Achievement of pre-specified target for resuscitation (eg target central venous pressure, urine output, lactate levels, PiCCO measurements) at <1 year; Length of stay (in intensive therapy unit or hospital) at <1 year; Local complications (fluid collection; cystic collection; pancreas necrosis; peri-pancreatic necrosis; local infection) at <6 months

Study	Wu 2011[1160]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=40)
Countries and setting	Conducted in USA
Line of therapy	Adjunctive to current care
Duration of study	--:
Method of assessment of guideline condition	--
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Define
Exclusion criteria	Define
Age, gender and ethnicity	Age - --: . Gender (M:F): Define. Ethnicity: Not reported
Further population details	1. Age : <75 years 2. Severity of pancreatitis (as defined by study): Not stated / Unclear
Indirectness of population	--
Interventions	(n=19) Intervention 1: 'Aggressive' fluid administration - 'Aggressive' as defined by studies. Each patient received an initial fluid challenge with 20 mL/kg of either LR solution or NS during a period of 30 minutes. Participants then received continuous infusion of 3 mL/kg/h of intravenous hydration for volume

	maintenance. After 8-12 hours, study physicians reassessed patients with a bedside clinical examination as well as a BUN measurement. If refractory to initial volume challenge, participants received a second fluid challenge of 20 mL/kg to be administered during 30 minutes. They then continued to receive volume replacement at a rate of 3 mL/kg/h. An additional bolus of 20 mL/kg during a period of 30 minutes was initiated at 16-20 hours for patients who remained refractory to volume resuscitation.. Duration Unclear. Concurrent medication/care: Not reported (n=21) Intervention 2: 'Conservative' fluid administration - 'Conservative' as defined by studies. Patients randomised to standard fluid resuscitation had fluid adjustments managed by their treating physician.. Duration Unclear. Concurrent medication/care: Not reported
Funding	Academic or government funding (Dr Wu is supported by a 2009 Junior Faculty Career Development Award from the American College of Gastroenterology)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: GOAL DIRECTED RESUSCITATION versus STANDARD RESUSCITATION

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome for Adults (>16 years): Length of stay at Unclear; Risk of bias: ; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality at <1 year
- Actual outcome for Adults (>16 years): Mortality at Unclear; Group 1: 0/19, Group 2: 0/21; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 3: Local complications (fluid collection; cystic collection; pancreas necrosis; peri-pancreatic necrosis; local infection) at <6 months
- Actual outcome for Adults (>16 years): Necrosis at Unclear; Group 1: 1/19, Group 2: 0/21; Risk of bias: Very high; Indirectness of outcome: No indirectness
- Actual outcome for Adults (>16 years): Infections at Unclear; Group 1: 2/19, Group 2: 0/21; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 4: Systemic complications (persistent organ failure; fluid overload) at during admission

- Actual outcome for Adults (>16 years): Respiratory organ failure at Unclear; Group 1: 1/19, Group 2: 0/21; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome for Adults (>16 years): Shock at Unclear; Group 1: 1/19, Group 2: 0/21; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome for Adults (>16 years): Renal failure at Unclear; Group 1: 2/19, Group 2: 1/21; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 5: Serious adverse events at during admission - Actual outcome for Adults (>16 years): Transfer to CCU at Unclear; Group 1: 4/19, Group 2: 0/21; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Length of stay (in intensive therapy unit or hospital) at <1 year; Achievement of pre-specified target for resuscitation (eg target central venous pressure, urine output, lactate levels, PiCCO measurements) at <1 year

H.8 Route of feeding in people with severe acute pancreatitis

H.8.1 Randomised trials

Study (subsidiary papers)	Al-Omran 2010[22] (Abou-Assi 2002 [5]; Casas 2007 [197]; Gupta 2003 [425]; Kalfarentzos 1997 [565]; Louie 2005 [679]; Petrov 2006 [853])
Study type	Systematic Review
Number of studies (number of participants)	8 (n=348)
Countries and setting	Conducted in Multiple countries; Setting: Systematic review: mixed
Line of therapy	1st line
Duration of study	Systematic review: mixed
Method of assessment of guideline condition	Systematic review: method of assessment mixed
Stratum	Adults >16 years
Subgroup analysis within study	Systematic review – pre-specified in protocol: Severe acute pancreatitis
Inclusion criteria	Randomised trials comparing TPN with EN in acute pancreatitis
Exclusion criteria	No assessment of severity
Recruitment/selection of patients	Systematic review: mixed
Age, gender and ethnicity	Age - Range: 21-91 years. Gender (M:F): Define. Ethnicity:
Further population details	1. Patients in critical care: Systematic review: mixed
Indirectness of population	Serious indirectness: Includes mild acute pancreatitis patients
Interventions	Systematic review: see study characteristics
Funding	Academic or government funding
RESULTS See published systematic review for mortality and length of hospital stay, and some infection results RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ENTERAL versus PARENTERAL **Abou-Assi 2002** Protocol outcome 1: Serious adverse events at <1 year	

- Actual outcome: ARDS; Group 1: 5/27, Group 2: 3/26;
- Actual outcome: MODS; Group 1: 8/27, Group 2: 7/26
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 2 (switched – syndrome needed emergency surgery); Group 2 Number missing: 2 (switched – severe sepsis)
Protocol outcome 2: adverse events
- Actual outcome: necrosis or pseudocysts: Group 1: 3/26 Group 2: 4/27
- Actual outcome: hyperglycaemia: Group 1: 4/26, Group 2: 14/27
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 2 (switched – severe sepsis syndrome); Group 2 Number missing: 2 (switched – needed emergency surgery)
- Actual outcome: operative intervention: Group 1: 2/26, Group 2: 0/27
Risk of bias: All domain – Very high, Selection - High, Blinding - Low, Incomplete outcome data - high, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 2 (switched – severe sepsis syndrome); Group 2 Number missing: 2 (switched – needed emergency surgery)

Casas 2007
Protocol outcome 1: adverse events
- Actual outcome: necrosis: Group 1: 0/11, Group 2: 2/11
- Actual outcome: operative intervention: Group 1: 0/11, Group 2: 3/11
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0
Protocol outcome 2: achieving nutrition
- Actual outcome: kcal/kg/day at day 5: Group 1: mean 20.8 (SD 1.68) ; n=11, Group 2: mean 20.09 (SD 1.83); n=11
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0
Protocol outcome 3: infections
- Actual outcome: pancreatic infections: Group 1: 0/11, Group 2: 2/11
- Actual outcome: extra-pancreatic infections: Group 1: 1/11, Group 2: 0/11
- Actual outcome: systemic infections: Group 1: 0/11, Group 2: 5/11
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0
Protocol outcome 3: Serious adverse events
- Actual outcome: SIRS: Group 1: 2/11, Group 2: 2/11
- Actual outcome: MODS: Group 1: 0/11, Group 2: 2/11
- Actual outcome: systemic infections: Group 1: 0/11, Group 2: 5/11

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Gupta 2003

Protocol outcome 1: adverse events
- Actual outcome: tube displacement: Group 1: 0/11, Group 2: 0/9
- Actual outcome: operative intervention: Group 1: 3/8, Group 2: 2/9

Risk of bias: All domain – Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 3 withdrew or improved; Group 2 Number missing: 2withdrew [available case analysis]

Protocol outcome 2: infections
- Actual outcome: extra-pancreatic infections (urinary or respiratory): Group 1: 1/8, Group 2: 1/9
- Actual outcome: systemic infections (central line infection): Group 1: 0/8, Group 2: 1/9

Risk of bias: All domain – Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 3 withdrew or improved; Group 2 Number missing: 2withdrew [available case analysis]

Protocol outcome 3: Serious adverse events
- Actual outcome: single organ failure: Group 1: 0/8, Group 2: 6/9

Risk of bias: All domain – Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 3 withdrew or improved; Group 2 Number missing: 2withdrew [available case analysis]

Protocol outcome 4: length of hospital stay
- Actual outcome: Median Length of hospital stay (range): : Group 1: 7 (4-14) days, Group 2: 10 (7-26) days

Risk of bias: All domain – Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 3 withdrew or improved; Group 2 Number missing: 2withdrew [available case analysis]

Kalfarentzos 1997

Protocol outcome 1: adverse events
- Actual outcome: operative intervention: Group 1: 3/18, Group 2: 11/20; Comments: 3 procedures in 2 patients and 11 procedures in 4 patients
- Actual outcome: hyperglycaemia >200 mg/dl: Group 1: 4/18, Group 2: 9/20

Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 2 (unsuccessful tube placement); Group 2 Number missing: 0
- Actual outcome: fistula or pseudocysts: Group 1: 0/18 Group 2: 3/20

Risk of bias: All domain – Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 2 (unsuccessful tube placement); Group 2 Number missing: 0

Protocol outcome 2: infections
- Actual outcome: pancreatic infections (infected necrosis or abscess): Group 1: 2/18, Group 2: 4/20
- Actual outcome: systemic infections (blood culture or catheter-related sepsis): Group 1: 1/18, Group 2: 5/20

Risk of bias: All domain – Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 2 (unsuccessful tube placement); Group 2 Number missing: 0

- Actual outcome: extra-pancreatic infections (pneumonia or UTI): Group 1: 3/18, Group 2: 6/20
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Louie 2005
Protocol outcome 1: achieving nutrition
- Actual outcome: days to goal: Group 1: mean 3.3 (SD 2.6) ; n=10, Group 2: mean 1.9 (SD 2.4); n=18
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 1 (switched because of failure); Group 2 Number missing: 0
Protocol outcome 2: infections
- Actual outcome: pancreatic infections (Infected fluid collections): Group 1: 1/10, Group 2: 4/18
- Actual outcome: systemic infections (infected central line): Group 1: 0/10, Group 2: 2/18
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 1 (switched because of failure); Group 2 Number missing: 0
Protocol outcome 3: Serious adverse events
- Actual outcome: single organ failure: Group 1: 7/10, Group 2: 13/18
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 1 (switched because of failure); Group 2 Number missing: 0
Protocol outcome 4: adverse events
- Actual outcome: tube displacement: Group 1: 9/10, Group 2: 0/18
- Actual outcome: acute fluid collections: Group 1: 3/10, Group 2: 9/18
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 1 (switched because of failure); Group 2 Number missing: 0
- Actual outcome: operative intervention: Group 1: 1/10, Group 2: 4/18
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 1 (switched because of failure); Group 2 Number missing: 0

Petrov 2006
Protocol outcome 1: adverse events
- Actual outcome: operative intervention: Group 1: 8/35, Group 2: 25/34;
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 1 (withdrew)
- Actual outcome: tube displacement: Group 1: 5/35, Group 2: 0/34;
- Actual outcome: hyperglycaemia : Group 1: 1/35, Group 2: 5/35
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 1 (withdrew)

Protocol outcome 2: infections - Actual outcome: pancreatic infections (infected necrosis or abscess): Group 1: 7/35, Group 2: 16/34; - Actual outcome: extra-pancreatic infections (pneumonia or UTI): Group 1: 4/35, Group 2: 6/34; Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 1 (withdrew) - Actual outcome: systemic infections (central line infection): Group 1: 0/35, Group 2: 5/34 Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 1 (withdrew) Protocol outcome 3: Serious adverse events - Actual outcome: single organ failure: Group 1: 4/35, Group 2: 10/34; - Actual outcome: multiple organ failure: Group 1: 7/35, Group 2: 17/34; Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 1 (withdrew)	
Protocol outcomes not reported by the study	Quality of life at <1 year; Weight loss/BMI at <1 year; Achieving nutrition (meeting nutritional requirements; at least 20-25 kcal/kg) at <1 year; Requiring total parenteral nutrition at <1 year

Study	Doley 2009[302]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=50)
Countries and setting	Conducted in India; Setting: Hospital
Line of therapy	1st line
Duration of study	Intervention time: 14 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: acute pancreatitis was defined using the Atlanta criteria: clinical features, hyperamylasemia (three times the normal upper limit), and radiological evidence of severe acute pancreatitis (contrast enhanced CT (CECT) scan evidence of pancreatic necrosis and a computed tomography severity index (CTSI) equal to, or greater than, 7).
Stratum	Adults >16 years
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients admitted with severe acute pancreatitis
Exclusion criteria	Acute or chronic pancreatitis, patients who had undergone intervention prior to admission, patients requiring inotropic support at inclusion, or complications requiring surgical intervention at the time of inclusion
Recruitment/selection of patients	Consecutive
Age, gender and ethnicity	Age - Mean (SD): Enteral: 38.4 (13.8); parenteral: 41.1 (11.3). Range 17-70 years. Gender (M:F): Not stated. Ethnicity: Not stated
Further population details	1. Patients in critical care: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=25) Intervention 1: Enteral feeding - Jejunal or duodenal. Placement of the enteral tube was done endoscopically and a 16F single lumen 125 cm long red rubber feeding tube was placed over a 400 cm long stainless steel guidewire beyond the ligament of Treitz using fluoroscopic control. Seven of 25 patients required a second attempt at placement of the tube in the desired position. A test feed with 500 ml of normal saline was administered over a period of 4-5 hours and jejunostomy feed was started subsequently. Jejunal feeding was started at low flow rates - an initial rate of 20–30 ml/hour until achievement of the full regime of EN. Minor complications such as diarrhoea and distension were managed by altering the infusion rate and adding an antimotility agent. Duration 14 days. Concurrent medication/care: All patients were managed routinely by gastrointestinal decompression, prophylactic antibiotics (ciprofloxacin/metronidazole or imipenem/cilastatin),

	intravenous fluids and organ system support. Nutritional support was initiated within 72 hours of admission and was continued for a minimum of 14 days. The need for further continuation of nutritional support was decided on the basis of the patients' clinical status. Image-guided fine needle aspiration or percutaneous drainage of pancreatic or peripancreatic collection as a temporizing measure was resorted to in patients who continued to be toxic. Indirectness: No indirectness Comments: The targeted caloric and protein requirements were 2,500-2,700 kcal/day, and 120-130 g/day of protein. (n=25) Intervention 2: Parenteral feeding - Parenteral alone. A 16G central venous catheter was inserted through the subclavian or internal jugular vein. A chest X-ray was taken after insertion to check the catheter tip position and also to check for complications of central venous line placement. Commercially available parenteral nutrition formula (PNA: parenteral nutrition admixture) was administered. The target caloric and protein requirements were similar to the enteral group. Glycaemic control and metabolic parameters were monitored. All patients in the parenteral group could be weaned to oral diet (those managed conservatively) and feeding through a jejunostomy catheter placed intraoperatively (those operated on). Duration 14 days. Concurrent medication/care: All patients were managed routinely by gastrointestinal decompression, prophylactic antibiotics (ciprofloxacin/metronidazole or imipenem/cilastatin), intravenous fluids and organ system support. Nutritional support was initiated within 72 hours of admission and was continued for a minimum of 14 days. The need for further continuation of nutritional support was decided on the basis of the patients' clinical status. Image-guided fine needle aspiration or percutaneous drainage of pancreatic or peripancreatic collection as a temporizing measure was resorted to in patients who continued to be toxic. Indirectness: No indirectness Comments: The targeted caloric and protein requirements were 2,500-2,700 kcal/day, and 120-130 g/day of protein.
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: JEJUNAL versus PARENTERAL ALONE

Protocol outcome 1: Mortality at <1 year
- Actual outcome: Mortality at 14 days; Group 1: 5/25, Group 2: 4/16; Comments: In the EN group, all 5 deaths occurred due to sepsis and multiorgan failure; 4 out of 5 deaths occurred in the post-operative period. In the TPN group, all 4 deaths occurred in the post-operative phase: 3 due to sepsis and multiorgan failure and one due to operative haemorrhage
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Length of critical care or hospital stay at <1 year
- Actual outcome: Length of critical care stay at 14 days; ;

Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome: Length of hospital stay at 14 days; ; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Infections at <1 year - Actual outcome: Infection at 14 days; Group 1: 16/25, Group 2: 15/25 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Adverse events (for example, tube displacements, aspirational pneumonia, ischaemic gut and central line infections) at <1 year - Actual outcome: Locoregional complications at 14 days; Group 1: 13/25, Group 2: 10/25 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome: Surgical intervention at 14 days; Group 1: 14/25, Group 2: 15/25 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life at <1 year; Achieving nutrition (meeting nutritional requirements; at least 20-25 kcal/kg) at <1 year; Requiring total parenteral nutrition at <1 year; Serious adverse events at <1 year; Weight loss/BMI at <1 year

Study	Eatock 2005[329]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=50)
Countries and setting	Conducted in United Kingdom; Setting: Glasgow Royal Infirmary
Line of therapy	1st line
Duration of study	Intervention + follow-up: Duration of hospitalisation
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults >16 years
Subgroup analysis within study	Not applicable
Inclusion criteria	Predicted severe acute pancreatitis; abdominal pain, amylase ≥3-times ULN, onset of abdominal pain within 48h, APACHE II score ≥8 and/or CRP ≥150 mg/litre, and/or peripancreatic liquid shown on CT.
Exclusion criteria	AP due to surgery, IBD, stoma, short bowel, chronic pancreatitis with exacerbation.
Recruitment/selection of patients	Consecutive
Age, gender and ethnicity	Age - Median (IQR): NG: 63 (47-74); NJ: 58 (48-64). Gender (M:F): 53/47%. Ethnicity: Not stated
Further population details	1. Patients in critical care: Mixed (26% of NG and 36% of NJ group were admitted to CCU).
Extra comments	Feeding was started on average 72 hours from onset of pain
Indirectness of population	No indirectness
Interventions	(n=27) Intervention 1: Enteral feeding - Gastric. Nasogastric tubes placed on the ward with position checked by aspiration and pH check or chest X-ray. Feeds were commenced at a full strength and rate of 30 ml/hour increasing to 100 ml/hour over 24–48 hours. The caloric target was 2000 kcal/day. Low fat semi-elemental feed was used (Pepti 2000 LF), which contains 1 kcal/ml and 40 g protein/litre (5.9 g nitrogen/litre). Carbohydrate provides 75% of energy, protein 16% and fat 9%. Duration Unclear. Concurrent medication/care: Unclear. Indirectness: No indirectness (n=22) Intervention 2: Enteral feeding - Jejunal or duodenal. Nasojejunal tubes placed under endoscopic guidance to the proximal jejunum. Feeds were commenced at a full strength and rate of 30 ml/hour increasing to 100 ml/hour over 24–48 hours. The caloric target was 2,000 kcal/day.

	Low fat semi-elemental feed was used (Pepti 2000 LF), which contains 1 kcal/ml and 40 g protein/litre (5.9 g nitrogen/litre). Carbohydrate provides 75% of energy, protein 16% and fat 9%. Duration Unclear. Concurrent medication/care: Unclear. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: GASTRIC versus JEJUNAL (PROXIMAL)

Protocol outcome 1: Mortality at <1 year
- Actual outcome for Adults >16 years: Mortality at During hospital stay; Group 1: 5/27, Group 2: 7/22; Comments: Mostly due to multiorgan failure. Only 2 of the deaths occurred within the first week of illness.
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Numbers not equal; Group 1 Number missing: 0; Group 2 Number missing: 3, Reason: 1 Misdiagnosis excluded; 2 switched to NG because tube could not be passed into the jejunum

Protocol outcome 2: Length of critical care or hospital stay at <1 year
- Actual outcome for Adults >16 years: Length of hospital stay at During hospital stay; ;
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Numbers not equal; Group 1 Number missing: 0; Group 2 Number missing: 3, Reason: 1 Misdiagnosis excluded; 2 switched to NG because tube could not be passed into the jejunum

Protocol outcome 3: Achieving nutrition (meeting nutritional requirements; at least 20-25 kcal/kg) at <1 year
- Actual outcome for Adults >16 years: Tolerating administration of at least 75% of target at Within 48h of feed commencement; Group 1: 19/27, Group 2: 17/22
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Numbers not equal; Group 1 Number missing: 0; Group 2 Number missing: 3, Reason: 1 Misdiagnosis excluded; 2 switched to NG because tube could not be passed into the jejunum
- Actual outcome for Adults >16 years: Tolerating administration of at least 75% of target at Within 60h of feed commencement; Group 1: 21/27, Group 2: 17/22
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Numbers not equal; Group 1 Number missing: 0; Group 2 Number missing: 3, Reason: 1 Misdiagnosis excluded; 2 switched to NG because tube could not be passed into the jejunum

Protocol outcome 4: Requiring total parenteral nutrition at <1 year
- Actual outcome for Adults >16 years: Converted to IV feeding at Unclear; Group 1: 0/27, Group 2: 1/22; Comments: Duodenal obstruction
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Numbers not equal; Group 1 Number missing: 0; Group 2 Number missing: 3, Reason: 1 Misdiagnosis

excluded; 2 switched to NG because tube could not be passed into the jejunum Protocol outcome 5: Adverse events (for example, tube displacements, aspirational pneumonia, ischaemic gut and central line infections) at <1 year - Actual outcome for Adults >16 years: Tube displacement at During hospital stay; Group 1: 1/27, Group 2: 1/22 Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Numbers not equal; Group 1 Number missing: 0; Group 2 Number missing: 3, Reason: 1 Misdiagnosis excluded; 2 switched to NG because tube could not be passed into the jejunum	
Protocol outcomes not reported by the study	Quality of life at <1 year; Infections at <1 year; Serious adverse events at <1 year; Weight loss/BMI at <1 year

Study	Eckerwall 2006[332]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=50)
Countries and setting	Conducted in Sweden; Setting: Lund University Hospital
Line of therapy	1st line
Duration of study	Intervention + follow-up: 10 days observation and 3-month follow-up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults >16 years
Subgroup analysis within study	Not applicable
Inclusion criteria	Predicted severe acute pancreatitis; abdominal pain, amylase ≥3-times ULN, onset of abdominal pain within 48h, APACHE II score ≥8 and/or CRP ≥150 mg/litre, and/or peripancreatic liquid shown on CT
Exclusion criteria	AP due to surgery, IBD, stoma, short bowel, chronic pancreatitis with exacerbation.
Recruitment/selection of patients	Unclear
Age, gender and ethnicity	Age - Median (IQR): TPN: 68 (60-80); EN: 71 (58-80). Gender (M:F): 48/52%. Ethnicity: Not stated
Further population details	1. Patients in critical care: Mixed (12% were admitted to CCU).
Extra comments	Median (IQR) APACHE II score TPN: 9 (8-10); EN: 10 (8-13)
Indirectness of population	No indirectness
Interventions	(n=26) Intervention 1: Parenteral feeding - Parenteral alone. TPN (Kabiven PI) infused via central or peripheral venous catheter. Energy target of 25 kcal/kg per day based on admission weight. Duration 10 days. Concurrent medication/care: Fluids, such as crystalloids or colloids, were added in both groups to fulfil the individual's needs of fluid and energy (in case of reduced rate). Oral feeding was reintroduced when amylase and CRP levels had decreased and abdominal pain had resolved. Regular hospital diet was introduced gradually, in general initially starting with liquid and then solid food. Patients were treated according to clinical routine including pain control, symptomatic and organ supportive treatment and, when indicated, restrictive indications for surgery. Broad-spectrum antibiotic therapy was used according to current recommendations. Indirectness: No indirectness Comments: To maintain isocaloric groups, the TPN group did not receive Kabiven on day 1 (n=24) Intervention 2: Enteral feeding - Gastric. Early nasogastric enteral nutrition with 'Fresubin original' infused at an initial rate of 25 ml/hour and gradually increased up to 100 ml/hour as tolerated and as needed.

	Duration 10 days. Concurrent medication/care: Fluids, such as crystalloids or colloids, were added in both groups to fulfil the individual's needs of fluid and energy (in case of reduced rate). Oral feeding was reintroduced when amylase and CRP levels had decreased and abdominal pain had resolved. Regular hospital diet was introduced gradually, in general initially starting with liquid and then solid food. Patients were treated according to clinical routine including pain control, symptomatic and organ supportive treatment and, when indicated, restrictive indications for surgery. Broad-spectrum antibiotic therapy was used according to current recommendations. Indirectness: No indirectness
Funding	Academic or government funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PARENTERAL ALONE versus GASTRIC

Protocol outcome 1: Mortality at <1 year
- Actual outcome for Adults >16 years: Mortality at 3 months; Group 1: 0/25, Group 2: 1/23
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Note: fixed block size and no blinding means investigators will know what the last patient in a block will receive personnel recruiting the patients would know the assignments for the patients at the end of a 'block'.; Group 1 Number missing: 1, Reason: Protocol violation; Group 2 Number missing: 1, Reason: Protocol violation

Protocol outcome 2: Length of critical care or hospital stay at <1 year
- Actual outcome for Adults >16 years: Length of hospital stay at 3 months;
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Note: fixed block size and no blinding means investigators will know what the last patient in a block will receive personnel recruiting the patients would know the assignments for the patients at the end of a 'block'. Group 1 Number missing: 1, Reason: Protocol violation; Group 2 Number missing: 1, Reason: Protocol violation

Protocol outcome 3: Achieving nutrition (meeting nutritional requirements; at least 20-25 kcal/kg) at <1 year
- Actual outcome for Adults >16 years: Achieving nutrition (25 kcal/kg/day) at 10 days; Group 1: 17/26, Group 2: 16/24
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Note: fixed block size and no blinding means investigators will know what the last patient in a block will receive personnel recruiting the patients would know the assignments for the patients at the end of a 'block'.; Group 1 Number missing: 1, Reason: Protocol violation; Group 2 Number missing: 1, Reason: Protocol violation

Protocol outcome 4: Infections at <1 year
- Actual outcome for Adults >16 years: Sepsis or infected pancreatic necrosis at 3 months; Group 1: 0/25, Group 2: 3/23

Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Note: fixed block size and no blinding means investigators will know what the last patient in a block will receive personnel recruiting the patients would know the assignments for the patients at the end of a 'block'.; Group 1 Number missing: 1, Reason: Protocol violation; Group 2 Number missing: 1, Reason: Protocol violation Protocol outcome 5: Adverse events (for example, tube displacements, aspirational pneumonia, ischaemic gut and central line infections) at <1 year - Actual outcome for Adults >16 years: Surgical intervention at 3 months; Group 1: 1/26, Group 2: 1/24; Comments: Cholecystectomy and necrosectomy Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Note: fixed block size and no blinding means investigators will know what the last patient in a block will receive personnel recruiting the patients would know the assignments for the patients at the end of a 'block'.; Group 1 Number missing: 1, Reason: Protocol violation; Group 2 Number missing: 1, Reason: Protocol violation Protocol outcome 6: Serious adverse events at <1 year - Actual outcome for Adults >16 years: Multiple organ failure at 3 months; Group 1: 1/25, Group 2: 1/23 Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Note: fixed block size and no blinding means investigators will know what the last patient in a block will receive personnel recruiting the patients would know the assignments for the patients at the end of a 'block'. ; Group 1 Number missing: 1, Reason: Protocol violation; Group 2 Number missing: 1, Reason: Protocol violation	
Protocol outcomes not reported by the study	Quality of life at <1 year; Requiring total parenteral nutrition at <1 year; Weight loss/BMI at <1 year

Study	**Kumar 2006[621]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=31)
Countries and setting	Conducted in India; Setting: Gastroenterology ward
Line of therapy	1st line
Duration of study	Intervention + follow-up: 7 day intervention plus follow-up to death, surgery or hospital discharge
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults >16 years
Subgroup analysis within study	Not applicable

Inclusion criteria	Severe acute pancreatitis; defined according to Atlanta criteria
Exclusion criteria	Delay of >4 weeks between onset of symptoms and presentation; already taking oral feeding; acute exacerbation of chronic pancreatitis; in shock (sBP <90mmHg)
Recruitment/selection of patients	Consecutive
Age, gender and ethnicity	Age - Mean (SD): NJ: 33.57 (12.53); NG: 43.25 (12.76). Gender (M:F): 25/5. Ethnicity:
Further population details	1. Patients in critical care: Not in critical care
Extra comments	Mean days from onset to admission to study hospital: NJ: 5.7; NG: 7.8 Mean APACHE II score: NJ: 9.64; NG: 10.50 87% had single or multiple organ failure at baseline
Indirectness of population	No indirectness
Interventions	(n=16) Intervention 1: Enteral feeding - Gastric. Tubes were placed under endoscopic guidance by the nasal route into the stomach. 'Re-feeding' started 48h after admission and used Paptamen, a semi-elemental formula through an enteral tube. Given as a slow infusion rate of 1-1.5 ml/min. Duration 7 days. Concurrent medication/care: Not stated Comments: After 7 days oral feeding was instituted (n=14) Intervention 2: Enteral feeding - Jejunal or duodenal. Tubes were placed under endoscopic guidance by the nasal route into the third part of the duodenum. 'Re-feeding' started 48h after admission and used Paptamen, a semi-elemental formula through an enteral tube. Given as a slow infusion rate of 1-1.5 ml/min and with an increase in caloric intake from 250 kcal to 1800 kcal over 7 days. Duration 7 days. Concurrent medication/care: Not stated. Indirectness: No indirectness Comments: After 7 days oral feeding was instituted
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: JEJUNAL OR DUODENAL (D3) versus GASTRIC

Protocol outcome 1: Mortality at <1 year
- Actual outcome for Adults >16 years: Mortality at Unclear; Group 1: 4/14, Group 2: 5/16
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Length of critical care or hospital stay at <1 year
- Actual outcome for Adults >16 years: Length of hospital stay at 7 days; Group 1: mean 29.93 days (SD 25.54); n=14, Group 2: mean 24.06 days (SD 14.35); n=16

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Achieving nutrition (meeting nutritional requirements; at least 20-25 kcal/kg) at <1 year - Actual outcome for Adults >16 years: Partial parenteral nutrition at 7 days; Group 1: 4/14, Group 2: 6/16 Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Infections at <1 year - Actual outcome for Adults >16 years: Infection (blood or bile culture, tracheal or pancreatic aspirate) at 7 days; Group 1: 6/14, Group 2: 7/16 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 5: Adverse events (for example, tube displacements, aspirational pneumonia, ischaemic gut and central line infections) at <1 year - Actual outcome for Adults >16 years: Tube displacement at 7 days; Group 1: 1/14, Group 2: 1/16 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults >16 years: Surgical intervention at Unclear; Group 1: 2/14, Group 2: 1/16 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 6: Serious adverse events at <1 year - Actual outcome for Adults >16 years: Serious complications requiring tube withdrawal at 7 days; Group 1: 0/14, Group 2: 0/16 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life at <1 year; Requiring total parenteral nutrition at <1 year; Weight loss/BMI at <1 year

Study (subsidiary papers)	**PYTHON trial: Bakker 2014[71] (Bakker 2011[73])**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=205)
Countries and setting	Conducted in Netherlands; Setting: 20 hospitals (Dutch Pancreatitis Study Group)

Line of therapy	1st line
Duration of study	Intervention plus 6 months follow-up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults >16 years
Subgroup analysis within study	Not applicable
Inclusion criteria	Diagnosis of acute pancreatitis if at least 2 of the 3 following features are present: 1) upper abdominal pain, 2) serum lipase or amylase levels above 3 times the upper level of normal and 3) characteristic findings of acute pancreatitis on cross-sectional abdominal imaging. Age ≥ 18 years and written informed consent Predicted severe pancreatitis within 24 hours after admission defined as one or more of the following: APACHE-II score ≥ 8 Imrie-score ≥ 3 CRP level >150 mg/litre
Exclusion criteria	History of acute or chronic pancreatitis Identification of patients >24 hours after admission Onset of symptoms >96 hours (4 days) before admission Acute pancreatitis due to malignancy or post-ERCP pancreatitis Diagnosis of acute pancreatitis confirmed during laparotomy for acute abdomen Artificial nutrition at admission (EN or PN) Pregnancy
Recruitment/selection of patients	Consecutive
Age, gender and ethnicity	Age - Mean (SD): 65 (15) years. Gender (M:F): 56/44%. Ethnicity: Not stated
Further population details	1. Patients in critical care: Mixed (19% had CCU admission after randomisation).
Extra comments	. Patients were stratified according to APACHE-II <13 or ≥13 prior to randomisation
Indirectness of population	No indirectness
Interventions	(n=104) Intervention 1: Enteral feeding - Jejunal or duodenal. A nasojejunal feeding tube was placed with the tip of the tube is beyond Treitz' ligament. If placed endoscopically, an abdominal X-ray is performed to check the tube's position and in case of radiological placement, fluoroscopy is used. After tube placement, EN started immediately using a very strict volume regimen: 20 ml/hour in the first 24 hours, 45 ml/hour, between 24–48 hour, 65 ml/hour, between 48–72 hours and, at 72 hours and thereafter: full nutrition, defined as an energy target of 25 kcal/kg/day (CCU patients) and 30 kcal/kg/day (non CCU patients). Nasoenteric feeding was administered as Nutrison Protein Plus. Per 100 ml this provided 125 kcal, 6.3 g protein, 4.9 g fat and 14.2 g carbohydrate. Standard amounts of minerals, vitamins and trace

	elements were included. For both study groups, full nutrition was defined as an energy target of 25 kcal/kg/day for patients in the intensive care unit and 30 kcal/kg/day for patients in the ward. At 3 and 7 days after admission a dietitian assessed nutritional status and nutritional requirements and made adjustments accordingly. Duration Follow-up 3- and 6-months after discharge. Concurrent medication/care: All patients had contrast enhanced CT within 5-7 days after admission. Intravenous antibiotics were administered based on culture results and not as prophylaxis in case of necrotizing pancreatitis without documented infection. Invasive intervention for (suspected) infected necrosis was preferably postponed until the fluid collections are walled-off and demarcated on CT-scan. ERCP was performed in case of suspected cholangitis or in case of biliary pancreatitis with clinically important persistent cholestasis. . Indirectness: No indirectness Comments: At 72 hours after the start of enteral feeding, the nutritional status will be evaluated and in case of intolerance, the type of EN will be changed accordingly (for example, additional proteins, calories, fibre). If feeding is not tolerated EN is reduced to 50% and stepwise rebuilt gradually until tolerated. If, after two of such attempts, full nutrition cannot be attained, PN will be started to reach the required energy target. Oral normal feeding is started, when abdominal pain has resolved and organ failure has subsided. In case of full tolerance of oral food nasojejunal feeding is gradually decreased. If pain relapses, EN is restarted. In case of nausea or vomiting, lowered consciousness (Glasgow Coma Score [GCS] 14 or lower in a non-intubated patient), or gastric residual volume (GRV) >250 ml/6 hours, the position of the feeding tube is checked. In case of CCU admission, irrespective of time from admission, the patient is fed according to the attending intensivist's preference (nasogastric or nasojejunal; enteral or parenteral). These patients are analysed according to the treatment assigned. (n=104) Intervention 2: Oral feeding. 'Nil by mouth' without any artificial nutrition during the first 72 hours after admission. If patients spontaneously request for oral food within these 72 hours, liquid and solid food are offered as requested and tolerated. If, at 72 hours after admission, patients develop organ failure, they will receive nasojejunal feeding with the same regimen as the intervention group. If, at 72 hours, there is no organ failure, patients are offered oral food ad libitum. If oral food is not tolerated, there is a re-challenge the next morning and if still not tolerated, EN is started through a nasojejunal feeding tube. Duration Follow-up 3- and 6-months after discharge. Concurrent medication/care: All patients had contrast enhanced CT within 5-7 days after admission. Intravenous antibiotics were administered based on culture results and not as prophylaxis in case of necrotizing pancreatitis without documented infection. Invasive intervention for (suspected) infected necrosis was preferably postponed until the fluid collections are walled-off and demarcated on CT-scan. ERCP was performed in case of suspected cholangitis or in case of biliary

	pancreatitis with clinically important persistent cholestasis. Indirectness: No indirectness Comments: 31% needed a nasoenteric feeding tube. 5% requested and received food within the first 72 h after presentation
Funding	Academic or government funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: JEJUNAL (EARLY) versus ORAL FEEDING

Protocol outcome 1: Mortality at <1 year
- Actual outcome for Adults >16 years: Mortality at 6 months; Group 1: 11/101, Group 2: 7/104
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Mean BMI 29 in early group and 27 in the on-demand group; Group 1 Number missing: 3, Reason: Incorrect diagnosis; Group 2 Number missing: 0

Protocol outcome 2: Length of critical care or hospital stay at <1 year
- Actual outcome for Adults >16 years: critical care admission at 6 months; Group 1: 18/101, Group 2: 20/103
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Mean BMI 29 in early group and 27 in the on-demand group; Group 1 Number missing: 3, Reason: Incorrect diagnosis; Group 2 Number missing: 0

Protocol outcome 3: Achieving nutrition (meeting nutritional requirements; at least 20-25 kcal/kg) at <1 year
- Actual outcome for Adults >16 years: Days from admission to full tolerance of oral diet at 6 months; ;
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Mean BMI 29 in early group and 27 in the on-demand group; Group 1 Number missing: 3, Reason: Incorrect diagnosis; Group 2 Number missing: 0

Protocol outcome 4: Requiring total parenteral nutrition at <1 year
- Actual outcome for Adults >16 years: Requiring parenteral nutrition at 6 months; Group 1: 5/101, Group 2: 10/103
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Mean BMI 29 in early group and 27 in the on-demand group; Group 1 Number missing: 3, Reason: Incorrect diagnosis; Group 2 Number missing: 0

Protocol outcome 5: Infections at <1 year
- Actual outcome for Adults >16 years: Infection at 6 months; Group 1: 25/101, Group 2: 27/104; Comments: Included infected pancreatic necrosis (9 versus 15); bacteraemia (17 versus 18); and pneumonia (12 versus 13)

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Mean BMI 29 in early group and 27 in the on-demand group; Group 1 Number missing: 3, Reason: Incorrect diagnosis; Group 2 Number missing: 0 Protocol outcome 6: Adverse events (for example, tube displacements, aspirational pneumonia, ischaemic gut and central line infections) at <1 year - Actual outcome for Adults >16 years: Nasoenteric tube displacement at 6 months; Group 1: 38/99, Group 2: 14/32; Comments: 2 patients in the early group declined tube insertion Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Mean BMI 29 in early group and 27 in the on-demand group; Group 1 Number missing: 3, Reason: Incorrect diagnosis; Group 2 Number missing: 0 - Actual outcome for Adults >16 years: Ileus at 6 months; Group 1: 10/101, Group 2: 10/103 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Mean BMI 29 in early group and 27 in the on-demand group; Group 1 Number missing: 3, Reason: Incorrect diagnosis; Group 2 Number missing: 0 - Actual outcome for Adults >16 years: Necrotising pancreatitis at 6 months; Group 1: 64/104, Group 2: 65/104 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Mean BMI 29 in early group and 27 in the on-demand group; Group 1 Number missing: 3, Reason: Incorrect diagnosis; Group 2 Number missing: 0 Protocol outcome 7: Serious adverse events at <1 year - Actual outcome for Adults >16 years: Multiple organ failure (among subset without organ failure at baseline) at 6 months; Group 1: 7/67, Group 2: 6/73 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Mean BMI 29 in early group and 27 in the on-demand group; Group 1 Number missing: 3, Reason: Incorrect diagnosis; Group 2 Number missing: 0 - Actual outcome for Adults >16 years: Single organ failure (among subset without organ failure at baseline) at 6 months; Group 1: 26/67, Group 2: 31/73 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Mean BMI 29 in early group and 27 in the on-demand group; Group 1 Number missing: 3, Reason: Incorrect diagnosis; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Quality of life at <1 year; Weight loss/BMI at <1 year

Study	**Singh 2012[997]**
Study type	RCT (Patient randomised; Parallel)

Number of studies (number of participants)	1 (n=78)
Countries and setting	Conducted in India; Setting: Tertiary care academic centre (CCU initially)
Line of therapy	1st line
Duration of study	Not clear:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults >16 years
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients with SAP admitted within 7 days of onset of pain AP diagnosis was based on clinical features, raised (>3 times the reference) amylase levels, and evidence of AP on imaging studies Severe AP was defined by at least 1 of the following criteria: (i) Presence of 1 or more organ failure as defined by the Atlanta classification. (ii) An APACHE II score of 8 or higher. (iii) CT severity index greater than 7.
Exclusion criteria	Patient already on oral feeds at the time of presentation; patients in shock (that is, systolic blood pressure <90 mmHg at the time of randomisation); not willing to give consent to participate in the study.
Recruitment/selection of patients	Consecutive
Age, gender and ethnicity	Age - Mean (SD): NG: 39.1 (16.70; NJ: 39.7 (12.3). Gender (M:F): 68/32%. Ethnicity: Not stated
Further population details	1. Patients in critical care: In critical care (All in CCU initially).
Extra comments	Median (range) APACHE II score: NG 8.5 (2-19); NJ 8 (2-24)
Indirectness of population	No indirectness
Interventions	(n=39) Intervention 1: Enteral feeding - Gastric. Nasogastric tube placed in the ward with the position being confirmed at the bedside by air test and aspirating gastric contents. 'Refeeding' was attempted in all included patients 48 hours after admission. Novasource, a commercially available semielemental enteral formula, was used to reach the nutrient goal (25 kcal/kg per day) in 3 to 4 days. The composition of feed was similar in both groups and was aimed to be of equal energy value in both groups. If the elemental feed was tolerated well, with no postfeeding pain, distension, and vomiting for 7 days, it was switched to a polymeric feed and then from oral soft to solid hospital diet reintroduced gradually. Duration Unclear; minimum 7 days; tube removed once oral feeds were taken. Concurrent medication/care: All patients were treated in an intensive care unit initially with nil by mouth, analgesics, aggressive fluid resuscitation, and supportive

	treatment. Antibiotics were prescribed if patients had infected pancreatic necrosis or if there was documented infection at the extrapancreatic sites. The antibiotics chosen were according to the culture and sensitivity report whenever available. In all patients with severe pancreatitis, enteral feeding was started early, unless the patient had persistent ileus or active gastrointestinal bleeding. In patients with organ failure, all possible organ support systems were used including ventilator support, vasopressors, and dialysis as and when required. Patients with biliary obstruction or cholangitis underwent an endoscopic retrograde cholangiography. All patients with infected pancreatic necrosis were treated initially with antibiotics, early EN, organ support, and percutaneous catheter drainage. Patients who did not improve despite maximal supportive management underwent open necrosectomy with lavage usually 4 weeks after the onset of pancreatitis. Indirectness: No indirectness (n=39) Intervention 2: Enteral feeding - Jejunal or duodenal. Nasojejunal tube placed under endoscopic guidance. A commercially available single-port tube, 200 cm long was placed in the jejunum beyond the ligament of Trietz and confirmed radiologically. 'Refeeding' was attempted in all included patients 48 hours after admission. Novasource, a commercially available semielemental enteral formula, was used to reach the nutrient goal (25 kcal/kg per day) in 3 to 4 days. The composition of feed was similar in both groups and was aimed to be of equal energy value in both groups. If the elemental feed was tolerated well, with no postfeeding pain, distension, and vomiting for 7 days, it was switched to a polymeric feed and then from oral soft to solid hospital diet reintroduced gradually. Duration Unclear; minimum 7 days; tube removed once oral feeds were taken. Concurrent medication/care: All patients were treated in an intensive care unit initially with nil by mouth, analgesics, aggressive fluid resuscitation, and supportive treatment. Antibiotics were prescribed if patients had infected pancreatic necrosis or if there was documented infection at the extrapancreatic sites. The antibiotics chosen were according to the culture and sensitivity report whenever available. In all patients with severe pancreatitis, enteral feeding was started early, unless the patient had persistent ileus or active gastrointestinal bleeding. In patients with organ failure, all possible organ support systems were used including ventilator support, vasopressors, and dialysis as and when required. Patients with biliary obstruction or cholangitis underwent an endoscopic retrograde cholangiography. All patients with infected pancreatic necrosis were treated initially with antibiotics, early EN, organ support, and percutaneous catheter drainage. Patients who did not improve despite maximal supportive management underwent open necrosectomy with lavage usually 4 weeks after the onset of pancreatitis. Indirectness: No indirectness
Funding	Academic or government funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: GASTRIC versus JEJUNAL Protocol outcome 1: Mortality at <1 year - Actual outcome for Adults >16 years: Mortality at Unclear; Group 1: 4/39, Group 2: 7/39	

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 2, Reason: Inadvertent removal of NJ tube and refused re-insertion Protocol outcome 2: Length of critical care or hospital stay at <1 year - Actual outcome for Adults >16 years: Length of hospital stay at unclear; ; Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 2, Reason: Inadvertent removal of NJ tube and refused re-insertion Protocol outcome 3: Achieving nutrition (meeting nutritional requirements; at least 20-25 kcal/kg) at <1 year - Actual outcome for Adults >16 years: Achieving goal nutrient requirements at within 3 days; Group 1: 39/39, Group 2: 39/39 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 2, Reason: Inadvertent removal of NJ tube and refused re-insertion Protocol outcome 4: Infections at <1 year - Actual outcome for Adults >16 years: Infection: any positive culture (blood or bile culture; tracheal or pancreatic aspirate) at Unclear; Group 1: 9/39, Group 2: 14/39 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 2, Reason: Inadvertent removal of NJ tube and refused re-insertion Protocol outcome 5: Adverse events (for example, tube displacements, aspirational pneumonia, ischaemic gut and central line infections) at <1 year - Actual outcome for Adults >16 years: Surgical intervention at Unclear; Group 1: 4/39, Group 2: 2/39 Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 2, Reason: Inadvertent removal of NJ tube and refused re-insertion	
Protocol outcomes not reported by the study	Quality of life at <1 year; Requiring total parenteral nutrition at <1 year; Serious adverse events at <1 year; Weight loss/BMI at <1 year

Study	**Wu 2010[1161]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=107)
Countries and setting	Conducted in China; Setting: CCU
Line of therapy	1st line
Duration of study	Not clear:

Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Mean APACHE II score for TPN 16 (4.4); TEN 14 (2.1)
Stratum	Adults >16 years
Subgroup analysis within study	Not applicable
Inclusion criteria	Severe acute pancreatitis with pancreatic necrosis (determined by dynamic spiral CT and confirmed by CRP >19.5mg/dl, 48h after onset of disease) and sufficient prophylactic antibiotics with concomitant parenteral or enteral nutrition within the first 7 days of hospitalisation.
Exclusion criteria	Not stated
Recruitment/selection of patients	Consecutive
Age, gender and ethnicity	Age - Mean (SD): TPN: 54 (11.2); TEN: 52 (12.1). Gender (M:F): 58/42%. Ethnicity: Not stated
Further population details	1. Patients in critical care: In critical care
Indirectness of population	No indirectness
Interventions	(n=53) Intervention 1: Enteral feeding - Jejunal or duodenal. Total enteral nutrition. An 8F or 12F nasojejunal-gastric feeding tube was placed by endoscopy, which confirmed the feeding port position to be distal to the ligament of Treitz. (NJ) Enteral feeding with an elemental formula TEN, peptide enteral nutritional formulae was given at 20 ml/hour for 20 hours with feeding rates that provided 1.5 g of protein per kilogram per day and 105 to 126 kJ of energy intake per kilogram per day. The feeding was gradually increased in volume according to patient's condition Duration Not stated. Concurrent medication/care: Prophylactic antibiotics (IV metronidazol/ciprofloxacin). Indirectness: No indirectness (n=54) Intervention 2: Parenteral feeding - Parenteral alone. Total parenteral nutrition solution, containing nitrogen, glucose, calcium, magnesium, potassium, trace elements, and multiple vitamins in a volume of 2000 ml, was continuously infused within 24 hours, along with 250 ml of 20% introlipid, with infusion rates that provided 1.2 g of protein per kilogram per day and 105 to 126 kJ of energy intake per kilogram per day. Total parenteral nutrition was infused by single lumen polyurethane catheters through the anterior chests. Duration Not stated. Concurrent medication/care: Prophylactic antibiotics (IV metronidazol/ciprofloxacin). Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PARENTERAL ALONE versus JEJUNAL	

Protocol outcome 1: Mortality at <1 year - Actual outcome for Adults >16 years: Mortality at Unclear; Group 1: 23/54, Group 2: 6/53; Comments: TPN group: 70% of deaths were due to septic shock; TEN group: 4 aspiration pneumonia; 2 multiple organ failure Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Adverse events (for example, tube displacements, aspirational pneumonia, ischaemic gut and central line infections) at <1 year - Actual outcome for Adults >16 years: Surgical intervention at Unclear; Group 1: 43/54, Group 2: 12/53 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults >16 years: Infected pancreatic necrosis at Unclear; Group 1: 39/54, Group 2: 12/53 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Serious adverse events at <1 year - Actual outcome for Adults >16 years: Single organ failure at Unclear; Group 1: 9/54, Group 2: 3/53 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults >16 years: Multiple organ failure at Unclear; Group 1: 35/54, Group 2: 8/53 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life at <1 year; Length of critical care or hospital stay at <1 year; Achieving nutrition (meeting nutritional requirements; at least 20-25 kcal/kg) at <1 year; Requiring total parenteral nutrition at <1 year; Infections at <1 year; Weight loss/BMI at <1 year

Study	**Zhao 2015[1189]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=146)
Countries and setting	Conducted in China; Setting: National research centre for pancreatic disease
Line of therapy	1st line

Duration of study	Not clear:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: The diagnosis and severity of AP were established according to the 2012 revision of the Atlanta classification
Stratum	Adults >16 years
Subgroup analysis within study	Not applicable
Inclusion criteria	Acute abdominal pain accompanied by elevated serum amylase and/or lipase levels (>3-fold above the upper reference limit) and unequivocal evidence of AP on ultrasound and CT.
Exclusion criteria	1. Age <18 y or >70 y; 2. Abdominal pain lasting >72 h before admission; 3. Mild AP; 4. Pregnant or breastfeeding; 5. Pancreatic neoplasm, ERCP, or trauma aetiology; 6. The possibility of poor oral intake or prolonged hospitalisation for reasons other than pancreatitis, such as gastroparesis or surgical intervention; 7. Admission to the intensive care unit for intubation; and 8. Surgical intervention for infected pancreatic necrosis or pancreatic haemorrhage
Recruitment/selection of patients	Consecutive
Age, gender and ethnicity	Age - Median (range): Early group: 51 (24-72); Conventional group: 48 (21-74). Gender (M:F): 62/38%. Ethnicity: Not reported
Further population details	1. Patients in critical care: Not stated / Unclear
Extra comments	Mean Ranson score: Early - 3.4 (1.8); conventional - 3.9 (1.1) Moderate severity: Early - 67.2%; conventional - 78.9%
Indirectness of population	No indirectness
Interventions	(n=70) Intervention 1: Oral feeding - Early oral feeding. Recommenced oral feeding once they felt hungry regardless of laboratory parameters. The diet was gradually progressed from clear liquid to a low-fat solid diet. Duration Unclear. Concurrent medication/care: All patients received conservative treatment according to their individual conditions, including limited PN if they were in malnutrition and EN was contraindicated or not feasible, prophylactic antibiotics if they were at risk for infection, glucose control (insulin or acarbose oral) if they were at risk for hyperglycaemia, treatment to maintain the homeostasis, appropriate fluid resuscitation therapy, and Traditional Chinese Medicine (TCM) formulation. PN was given after adequate fluid resuscitation and when the patient had achieved full hemodynamic stabilisation (usually 48–72 h after admission). Adequate protein delivery (1.2–2.0 g/kg

	daily) and calories (15–30 kcal/kg daily) were given to patients according to their individual condition. The volume of PN was gradually reduced after oral 'refeeding' (usually 12–24 h after the first oral intake). Indirectness: No indirectness (n=76) Intervention 2: Oral feeding. Conventional oral 'refeeding' (recommenced oral feeding once their abdominal pain resolved and biochemical markers had normalised.) Duration Unclear. Concurrent medication/care: All patients received conservative treatment according to their individual conditions, including limited PN if they were in malnutrition and EN was contraindicated or not feasible, prophylactic antibiotics if they were at risk for infection, glucose control (insulin or acarbose oral) if they were at risk for hyperglycaemia, treatment to maintain the homeostasis, appropriate fluid resuscitation therapy, and Traditional Chinese Medicine (TCM) formulation. PN was given after adequate fluid resuscitation and when the patient had achieved full hemodynamic stabilisation (usually 48–72 h after admission). Adequate protein delivery (1.2–2.0 g/kg daily) and calories (15–30 kcal/kg daily) were given to patients according to their individual condition. The volume of PN was gradually reduced after oral feeding (usually 12–24 h after the first oral intake). Indirectness: No indirectness
Funding	Academic or government funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EARLY ORAL FEEDING versus CONVENTIONAL ORAL FEEDING

Protocol outcome 1: Length of critical care or hospital stay at <1 year
- Actual outcome for Adults >16 years: Length of hospital stay at Unclear; Group 1: mean 13.7 (SD 5.4); n=67, Group 2: mean 15.7 (SD 6.2); n=71
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: Refusal to follow prescribed feeding schedule; Group 2 Number missing: 5, Reason: Refusal to follow prescribed feeding schedule

Protocol outcome 2: Requiring total parenteral nutrition at <1 year
- Actual outcome for Adults >16 years: Parenteral nutrition at Unclear; Group 1: 65/67, Group 2: 69/71
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: Refusal to follow prescribed feeding schedule; Group 2 Number missing: 5, Reason: Refusal to follow prescribed feeding schedule

Protocol outcome 3: Adverse events (for example, tube displacements, aspirational pneumonia, ischaemic gut and central line infections) at <1 year
- Actual outcome for Adults >16 years: Abdominal pain relapse at Unclear; Group 1: 7/67, Group 2: 10/71

Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: Refusal to follow prescribed feeding schedule; Group 2 Number missing: 5, Reason: Refusal to follow prescribed feeding schedule	
Protocol outcomes not reported by the study	Quality of life at <1 year; Weight loss/BMI at <1 year; Achieving nutrition (meeting nutritional requirements; at least 20-25 kcal/kg) at <1 year; Infections at <1 year; Serious adverse events at <1 year; Mortality at <1 year

H.8.2 Observational studies

Study	**Individual patient data meta-analysis of single-arm from RCTs trial: Bakker 2014[70]**
Study type	Systematic Review
Number of studies (number of participants)	8 (n=165 (95 with predicted severe AP))
Countries and setting	Conducted in Canada, Greece, Hungary, New Zealand, Spain, United Kingdom, USA; Setting: Systematic review: mixed
Line of therapy	1st line
Duration of study	Intervention + follow up: systematic review - mixed
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults >16 years
Subgroup analysis within study	Sys review – pre-specified in protocol: Predicted severe pancreatitis (defined as APACHE-II score ≥8, Imrie score ≥3, Ranson score ≥3, or CRP >150 mg/L)
Inclusion criteria	Randomised trials with early EN in one arm of the study in adults with acute pancreatitis. The following inclusion criteria were used: consecutive patients with acute pancreatitis, use of a validated classification system or generally accepted parameter to predict severity on admission, and initiation of EN according to a pre-specified protocol.
Exclusion criteria	Not stated

Recruitment/selection of patients	Consecutive within each trial
Age, gender and ethnicity	Age - Median (IQR): Early EN: 53 (42-66); delayed EN: 55 (45-70) years. Gender (M:F): 64/36%. Ethnicity: Not stated
Further population details	1. Patients in critical care: Systematic review: mixed
Extra comments	.
Indirectness of population	No indirectness
Interventions	(n=47) Intervention 1: Enteral feeding - Early gastric feeding. Enteral feeding within 24 hours of admission. Duration Systematic review: mixed. Concurrent medication/care: Systematic review: mixed. Indirectness: No indirectness (n=48) Intervention 2: Enteral feeding - Late enteral feeding. Enteral feeding 24 hours or more after admission. Duration Systematic review: mixed. Concurrent medication/care: Systematic review: mixed. Indirectness: No indirectness
Funding	Academic or government funding
Protocol outcomes not reported by the study	Quality of life at <1 year; Length of critical care or hospital stay at <1 year; Achieving nutrition (meeting nutritional requirements; at least 20-25 kcal/kg) at <1 year; Requiring total parenteral nutrition at <1 year; Adverse events (e.g. tube displacements, aspirational pneumonia, ischemic gut and central line infections) at <1 year; Weight loss/BMI at <1 year

Study	**Propensity matched cohort trial: Jin 2017[537]**
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=104)

Countries and setting	Conducted in China; Setting: Single hospital
Line of therapy	Unclear
Duration of study	Intervention + follow up: unclear
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Revised Atlanta classification
Stratum	Adults >16 years
Subgroup analysis within study	Not applicable
Inclusion criteria	Moderately severe or severe acute pancreatitis
Exclusion criteria	GI bleeding or GI obstruction; allergic to components of the EN fluid; malignant tumours; multiple onsets; unable to describe subjective symptoms; pregnancy
Recruitment/selection of patients	Prospective, consecutive sample
Age, gender and ethnicity	Age - Mean (SD): Early: 43.9 (15.9); late: 45.2 (13.5). Gender (M:F): 68/32%. Ethnicity: Not stated
Further population details	1. Patients in critical care: Mixed (54.3% in the early group and 48.1% in the late group were in CCU).
Extra comments	42% severe; 58% moderately severe. 100% had abdominal pain
Indirectness of population	No indirectness
Interventions	(n=35) Intervention 1: Enteral feeding - Early gastric feeding. Early (within 3 days of hospital admission) enteral feeding with a nasojejunal feeding tube placed under X ray guidance, with peptide formulation. Enteral nutrition was given continuously using an infusion pump at 20 ml/h in the first 24 h, 40 ml/h from 24 to 48 h, 60-80 ml/h between 48 and 72 h to reach 25 kcal/kg/d based on ideal weight at 72 h. PN was initiated if full nutrition could not be achieved using the enteral route after 3 attempts. Duration Unclear. Concurrent medication/care: Rehydration, correction of electrolyte disorders and organ function support

	(n=52) Intervention 2: Enteral feeding - Late enteral feeding. Late (starting after 3 days from hospital admission) enteral feeding with a nasojejunal feeding tube placed under X ray guidance, with peptide formulation. Enteral nutrition was given continuously using an infusion pump at 20 ml/h in the first 24 h, 40 ml/h from 24 to 48 h, 60-80 ml/h between 48 and 72 h to reach 25 kcal/kg/d based on ideal weight at 72 h. PN was initiated if full nutrition could not be achieved using the enteral route after 3 attempts. Duration Unclear. Concurrent medication/care: Rehydration, correction of electrolyte disorders and organ function support. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EARLY ENTERAL FEEDING versus LATE ENTERAL FEEDING

Protocol outcome 1: Mortality at <1 year
- Actual outcome for Adults >16 years: Mortality at unclear; Group 1: 0/35, Group 2: 1/52
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Key confounders: matched for age, sex, aetiology, disease severity, abdominal pain, VAS of abdominal pain, abdominal distension, AGI grade and serum albumin level at admission; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Length of critical care or hospital stay at <1 year
- Actual outcome for Adults >16 years: Length of hospital stay at unclear;
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Key confounders: matched for age, sex, aetiology, disease severity, abdominal pain, VAS of abdominal pain, abdominal distension, AGI grade and serum albumin level at admission; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Infections at <1 year
- Actual outcome for Adults >16 years: Pancreatic infections at unclear; Group 1: 1/35, Group 2: 6/52
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Key confounders: matched for age, sex, aetiology, disease severity, abdominal pain, VAS of abdominal pain, abdominal distension, AGI grade and serum albumin level at admission; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults >16 years: Extra-pancreatic infections (systemic or localised) at unclear; Group 1: 2/35, Group 2: 15/52
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Key confounders: matched for age, sex, aetiology, disease severity, abdominal pain, VAS of abdominal pain, abdominal distension, AGI grade and serum albumin level at admission; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults >16 years: Multi-site infections at unclear; Group 1: 0/35, Group 2: 6/52

Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Key confounders: matched for age, sex, aetiology, disease severity, abdominal pain, VAS of abdominal pain, abdominal distension, AGI grade and serum albumin level at admission; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Adverse events (e.g. tube displacements, aspirational pneumonia, ischemic gut and central line infections) at <1 year - Actual outcome for Adults >16 years: Abnormal glucose metabolism at unclear; Group 1: 22/35, Group 2: 31/52 Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Key confounders: matched for age, sex, aetiology, disease severity, abdominal pain, VAS of abdominal pain, abdominal distension, AGI grade and serum albumin level at admission; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults >16 years: Surgical or percutaneous intervention at unclear; Group 1: 2/35, Group 2: 11/52; Comments: Early:1 percutaneous and 1 surgical; late: 8 percutaneous and 3 surgical Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Key confounders: matched for age, sex, aetiology, disease severity, abdominal pain, VAS of abdominal pain, abdominal distension, AGI grade and serum albumin level at admission; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults >16 years: Non-infective pancreatic complications at unclear; Group 1: 31/35, Group 2: 50/52 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Key confounders: matched for age, sex, aetiology, disease severity, abdominal pain, VAS of abdominal pain, abdominal distension, AGI grade and serum albumin level at admission; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life at <1 year; Achieving nutrition (meeting nutritional requirements; at least 20-25 kcal/kg) at <1 year; Requiring total parenteral nutrition at <1 year; Serious adverse events at <1 year; Weight loss/BMI at <1 year

Study	**Wereszczynska-siemiatkowska 2013[1142]**
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=197)
Countries and setting	Conducted in Poland; Setting: Hospital inpatients
Line of therapy	1st line

Duration of study	Intervention + follow up: unclear
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Two of the following characteristics: upper abdominal pain, serum amylase or lipase activities at least 3 times higher than normal, and findings of abdominal contrast-enhanced computed tomography (CT), magnetic resonance imaging, or ultrasonography suggesting AP.
Stratum	Adults >16 years
Subgroup analysis within study	Not applicable
Inclusion criteria	Severe AP within the first 48 hours of admission to hospital and treatment with total enteral feeding
Exclusion criteria	Younger than 18 years of age; admission after 72 hours of the onset of symptoms; acute exacerbation of chronic pancreatitis; AP confirmed during laparotomy for acute abdomen; treatment with total parenteral feeding alone; early deaths of patients with severe AP who did not receive total enteral feeding.
Recruitment/selection of patients	Consecutive
Age, gender and ethnicity	Age - Median (IQR): Early: 49 (39-56); delayed: 50 (41-62.5). Gender (M:F): Early: 74/26%; delayed: 61/39%. Ethnicity:
Further population details	1. Patients in critical care: Not stated / Unclear
Extra comments	The diagnosis of severe AP was established by the presence of one or more of the following within the first 48 hours: SIRS; Acute Physiology and Chronic Health Evaluation (APACHE) II score, 8 or greater; Bedside Index of Severity in AP (BISAP), 3 or greater; Panc 3 score; Ranson score, 3 or greater; Balthazar score C-E; or organ failure assessed using Sequential Organ Failure Assessment (SOFA) score
Indirectness of population	No indirectness
Interventions	(n=97) Intervention 1: Enteral feeding - Early gastric feeding. Enteral nutrition started within the first 48 hours after admission to hospital. Duration Unclear. Concurrent medication/care: Patients were managed by standard medical treatment in AP: intravenous fluid and electrolytes, analgesia, prophylactic antibiotics, and other supportive therapies

	for organ failure, as indicated. Emergency endoscopic retrograde cholangiopancreatography was performed within 24 to 72 hours on patients with suspected choledocholithiasis.. Indirectness: No indirectness (n=100) Intervention 2: Enteral feeding - Late enteral feeding. Enteral nutrition started more than 48 hours after admission to hospital. Duration Unclear. Concurrent medication/care: Patients were managed by standard medical treatment in AP: intravenous fluid and electrolytes, analgesia, prophylactic antibiotics, and other supportive therapies for organ failure, as indicated. Emergency endoscopic retrograde cholangiopancreatography was performed within 24 to 72 hours on patients with suspected choledocholithiasis.. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EARLY ENTERAL FEEDING versus DELAYED ENTERAL FEEDING

Protocol outcome 1: Mortality at <1 year
- Actual outcome for Adults >16 years: Mortality at Unclear; Group 1: 0/97, Group 2: 9/100
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Length of critical care or hospital stay at <1 year
- Actual outcome for Adults >16 years: Length of hospital stay at Unclear; ;
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Infections at <1 year
- Actual outcome for Adults >16 years: Infected necrosis or infected fluid collection at Unclear; OR; 4.094 (95%CI 1.169 to 14.343, Comments: Adjusted for APACHE II score at day 3, persistence of SIRS after 48 hours);
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults >16 years: Localised infections (pneumonia or UTI) at Unclear; Group 1: 26/97, Group 2: 39/100
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults >16 years: Pancreatic infections at Unclear; Group 1: 4/97, Group 2: 18/100
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;

	Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults >16 years: Systemic infections (sepsis) at Unclear; Group 1: 2/97, Group 2: 4/100 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Adverse events (e.g. tube displacements, aspirational pneumonia, ischemic gut and central line infections) at <1 year - Actual outcome for Adults >16 years: Requiring surgery at Unclear; Group 1: 7/97, Group 2: 11/100 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults >16 years: Pancreatic complications (necrosis, pseudocyst, ascites, haemorrhage, fistula) at Unclear; Group 1: 63/97, Group 2: 86/100 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 5: Serious adverse events at <1 year - Actual outcome for Adults >16 years: Multi-organ failure at Unclear; Group 1: 9/97, Group 2: 16/100 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
Protocol outcomes not reported by the study	Quality of life at <1 year; Achieving nutrition (meeting nutritional requirements; at least 20-25 kcal/kg) at <1 year; Requiring total parenteral nutrition at <1 year; Weight loss/BMI at <1 year

H.9 Early versus late nutritional intervention in people with chronic pancreatitis

None.

H.10 Specialist versus non-specialist nutritional assessment in people with chronic pancreatitis

None.

H.11 Prophylactic antimicrobial agents to prevent infection in people with acute pancreatitis

Study	Bassi 1998[100]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=60)
Countries and setting	Conducted in Greece, Italy; Setting: University of Verona; Pancreatic Disease Center, Cardarelli Hospital, naples; Agia Holga Hospital; Mestre Hospital
Line of therapy	Not applicable
Duration of study	Intervention time: 2 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Evidence of pancreatic necrosis was detected by CT and intravenous contrast medium and confirmed by CRP values above 100 mg/L and extending to at least 50% volume of the gland.
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	No history of pancreatic disease; definite diagnosis of severe pancreatitis of any etiology with onset of pain symptoms occurring not more than 5 days before admission; definite evidence of pancreatic necrosis as detected by CT and intravenous contrast medium and confirmed by CRP values above 100 mg/L and extending to at least 50% volume of the gland; and no antibiotic intake during the hours immediately before admission.
Exclusion criteria	Not reported
Recruitment/selection of patients	Patients admitted to the participating centers with acute necrotising pancreatitis were screened
Age, gender and ethnicity	Age - Range: 34-70. Gender (M:F): 34/26. Ethnicity: Not reported
Further population details	1. Severity of pancreatitis (as defined by study): Severe pancreatitis (ranson score 4.4 (3-6), 4.7 (3-6); Apache II score 12 (10-21), 11 (9-22); CRP mg dl 301 (155-485), 314 (145-510), pancreatic necrosis >50%).
Extra comments	n or mean (range) in the imipenem and pefloxacin groups, respectively: ranson score 4.4 (3-6), 4.7 (3-6); Apache II score 12 (10-21), 11 (9-22); CRP mg dl 301 (155-485), 314 (145-510), biliary etiology 18, 19; biliary + alcoholic 4, 4; alcoholic 4, 5; post ERCP 2, 0; idiopathic 2, 2; days from abdominal pain to admission 2.1 (1.5-5), 1.9 (0.5-5). Severe necrotic component >50% pancreatic volume
Indirectness of population	No indirectness
Interventions	(n=30) Intervention 1: Prophylactic antimicrobial therapy - Quinolone. 400 mg Pefloxin IV, 2 times daily. Duration 2 weeks. Concurrent medication/care: Patients with pancreatitis of biliary etiology underwent endoscopic sphincterotomy

	within 72 hours of admission Further details: 1. Drug class: Quinolones 2. Drug dose: Not stated / Unclear 3. Drug route: Intravenous 4. Duration of therapy: Not stated / Unclear (n=30) Intervention 2: Prophylactic antimicrobial therapy - Carbapenem. 500 mg Imipenem IV, given 3 times daily. Duration 2 weeks . Concurrent medication/care: Patients with pancreatitis of biliary etiology underwent endoscopic sphincterotomy within 72 hours of admission Further details: 1. Drug class: Quinolones 2. Drug dose: Not stated / Unclear 3. Drug route: Intravenous 4. Duration of therapy: Not stated / Unclear
Funding	Academic or government funding (Supported by Italian Ministry of the University grant)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PEFLOXACIN versus IMIPENEM Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year - Actual outcome for Adults (>16 years): Length of hospital stay at 2 weeks; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 2: Mortality at <1 year - Actual outcome for Adults (>16 years): Mortality (postoperative) at 2 weeks; Group 1: 5/30, Group 2: 3/30; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 3: Infected necrosis at <1 year - Actual outcome for Adults (>16 years): Infected necrosis at 2 weeks; Group 1: 10/30, Group 2: 3/30; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 4: Extra-pancreatic infection at <1 year - Actual outcome for Adults (>16 years): Extra-pancreatic infection at 2 weeks; Group 1: 13/30, Group 2: 6/30; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Colonisation by resistant organisms at >6 months; Serious adverse events at <6 months; Serious adverse events at >6 months; Colonisation by resistant organisms at <6 months

Study	**Delcenserie 1996[278]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=23)

Countries and setting	Conducted in France; Setting: Departments of Gastroenterology and Internal Medicine, CHU Nord, Amiens Cedex, France
Line of therapy	Not applicable
Duration of study	Intervention time: 10 days
Method of assessment of guideline condition	Unclear method of assessment/diagnosis
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	No previous pancreatic disease; admission within 48 hours of onset; no previous antibiotic treatment; and acute alcoholic pancreatitis, with two or more fluid collections demonstrated by CT within 48 hours.
Exclusion criteria	<18 years; antibiotic allergy; and the need to carry out endoscopic retrograde cholangiopancreatography (ERCP)
Recruitment/selection of patients	Patients admitted into hospital with severe alcoholic acute pancreatitis were recruited
Age, gender and ethnicity	Age - Range: 21-74. Gender (M:F): 21/2. Ethnicity: Not reported
Further population details	1. Severity of pancreatitis (as defined by study): Severe pancreatitis
Extra comments	The Ranson early objective signs ranged from 0 to 7, with a mean value of 2.3 ± 2.
Indirectness of population	No indirectness
Interventions	(n=11) Intervention 1: Prophylactic antimicrobial therapy – Combination of antimicrobials. Subjects received intravenous ceftazidime, 2 g every 8 hours; intravenous amikacin, 7.5 mg/kg every 12 hours; and intravenous metronidazole, 0.5 g every 8 hours for 10 days. Duration 10 days . Concurrent medication/care: All patients also received medical treatment. Further details: 1. Drug class: Systematic review: mixed 2. Drug dose: Not stated / Unclear 3. Drug route: Intravenous 4. Duration of therapy: Not stated / Unclear (n=12) Intervention 2: No prophylactic antimicrobial therapy. Subjects received medical treatment only. Duration 10 days. Concurrent medication/care: None reported Further details: 1. Drug class: Not applicable 2. Drug dose: Not applicable 3. Drug route: Not applicable 4. Duration of therapy: Not applicable
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CEFTAZIDIME, AMIKACIN, METRONIDAZOLE versus NO PROPHYLACTIC ANTIMICROBIAL THERAPY

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year - Actual outcome for Adults (>16 years): Length of hospitalisation at 10 days; Group 1: mean 22 days (SD 10.7); n=11, Group 2: mean 27.8 days (SD 24.6); n=12; Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 2: Mortality at <1 year - Actual outcome for Adults (>16 years): Mortality at 10 days; Group 1: 1/11, Group 2: 3/12; Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 3: Infected necrosis at <1 year - Actual outcome for Adults (>16 years): Superinfection of necrotic pancreatic tissue at 10 days; Group 1: 0/11, Group 2: 3/12; Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 4: Extra-pancreatic infection at <1 year - Actual outcome for Adults (>16 years): Patients with infection at 10 days; Group 1: 0/11, Group 2: 7/12; Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 5: Serious adverse events at <6 months - Actual outcome for Adults (>16 years): Multiorgan failure at 10 days; Group 1: 1/11, Group 2: 1/12; Risk of bias: Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Colonisation by resistant organisms at >6 months; Serious adverse events at >6 months; Colonisation by resistant organisms at <6 months

Study	**Dellinger 2007[280]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=100)
Countries and setting	Conducted in Austria, Belgium, Canada, Estonia, Germany, Latvia, Lithuania, Portugal, Spain, United Kingdom, USA; Setting: 32 sites within North America and Europe
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 42 days (at least 35 days follow up)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable:

Inclusion criteria	Male or female patients ≥18 years of age with a confirmed diagnosis of necrotising pancreatitis within 120 hours of onset of symptoms. Patients with ≥30% necrosis of the pancreas confirmed by contrast-enhanced CT were eligible for inclusion. Alternatively, patients who were unsuitable for CT scan in the judgment of the investigator, and who had non-contrast scans with extensive or multiple peripancreatic fluid collections and pancreatic edema (Balthazar grade E), and had either CRP >120 mg/L or a multiple organ dysfunction (MOD) score >2 were also eligible. In addition randomisation and receipt of first dose of study treatment was required within 120 hours of the onset of symptoms for inclusion in the study.
Exclusion criteria	Patients diagnosed with concurrent pancreatic or peripancreatic infection were excluded from the study, as were patients who had received an investigational drug <30 days prior to enrollment, antimicrobial therapy for >48 hours prior to randomisation, or who had allergy to beta-lactam antimicrobial agents. In addition, patients who received or were likely to require probenecid or who had progressing underlying disease, neutropenia, or cirrhosis (Child-Pugh class C), and pregnant or lactating females were also excluded.
Age, gender and ethnicity	Age - Other: 18-64 years, n=68; 65-74 years, n=18; >75 years, n=14. Gender (M:F): 70/30. Ethnicity: white 98, black 2
Further population details	1. Severity of pancreatitis (as defined by study): Severe pancreatitis
Extra comments	Baseline characteristics (n) for intervention and control group, respectively: biliary etiology 22, 12; alcohol etiology 18, 26; other etiology 10, 12; <30% necrosis at CECT 15, 10; ≥30% necrosis at CECT 26, 31; not recorded 9,9. . Baseline characteristics, mean (range) for intervention and control group, respectively: days between symptom onset and 1st dose 3(1-6), 3(1-8); ranson score 4.5(1-8), 3.8(0-8); modified Glasgow score 4.2(1-8), 3.4(0-7); APACHE II 12.7(2-30), 11.5(0-39); CTSI 7.1(6-10), 7.7(6-10); MOD 3.7(0-13), 2.8(0-12); CRP 274(120-456), 262(50-661).
Indirectness of population	No indirectness
Interventions	(n=50) Intervention 1: Prophylactic antimicrobial therapy - Carbapenem. Meropenem 1 g powder reconstituted in fluid administered by intravenous infusion over 15 to 30 minutes every 8 hours. . Duration 7-21 days (14 days recommended). Concurrent medication/care: The use of non-protocol antibiotics during this time was discouraged but could not be prohibited in these seriously ill patients. Most patients received nutritional support and the incidence of support was not different between the meropenem and placebo arms. Further details: 1. Drug class: Carbapenems 2. Drug dose: (1g every 8 hours). 3. Drug route: Intravenous 4. Duration of therapy: Comments: 31 patients in this group received drug for a duration <14 days: 11 stopped as they were diagnosed an infection and started non-study antibiotic or received surgery; 5 recovered; 2 died; 1 refused further drug. 25 patients received additional antibiotics other than study drug for clinical indications. (n=50) Intervention 2: Placebo. dose-and administration-matched placebo. Duration 7-21 days (14 days recommended).

	Concurrent medication/care: The use of non-protocol antibiotics during this time was discouraged but could not be prohibited in these seriously ill patients. Most patients received nutritional support and the incidence of support was not different between the meropenem and placebo arms. Further details: 1. Drug class: 2. Drug dose: 3. Drug route: 4. Duration of therapy: Comments: 32 patients in this group received drug for a duration <14 days: 10 stopped as they were diagnosed an infection and started non-study antibiotic or received surgery; 2 recovered; 4 died. 27 patients received additional antibiotics other than study drug for clinical indications.
Funding	Equipment / drugs provided by industry (Supported by a grant from AstraZeneca Pharmaceuticals)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: MEROPENEM versus PLACEBO Protocol outcome 1: Mortality at <1 year - Actual outcome for Adults (>16 years): Mortality at within 42 days of randomisation; Group 1: 10/50, Group 2: 9/50; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 2: Infected necrosis at <1 year - Actual outcome for Adults (>16 years): Pancreatic infection at within 42 days of randomisation; Group 1: 9/40, Group 2: 6/40; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 3: Extra-pancreatic infection at <1 year - Actual outcome for Adults (>16 years): Nonpancreatic nosocomial infections at within 42 days of randomisation; Group 1: 16/50, Group 2: 24/50; Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 4: Colonisation by resistant organisms at <6 months - Actual outcome for Adults (>16 years): Pancreatic infection by meropenem-resistant bacteria at within 42 days of randomisation; Group 1: 5/40, Group 2: 2/40; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 5: Serious adverse events at <6 months - Actual outcome for Adults (>16 years): Serious adverse events at within 42 days of randomisation; Group 1: 6/50, Group 2: 9/50; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Colonisation by resistant organisms at >6 months; Serious adverse events at >6 months; Length of stay (in intensive therapy unit or hospital) at <1 year

Study	Garcia-Barrasa 2009[384]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=41)
Countries and setting	Conducted in Spain; Setting: Surgical Gastrointestinal Service of Bellvitge Hospital
Line of therapy	Not applicable
Duration of study	Intervention time: 10 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosed according to the Atlanta criteria
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	All patients without previous antibiotic treatment and with detectable pancreatic necrosis in a CECT scan performed within 48-72 hours of admission.
Exclusion criteria	Patients with a quinolone allergy or clinical evidence of sepsis on admission.
Recruitment/selection of patients	Patients admitted to hospital with acute pancreatitis and pancreatic necrosis were recruited.
Age, gender and ethnicity	Age - Range: 31-84. Gender (M:F): 29/12. Ethnicity: Not reported
Further population details	1. Severity of pancreatitis (as defined by study): Severe pancreatitis (Severe pancreatitis according to the Atlanta classification).
Extra comments	Percentage in intervention and control group, respectively: biliary 72.7, 57.9; alcohol 9.1, 26.3; others 18.2, 15.8. Number of patients in the intervention and control group, respectively: necrosis <30% 11, 9; necrosis 30-50% 3, 6; necrosis >50% 8,4. Mean in intervention and control group, respectively: APACHE score 10, 14; CRP mg/L in first 48 h 313(25-431), 326(106-453).
Indirectness of population	No indirectness
Interventions	(n=22) Intervention 1: Prophylactic antimicrobial therapy - Quinolone. 300 mg ciprofloxacin q. 12 hours for 10 days. Duration 10 days. Concurrent medication/care: All patients were treated medically on admission (aggressive fluid resuscitation along with electrolyte imbalance, complete avoidance of oral intake, pain control and total parenteral nutrition Further details: 1. Drug class: Quinolones 2. Drug dose: Low dose (BNF dose: 400 mg). 3. Drug route: Not stated / Unclear 4. Duration of therapy: Not stated / Unclear Comments: In 7 patients, medication had to be discontinued and open antibiotic treatment had to be started after a mean of 7 days (range 3-9)

	(n=19) Intervention 2: Placebo. Control patients were given placebo.. Duration 10 days. Concurrent medication/care: All patients were treated medically on admission (aggressive fluid resuscitation along with electrolyte imbalance, complete avoidance of oral intake, pain control and total parenteral nutrition Further details: 1. Drug class: Not applicable 2. Drug dose: Not applicable 3. Drug route: Not applicable 4. Duration of therapy: Not applicable Comments: In 8 patients placebo had to be discontinued and open antibiotic treatment had to be started instead after a mean of 6 days (range 4-8 days)
Funding	Academic or government funding (Supported by the Bellvitge Hospital)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CIPROFLOXACIN versus PLACEBO

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome for Adults (>16 years): Length of hospital stay at 10 days; Risk of bias: Very high; Indirectness of outcome: No indirectness
- Actual outcome for Adults (>16 years): Length of CCU stay at 10 days; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality at <1 year
- Actual outcome for Adults (>16 years): Mortality at 10 days; Group 1: 4/22, Group 2: 2/19; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 3: Infected necrosis at <1 year
- Actual outcome for Adults (>16 years): Infected necrosis at 10 days; Group 1: 8/22, Group 2: 8/19; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 4: Extra-pancreatic infection at <1 year
- Actual outcome for Adults (>16 years): Number of people with one or more extra-pancreatic infections at 10 days; Group 1: 6/22, Group 2: 8/22; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 5: Serious adverse events at <6 months
- Actual outcome for Adults (>16 years): Organ failure at 10 days; Group 1: 13/22, Group 2: 10/19; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcomes not reported by the study	Quality of life at <1 year; Colonisation by resistant organisms at >6 months; Serious adverse events at >6 months; Colonisation by resistant organisms at <6 months

Study	He 2003[450]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=70)
Countries and setting	Conducted in China; Setting: Not reported
Line of therapy	Not applicable
Duration of study	Not clear:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosed with the diagnosis criteria proposed by the Pancreas Surgery Group of the Chinese Medical Association in 1997
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Subjects with a clinical diagnosis and one of the following predisposing factors of deep fungal infections, such as gerontism, history of diabetes, dysfunction of one or more organs, non-iatrogenic fasting hyperglycemia (≥ 9 mmol/L), central venous catheter, TPN, retaining urethral catheterisation, operation, gastrointestinal fistula, CCU, breathing machine supported ≥ 5 days, administration of broad spectrum antibiotics ≥ 5 days or super broad spectrum antibiotics ≥ 3 days
Exclusion criteria	Not reported
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - --: . Gender (M:F): 37/33. Ethnicity: Not reported
Further population details	1. Severity of pancreatitis (as defined by study): Severe pancreatitis
Extra comments	Etiological factors - Fluconazole group: Biliary - 11, Alcoholemia - 6, Others - 5; Control group: Biliary - 11, Alcoholemia - 7, Injury - 1, Others - 4 APACHIII scores - Fluconazole group: 13.2 ± 2.5, Control group: 11.6 ± 4.7
Indirectness of population	No indirectness
Interventions	(n=22) Intervention 1: Prophylactic antimicrobial therapy - Imidazole antifungal. Subjects were given venous instillation of 100 mg fluconazole once a day plus routine treatment. Duration Until relief of predisposing factors. Concurrent medication/care: All patients received routine treatment Further details: 1. Drug class: Imidazole antifungals 2. Drug dose: Not stated / Unclear 3. Drug route: Intravenous 4. Duration of therapy: Not stated / Unclear

	(n=23) Intervention 2: No prophylactic antimicrobial therapy. Subjects received routine treatment only. Duration For the duration of the study. Concurrent medication/care: Not reported Further details: 1. Drug class: Not applicable 2. Drug dose: Not applicable 3. Drug route: Not applicable 4. Duration of therapy: Not applicable
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: FLUCONAZOLE versus NO PROPHYLACTIC ANTIMICROBIAL THERAPY Protocol outcome 1: Extra-pancreatic infection at <1 year - Actual outcome for Adults (>16 years): Fungal infections at Duration of study; Group 1: 2/22, Group 2: 7/23; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Mortality at <1 year; Infected necrosis at <1 year; Colonisation by resistant organisms at <6 months; Colonisation by resistant organisms at >6 months; Serious adverse events at <6 months; Serious adverse events at >6 months; Length of stay (in intensive therapy unit or hospital) at <1 year

Study (subsidiary papers)	Isenmann 2004[500] (Forsmark 2005[363])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=114)
Countries and setting	Conducted in Germany; Setting: Universities of Ulm, Essen, Nuremberg, Magdeburg and Heidenheim, Germany
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 21 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Acute pancreatitis was defined as abdominal pain in combination with a 3-fold elevation of serum amylase and/or lipase. A serum CRP >150 mg/dl and/or presence of pancreatic necrosis on contrast enhanced CT scanning (CECT) were chosen to define severity.
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable:
Inclusion criteria	Patients with a predicted severe attack of acute pancreatitis. Acute pancreatitis was defined as abdominal pain in combination with a 3-fold elevation of serum amylase and/or lipase. A serum CRP >150 mg/dl and/or presence of pancreatic necrosis on contrast enhanced CT scanning (CECT) were chosen to define severity. Study inclusion had to be performed within 72h after the onset of upper abdominal pain.
Exclusion criteria	Not stated
Recruitment/selection of patients	Patients with predicted severe attack of acute pancreatitis presenting at participating hospitals
Age, gender and ethnicity	Age - Median (range): Ciprofloxacin/metronidazole group: 47.9(25.1-72.5), control group: 45.6(21.9-78.4). Gender (M:F): 87/27. Ethnicity: Not reported
Further population details	1. Severity of pancreatitis (as defined by study): Severe pancreatitis (serum CRP at inclusion mg/L intervention group 175(1-790), control group 176(0-492); presence of pancreatic necrosis on CECT).
Extra comments	Baseline characteristics, N or median(range), for intervention and control group, respectively: alcohol etiology 32, 34; biliary etiology 13, 9; other etiology 13, 13; Ranson 48h points 2.5(0-6), 2(0-7); serum CRP at inclusion mg/L 175(1-790), 176(0-492); study inclusion after onset of symptoms, hrs 52(4-84), 41(11-89). End of study medication at day 14 or 21 with no additional antibiotics: rectal temperature <37 degrees for>72 hrs and at least two of the following: a) peripheral white blood cell count within normal limits, b) decrease of serum CPR <50% of recent maximum, c) decrease of serum lipase <50% of recent maximum, d) CECT without progression of necrotic areas, e) oral food intake tolerated. End of study medication and open antibiotic treatment if a) newly developed sepsis or SIRS, b) newly developed multi organ failure (2 or more organ systems), c) extrapancreatic infection (pneumonia, urinary tract infection, intra-abdominal infection, sepsis without known focus) or pancreatic infection proven by fine needle aspiration/positive

	intraoperative smears, d) increase of serum CRP and clinically suspected extrapancreatic/pancreatic infection
Indirectness of population	No indirectness
Interventions	(n=58) Intervention 1: Prophylactic antimicrobial therapy - Combination of antimicrobials. Ciprofloxacin 2x400 mg/day intravenously in combination with metronidazole 2x500 mg/day. Duration 14-21 days. Concurrent medication/care: Not stated Further details: 1. Drug class: Not applicable (Combination of florowuinolone and nitroimidazole derivative). 2. Drug dose: Not applicable (ciprofloxacin 2x400 mg/day, metronidazole 2x500mg/day). 3. Drug route: Intravenous 4. Duration of therapy: (21 days). Comments: Study medication was given for 3-23 days (median 14 days) after the onset of symptoms. 16 people discontinued study medication and switched to open antibiotic treatment (n=56) Intervention 2: Placebo. Placebo. Duration 14-21 days. Concurrent medication/care: Not stated Further details: 1. Drug class: Not applicable 2. Drug dose: Not applicable 3. Drug route: Not applicable 4. Duration of therapy: Not applicable Comments: Study medication was given for 2-19 days (median 12 days) after onset of symptoms in the placebo group. 26 people discontinued placebo and switched over to antibiotic open treatment
Funding	Equipment / drugs provided by industry (Supported by study medication provided from Bayer Vital and Ratiopharm as well as financial grant from Bayer Vital)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINATION (CIPROFLOXACIN PLUS METRONIDAZOLE) versus PLACEBO

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome for Adults (>16 years): CCU stay (days) at 21 days; Risk of bias: High; Indirectness of outcome: No indirectness
- Actual outcome for Adults (>16 years): Hospitalisation (days) at 21 days; Risk of bias: High; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality at <1 year
- Actual outcome for Adults (>16 years): Mortality at 21 days; Group 1: 3/58, Group 2: 4/56; Risk of bias: High; Indirectness of outcome: No indirectness

Protocol outcome 3: Infected necrosis at <1 year
- Actual outcome for Adults (>16 years): Infected pancreatic necrosis at 21 days; Group 1: 7/58, Group 2: 5/56; Risk of bias: High; Indirectness of outcome: No indirectness

Protocol outcome 4: Extra-pancreatic infection at <1 year

- Actual outcome for Adults (>16 years): Extra-pancreatic infections at 21 days; Group 1: 13/58, Group 2: 13/56; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 5: Serious adverse events at <6 months - Actual outcome for Adults (>16 years): Serious adverse events (pulmonary insufficiency) at 21 days; Group 1: 26/58, Group 2: 25/55; Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome for Adults (>16 years): Serious adverse events (renal insufficiency) at 21 days; Group 1: 7/58, Group 2: 6/55; Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome for Adults (>16 years): Serious adverse events (shock) at 21 days; Group 1: 5/58, Group 2: 7/55; Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome for Adults (>16 years): Serious adverse events (SIRS) at 21 days; Group 1: 31/58, Group 2: 24/55; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Colonisation by resistant organisms at >6 months; Serious adverse events at >6 months; Colonisation by resistant organisms at <6 months

Study (subsidiary papers)	Luiten 1995[686] (Luiten 1997[687])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=109)
Countries and setting	Conducted in Netherlands; Setting: 16 participating hospitals in the Netherlands
Line of therapy	Not applicable
Duration of study	Intervention + follow up: Selective decontamination was done until the risk of acquiring a new infection was absent and follow up was continued till discharge or death
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Clinical examination and elevated plasma levels of amylase (>1000 international units/L), or at diagnostic laparotomy
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Define
Exclusion criteria	Define
Recruitment/selection of patients	Patients admitted to participating hospitals with objective clinical signs of severe acute pancreatitis were recruited.
Age, gender and ethnicity	Age - Range: 20-91. Gender (M:F): Define. Ethnicity: Not reported
Further population details	1. Severity of pancreatitis (as defined by study): Severe pancreatitis
Extra comments	Etiology - SD group: Alcohol - 19, Gallstones - 17, Blunt abdominal trauma - 1, Postoperative - 2, ERCP-induced - 1, Unknown - 10; Control group - Alcohol - 12, Gallstones - 19, Hyperparathryoidism - 2, Postoperative - 2, ERCP-induced - 3, Unknown - 14
Indirectness of population	No indirectness
Interventions	(n=50) Intervention 1: Prophylactic antimicrobial therapy - Combination of antimicrobials. The selective decontamination regimen consisted of colistin sulfate (200 mg), amphotericin (500 mg) and norfloxacin (Noroxin, Merck & Co., West Point, PA; 50 mg) every 6 hours. A sticky paste containing 2% of the three selective decontamination drugs was smeared along the upper and lower gums every 6 hours and at the tracheostomy, if present. The aforementioned daily dose was also given in a rectal enema every day. A short-term systemic prophylaxis of cefotaxime sodium (Claforan, Hoechst-Roussel Pharm., Inc., Somerville NJ; 500 mg) was given every 8 hours until gram-negative bacteria were eliminated from the oral cavity and rectum. . Duration 7.4 days. Concurrent medication/care: A nasogastric tube was always inserted. Intravenous crystalloid solutions were given according to clinical requirements. Oxygen therapy, based on arterial blood gas analysis, was administered by face mask and was replaced by assisted

	ventilation if the patient developed respiratory insufficiency. Further details: 1. Drug class: Systematic review: mixed 2. Drug dose: Not stated / Unclear 3. Drug route: Systematic review: mixed (Oral, topical and rectal). 4. Duration of therapy: Not stated / Unclear (n=52) Intervention 2: No prophylactic antimicrobial therapy. A nasogastric tube was always inserted. Intravenous crystalloid solutions were given according to clinical requirements. Oxygen therapy, based on arterial blood gas analysis, was administered by face mask and was replaced by assisted ventilation if the patient developed respiratory insufficiency.. Duration Until the presence of infection was indicated. Concurrent medication/care: None reported Further details: 1. Drug class: Not applicable 2. Drug dose: Not applicable 3. Drug route: Not applicable 4. Duration of therapy: Not applicable
Funding	Equipment / drugs provided by industry (Supported by a grant from Merck Shard & Dohme B.V., the Netherlands and a grant from Roussel B.V., the Netherlands)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SELECTIVE DECONTAMINATION (COLISTIN SULFATE, AMPHOTERICIN, NORFLOXACIN) versus NO PROPHYLACTIC ANTIMICROBIAL THERAPY Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year - Actual outcome for Adults (>16 years): Length of hospital stay at Duration of study; Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 2: Mortality at <1 year - Actual outcome for Adults (>16 years): Mortality at Duration of study; Group 1: 11/50, Group 2: 18/52; Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 3: Infected necrosis at <1 year - Actual outcome for Adults (>16 years): Infected necrosis at Duration of study; Group 1: 9/50, Group 2: 20/52; Risk of bias: Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Colonisation by resistant organisms at <6 months; Colonisation by resistant organisms at >6 months; Serious adverse events at <6 months; Serious adverse events at >6 months; Extra-pancreatic infection at <1 year

Study	Manes 2003[707]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=176)
Countries and setting	Conducted in Italy; Setting: Carderelli Hospital, Napoli, Italy
Line of therapy	Not applicable
Duration of study	Intervention time: 14 days
Method of assessment of guideline condition	Unclear method of assessment/diagnosis
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	subjects older than 18 years, a diagnosis of AP with definite evidence of pancreatic necrosis as assessed by means of contrast-enhanced CT scan, admission within 72 hours of onset of symptoms, no intake of antibiotics in the 3 days before admission, and C-reactive protein concentration >120 mg/L within 48 hours of admission.
Exclusion criteria	Referred patients, immunocompromised patients, and patients with underlying chronic pancreatitis were excluded from the study.
Recruitment/selection of patients	Patients admitted to hospital with necrotising acute pancreatitis were recruited.
Age, gender and ethnicity	Age - Range: 19-91. Gender (M:F): 106/70. Ethnicity: Not reported
Further population details	1. Severity of pancreatitis (as defined by study): Severe pancreatitis (Glasgow score (mean, SD) for meropenem and imipenem groups, respectively: 6.0 (3.1), 5.0 (3.3)).
Extra comments	Number of patients in the meropenem and imipenem group, respectively: biliary etiology 57, 56; alcohol etiology 11, 9; other etiology 20, 23; necrosis <30% 51, 54; necrosis 30-50% 25, 21; necrosis >50% 12, 13. Mean (SD) for meropenem and imipenem groups, respectively: CRP mg/dl 219.3 (31.1), 235.2 (34.4); Glasgow score 6.0 (3.1), 5.0 (3.3); CE-CT score 7.0 (2.4), 7.0 (3.1)
Indirectness of population	No indirectness
Interventions	(n=88) Intervention 1: Prophylactic antimicrobial therapy - Carbapenem. 500 mg meropenem intravenously every 8 hours. Duration 14 days. Concurrent medication/care: All patients received the usual supportive medical treatment; endoscopic retrograde cholangiopancreatography with endoscopic sphincterotomy was performed in 96 patients with biliary forms. Further details: 1. Drug class: Carbapenems 2. Drug dose: Not stated / Unclear 3. Drug route: Intravenous 4. Duration of therapy: Not stated / Unclear

	(n=88) Intervention 2: Prophylactic antimicrobial therapy - Carbapenem. 500 mg imipenem intravenously every 6 hours. Duration 14 days. Concurrent medication/care: All patients received the usual supportive medical treatment; endoscopic retrograde cholangiopancreatography with endoscopic sphincterotomy was performed in 96 patients with biliary forms. Further details: 1. Drug class: 2. Drug dose: 3. Drug route: 4. Duration of therapy:
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: MEROPENEM versus IMIPENEM Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year - Actual outcome for Adults (>16 years): Length of hospital stay at 14 days; Mean imipenem group 24, meropenem group 23.3; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 2: Mortality at <1 year - Actual outcome for Adults (>16 years): Mortality at 14 days; Group 1: 12/88, Group 2: 10/88; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 3: Infected necrosis at <1 year - Actual outcome for Adults (>16 years): Infected necrosis at 14 days; Group 1: 10/88, Group 2: 12/88; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 4: Extra-pancreatic infection at <1 year - Actual outcome for Adults (>16 years): Extra-pancreatic infection at 14 days; Group 1: 19/88, Group 2: 21/88; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 5: Serious adverse events at <6 months - Actual outcome for Adults (>16 years): Multiorgan failure at 14 days; Group 1: 6/88, Group 2: 8/88; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Colonisation by resistant organisms at >6 months; Serious adverse events at >6 months; Colonisation by resistant organisms at <6 months

Study	Nordback 2001[806]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=58)
Countries and setting	Conducted in Finland; Setting: Single centre, Tampere University Hospital
Line of therapy	Unclear
Duration of study	Not clear:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Diagnosis of acute pancreatitis based on clinical criteria, an increase in serum amylase activity by at least three times the upper normal range, and CT verification of pancreatitis. The diagnosis of necrotizing pancreatitis was based on a serum C-reactive protein concentration >150 mg/L during the first 48 hours after admission and identification of necrotic areas in the pancreas with dynamic CT by the radiologist on duty.
Exclusion criteria	Those who had been started on antibiotics at the referring clinic, those admitted directly to intensive care unit because of early multi-organ failure, and those with frequent early need of antibiotic for other reasons, those who refused to participate in the study and those suspected of having a reaction to any of the study drugs
Recruitment/selection of patients	September 1995 to May 1999
Age, gender and ethnicity	Age - Mean (SD): intervention group 47(8); control group 46(7). Gender (M:F): 51/7. Ethnicity: not stated
Further population details	1. Severity of pancreatitis (as defined by study): Severe pancreatitis
Extra comments	Baseline characteristics, n or mean(SD) for intervention and control group, respectively: alcohol etiology 20, 25; biliary etiology 1, 2; other etiology 4, 6; CRP 211(44), 214(41); pancreatic necrosis on CT ,30% 8, 13; 30-50% 7, 10; >50% 10, 10. .
Indirectness of population	No indirectness
Interventions	(n=25) Intervention 1: Prophylactic antimicrobial therapy - Carbapenem. Imipenem 1.0 g plus cilastatin, IV three times a day. Duration unclear. Concurrent medication/care: non-operative conservative treatment was always attempted first. The three patients with gallstone pancreatitis underwent early ERCP. Patients with infected necrosis received surgery Further details: 1. Drug class: Carbapenems 2. Drug dose: 3. Drug route: Intravenous 4. Duration of therapy: Not stated / Unclear Comments: overall 11 patients received other antibiotics besides those originally used for this study

	(n=33) Intervention 2: No prophylactic antimicrobial therapy. No antimicrobial therapy. Duration unclear. Concurrent medication/care: non-operative conservative treatment was always attempted first. The three patients with gallstone pancreatitis underwent early ERCP. Patients with infected necrosis first received imipenem at a dosage similar to that used in the early imipenem group for 5 days and if indication to surgery persisted or patient deteriorated surgery was performed. Further details: 1. Drug class: 2. Drug dose: 3. Drug route: 4. Duration of therapy: Comments: overall 11 patients received other antibiotics besides those originally used for this study
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: IMIPENEM PLUS CILASTATIN versus NO PROPHYLACTIC ANTIMICROBIAL THERAPY Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year - Actual outcome for Adults (>16 years): length of hospital stay at unclear; Group 1: mean 20 (SD 13); n=23, Group 2: mean 17 (SD 10); n=28; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 2: Mortality at <1 year - Actual outcome for Adults (>16 years): Mortality at unclear; Group 1: 2/25, Group 2: 5/33; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 3: Serious adverse events at <6 months - Actual outcome for Adults (>16 years): major organ complications at unclear; Group 1: 5/25, Group 2: 11/33; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 4: infected pancreatic necrosis at <6 months - Actual outcome for Adults (>16 years): infected pancreatic necrosis at unclear; Group 1: 1/25, Group 2: 6/33; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 5: extra-pancreatic infection at <6 months - Actual outcome for Adults (>16 years): extra-pancreatic infection at unclear; Group 1: 4/25, Group 2: 1/33; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Extra-pancreatic infection at <1 year (available from published review that sought information from the author); Colonisation by resistant organisms at <6 months; Colonisation by resistant organisms at >6 months; Serious adverse events at >6 months; Infected necrosis at <1 year (available from published review that sought information from the author)

Study	Pederzoli 1993[847]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=74)
Countries and setting	Conducted in Italy; Setting: Six centers in Italy
Line of therapy	Not applicable
Duration of study	Intervention time: 14 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Necrotising AP was diagnosed on the basis of standard clinical criteria, ultrasonographic and computed tomographic scans.
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	No previous pancreatic disease, admission within 48 hours of onset, no clinical evidence of sepsis, no previous antibiotic treatment, availability of contrast enhanced CT scan within 72 hours of onset and presence of detectable pancreatic necrosis.
Exclusion criteria	Not reported
Recruitment/selection of patients	Patients admitted to hospital with necrotising AP were included
Age, gender and ethnicity	Age - Range: 20-84 years. Gender (M:F): 44/30. Ethnicity: Not reported
Further population details	1. Severity of pancreatitis (as defined by study): Not stated / Unclear (Mild, moderate and severe necrosis included).
Extra comments	n or mean in intervention and control group, respectively: biliary etiology 21, 16; alcohol etiology 13, 11; other etiology 7, 6; Ranson 3.7, 3.6; mild necrosis 15, 20; moderate necrosis 12, 11; severe necrosis 14, 2.
Indirectness of population	No indirectness
Interventions	(n=41) Intervention 1: Prophylactic antimicrobial therapy - Carbapenem. 500 mg Imipenem given intravenously every eight hours for 14 days.. Duration 14 days. Concurrent medication/care: All patients received the same medical treatment Further details: 1. Drug class: Carbapenems 2. Drug dose: Not stated / Unclear (BNF dose). 3. Drug route: Intravenous 4. Duration of therapy: Not stated / Unclear (n=33) Intervention 2: No prophylactic antimicrobial therapy. Patients in this group only received medical treatment. Duration 14 days. Concurrent medication/care: All patients received the same medical treatment. Further details: 1. Drug class: Not applicable 2. Drug dose: Not applicable 3. Drug route: Not applicable 4. Duration of

	therapy: Not applicable
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: IMIPENEM versus NO PROPHYLACTIC ANTIMICROBIAL THERAPY Protocol outcome 1: Mortality at <1 year - Actual outcome for Adults (>16 years): Mortality at 14 days; Group 1: 3/41, Group 2: 4/33; Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 2: Infected necrosis at <1 year - Actual outcome for Adults (>16 years): Pancreatic sepsis at 14 days; Group 1: 5/41, Group 2: 10/33; Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 3: Extra-pancreatic infection at <1 year - Actual outcome for Adults (>16 years): Non-Pancreatic sepsis at 14 days; Group 1: 6/41, Group 2: 16/33; Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 4: Serious adverse events at <6 months - Actual outcome for Adults (>16 years): Multiorgan failure at 14 days; Group 1: 12/41, Group 2: 13/33; Risk of bias: Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Colonisation by resistant organisms at <6 months; Colonisation by resistant organisms at >6 months; Serious adverse events at >6 months; Length of stay (in intensive therapy unit or hospital) at <1 year

Study	Røkke 2007[919]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=73)
Countries and setting	Conducted in Norway; Setting: Seven Norwegian hospitals
Line of therapy	Not applicable
Duration of study	Intervention time: 5-7 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis of acute pancreatitis was based on clinical examination, serum amylase levels above three times the normal upper limit or CT characteristics typical for acute pancreatitis.
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Criteria for inclusion included a duration of symptoms of less than 72h. Diagnosis of acute pancreatitis was based on clinical examination, serum amylase levels above three times the normal upper limit or CT characteristics typical for acute pancreatitis. The diagnosis of severe pancreatitis was based on a) CRP levels above 120 mg/l within the first 24 h or above 200 mg/l within 48h or b) pancreatitis necrosis as defined by dynamic CT.
Exclusion criteria	Age below 18 years, ongoing antibiotic treatment, previous episodes of acute pancreatitis, post-ERCP pancreatitis, concomitant bacterial infection such as cholangitis or cholecystitis, allergy to imipenem and pregnancy
Recruitment/selection of patients	Patients admitted to hospital with severe pancreatitis were eligible for inclusion
Age, gender and ethnicity	Age - Range: 19-84. Gender (M:F): 49/24. Ethnicity: Not reported
Further population details	1. Severity of pancreatitis (as defined by study): Severe pancreatitis (Imipenem and control group, respectively: APACHE II 7 (0-18), 6 (1-15); CRP 228 (122-448), 240 (49-457), CT pancreatic necrosis <30% 19, 18; CT necrosis 30-50% 3, 1; CT necrosis >50% 4, 9).
Extra comments	Imipenem and control group, n or mean (range), respectively: alcoholic cause 8, 10; biliary 20, 17; others 8, 10; APACHE II 7 (0-18), 6 (1-15); CRP 228 (122-448), 240 (49-457), CT pancreatic necrosis <30% 19, 18; CT necrosis 30-50% 3, 1; CT necrosis >50% 4, 9.
Indirectness of population	No indirectness
Interventions	(n=36) Intervention 1: Prophylactic antimicrobial therapy - Carbapenem. Early therapy with imipenem, 500 mg three times daily for 5-7 days. Duration 5-7 days. Concurrent medication/care: Not reported Further details: 1. Drug class: Carbapenems 2. Drug dose: Not stated / Unclear (BNF dose). 3. Drug route: Not stated / Unclear 4. Duration of therapy: Not stated / Unclear

	Comments: Patients in both groups were given antibiotics on demand when infection was diagnosed (n=37) Intervention 2: No prophylactic antimicrobial therapy. Patients in the control group did not receive any treatment.. Duration 5-7 days. Concurrent medication/care: Not reported Further details: 1. Drug class: Not applicable 2. Drug dose: Not applicable 3. Drug route: Not applicable 4. Duration of therapy: Not applicable Comments: Patients in both groups were given antibiotics on demand when infection was diagnosed
Funding	Study funded by industry (Supported by MSD)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: IMIPENEM versus NO THERAPY Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year - Actual outcome for Adults (>16 years): Hospitalisation at 4 weeks; Mean Imipenem: 18; control: 22; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 2: Mortality at <1 year - Actual outcome for Adults (>16 years): Mortality at 4 weeks; Group 1: 3/36, Group 2: 4/37; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 3: Extra-pancreatic infection at <1 year - Actual outcome for Adults (>16 years): Peri-pancreatic infection at 4 weeks; Group 1: 3/36, Group 2: 7/37; Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome for Adults (>16 years): Extra-pancreatic infection at 4 weeks; Group 1: 3/36, Group 2: 12/37; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 4: Serious adverse events at <6 months - Actual outcome for Adults (>16 years): Organ failure at 4 weeks; Group 1: 6/36, Group 2: 9/37; Risk of bias: Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Colonisation by resistant organisms at <6 months; Colonisation by resistant organisms at >6 months; Serious adverse events at >6 months; Infected necrosis at <1 year

Study	Sainio 1995[940]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=60)
Countries and setting	Conducted in Finland; Setting: Second department of surgery, Helsinki University central hospital.
Line of therapy	Not applicable
Duration of study	Intervention time: 14 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Dynamic CECT within 24 hours of admission, the pancreas was scanned at a preselected level for 60 seconds in a Siemens Somatom, Somatom DR2, or DRH
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	CRP concentration above 120 mg/L within 48 hours of admission and low contrast enhancement of the pancreas (below 30 Hounsfiels units [HU] on CECT. If CECT could not be done because of impaired renal function or allergy, early extrapancreatic scores were recorded and patients with scores of 4 or more points were included in the study.
Exclusion criteria	Treatment elsewhere for more than 2 days before admission to the hospital, continuing antimicrobial treatment, a previous severe episode of pancreatitis, and aetiology other than alcohol and no history of alcohol intake before admission.
Recruitment/selection of patients	60 consecutive patients admitted to hospital (July 1989 - November 1993)
Age, gender and ethnicity	Age - Mean (SD): 43 (11.3), 38.7 (8.4). Gender (M:F): 53/7. Ethnicity: Not reported
Further population details	1. Severity of pancreatitis (as defined by study): Not stated / Unclear
Extra comments	Alcohol-induced necrotising pancreatitis. Baseline characteristics for intervention and control group, respectively: mean (range) maximum C-reactive protein in first 48 hrs, mg/dl 308 (141-548), 343 (140-496); mean hospital (SD) stay 33.2 (22.1), 43.8 (43.1).
Indirectness of population	No indirectness
Interventions	(n=30) Intervention 1: Prophylactic antimicrobial therapy - Cephalosporin. Three doses of 1.5 g cefuroxime per day intravenously was started on admission and continued until clinical recovery and fall to normal of CRP concentrations. In cases of full recovery but moderately raised CRP concentrations, antibiotic treatment was continued with cefuroxime by mouth (two doses of 250 mg per day). Duration Up to 14 days. Concurrent medication/care: Adequate fluid replacement by central venous catheter, with monitoring of central venous pressure, and assistance of respiratory or renal function when needed.

	Further details: 1. Drug class: Cephalosporins 2. Drug dose: Not stated / Unclear (BNF dose). 3. Drug route: Intravenous 4. Duration of therapy: Not stated / Unclear (n=30) Intervention 2: No prophylactic antimicrobial therapy. No antibiotic treatment was given before infection had been clinically, microbiologically, or radiologically verified, or until there was a secondary rise in CRP of more than 20% after the acute phase.. Duration Up to 14 days. Concurrent medication/care: Adequate fluid replacement by central venous catheter, with monitoring of central venous pressure, and assistance of respiratory or renal function when needed. Further details: 1. Drug class: Not applicable 2. Drug dose: Not applicable 3. Drug route: Not applicable 4. Duration of therapy: Not applicable
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CEFUROXIME versus NO PROPHYLACTIC ANTIMICROBIAL THERAPY

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome for Adults (>16 years): Length of hospital stay at 14 days; MD 10.6 (p value 0.24); Risk of bias: High; Indirectness of outcome: No indirectness
- Actual outcome for Adults (>16 years): Length of CCU stay at 14 days; MD 10.9 (p value 0.06); Risk of bias: High; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality at <1 year
- Actual outcome for Adults (>16 years): Mortality at 14 days; Group 1: 1/30, Group 2: 7/30; Risk of bias: High; Indirectness of outcome: No indirectness

Protocol outcome 3: Infected necrosis at <1 year
- Actual outcome for Adults (>16 years): Abscess or infected necrosis at 14 days; Group 1: 9/30, Group 2: 12/30; Risk of bias: High; Indirectness of outcome: No indirectness

Protocol outcome 4: Extra-pancreatic infection at <1 year
- Actual outcome for Adults (>16 years): Peripancreatic infection at 14 days; Group 1: 21/30, Group 2: 18/30; Risk of bias: High; Indirectness of outcome: No indirectness
- Actual outcome for Adults (>16 years): Blood culture positive sepsis at 14 days; Group 1: 4/30, Group 2: 8/30; Risk of bias: High; Indirectness of outcome: No indirectness
- Actual outcome for Adults (>16 years): Urinary tract infection at 14 days; Group 1: 6/30, Group 2: 17/30; Risk of bias: High; Indirectness of outcome: No indirectness
- Actual outcome for Adults (>16 years): Pneumonia/ARDS at 14 days; Group 1: 11/30, Group 2: 17/30; Risk of bias: High; Indirectness of outcome: No indirectness

Protocol outcomes not reported by the study	Quality of life at <1 year; Colonisation by resistant organisms at >6 months; Serious adverse events at <6 months; Serious adverse events at >6 months; Colonisation by resistant organisms at <6 months

Study	Xue 2009[1167]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=59)
Countries and setting	Conducted in China; Setting: West China Hospital of Sichuan University
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 7-14 days and 1 month follow-up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: The diagnostic criteria for severe acute pancreatitis formulated at the 2002 Bangkok World Congress of Gastroenterology were adopted. Necrosis was confirmed by contrast-enhanced computerised tomography (CECT).
Stratum	Adults (>16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Hospitalised male and female patients (≥18 years of age) with a confirmed diagnosis of SAP. Patients with 30% or more necrosis of the pancreas (as proven by contrast enhanced CT) were eligible for inclusion.
Exclusion criteria	concurrent sepsis or (peri)pancreatic infection caused by a second disease; direct transfer to the intensive care unit due to multiple organ failure; recurrent or endoscopic retrograde cholangiopancreatography (ERCP), or traumatic or operative pancreatitis; pregnancy, malignancy or immunodeficiency; a history of allergy to imipenem-cliastin; a history of antibiotic administration within 48 hours prior to enrollment; and possible death within 48 hours after enrollment.
Recruitment/selection of patients	Patients admitted to hospital with a confirmed diagnosis of SAP in January-December 2007
Age, gender and ethnicity	Age - Mean (SD): Study group: 48.4 (15.1) Control group: 47.5 (12.3). Gender (M:F): 28/28. Ethnicity: Not reported
Further population details	1. Severity of pancreatitis (as defined by study): Severe pancreatitis (N or mean(SD) for intervention and control group, respectively: Ranson score 4.8(1.5), 5.3(1.7), 24h APACHE II Score 12.7(2.1), 11.9(3.7), pancreatic necrosis in CECT 30-50% 17, 18; pancreatic necrosis in CECT >50% 12, 9.).
Extra comments	N or mean (SD) for intervention and control group, respectively: biliary etiology 15, 14; alcoholic etiology 4, 2; hyperlipidemic 2, 2; idiopathic 8, 9; Ranson score 4.8(1.5), 5.3(1.7), 24h APACHE II Score 12.7(2.1), 11.9(3.7), pancreatic necrosis in CECT 30-50% 17, 18; pancreatic necrosis in CECT >50% 12, 9. . Patient who had been enrolled in the trial were withdrawn if they died, received surgery because of a lack of response to intensive care treatment within 72h of admission, or had serious adverse effect after administration of imipenem-cilastatin
Indirectness of population	No indirectness
Interventions	(n=30) Intervention 1: Prophylactic antimicrobial therapy - Carbapenem. 500mg imipenem-cilastatin every 8 hours by

	30 mins IV drip within 72 h of onset of symptoms. All 500mg doses were diluted in 100 mL normal saline solution.. Duration 7-14 days. Concurrent medication/care: The use of non-study antibiotics in the study group or any antibiotics in the control group was not encouraged until progressive pancreatitis was manifested by clinical deterioration, and/or infection was microbiologically verified or strongly suspected, or after an initial severe inflammatory response syndrome, a secondary rise in serum C-reactive protein (CRP) was measured. During the hospital stay, all patients received daily intensive care (monitoring of temperature, oxygen saturation, central venous pressure vis central venous catheter, liquid intake and output, and were given supportive care and nutritive administration. Further details: 1. Drug class: Carbapenems 2. Drug dose: Not stated / Unclear (BNF dose). 3. Drug route: Intravenous 4. Duration of therapy: Not stated / Unclear Comments: In patients who were switched to open antibiotic treatment, the choice of antibiotic was at the investigator's discretion and the recommendation of the study protocol was to use imipenem, possibly in combination to vancomycin. If the presence of bacteria was confirmed, appropriate antibiotic therapy was guided by the results of drug sensitivity testing. (n=29) Intervention 2: No prophylactic antimicrobial therapy. The control group did not receive any antibiotics. Duration 7-14 days. Concurrent medication/care: The use of non-study antibiotics in the study group or any antibiotics in the control group was not encouraged until progressive pancreatitis was manifested by clinical deterioration, and/or infection was microbiologically verified or strongly suspected, or after an initial severe inflammatory response syndrome, a secondary rise in serum C-reactive protein (CRP) was measured. During the hospital stay, all patients received daily intensive care (monitoring of temperature, oxygen saturation, central venous pressure vis central venous catheter, liquid intake and output, and were given supportive care and nutritive administration. Further details: 1. Drug class: Not applicable 2. Drug dose: Not applicable 3. Drug route: Not applicable 4. Duration of therapy: Not applicable Comments: In patients who were switched to open antibiotic treatment, the choice of antibiotic was at the investigator's discretion and the recommendation of the study protocol was to use imipenem, possibly in combination to vancomycin. If the presence of bacteria was confirmed, appropriate antibiotic therapy was guided by the results of drug sensitivity testing.
Funding	Academic or government funding (Supported by Sichuan Province Science and Technology Tackling Key Project)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: IMIPENEM-CILASTATIN versus NO PROPHYLACTIC ANTIMICROBIAL THERAPY

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome for Adults (>16 years): Hospital stay at 6 weeks; Other: Median (range) for intervention and control groups, respectively: 28.3 (23-71), 30.7(25-60); Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality at <1 year - Actual outcome for Adults (>16 years): Mortality at 6 weeks; Group 1: 3/29, Group 2: 4/27; Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 3: Infected necrosis at <1 year - Actual outcome for Adults (>16 years): Infected necrosis at 6 weeks; Group 1: 8/29, Group 2: 10/27; Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 4: Extra-pancreatic infection at <1 year - Actual outcome for Adults (>16 years): Extra-pancreatic infection (n of events - Lung, intestine, blood and urinary tract) at 6 weeks; Group 1: 18/29, Group 2: 15/27; Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 5: Serious adverse events at <6 months - Actual outcome for Adults (>16 years): Organ complication (n of events - Acute respiratory distress syndrome, Acute renal failure, Hepatic insufficiency, Shock, Pancreatic pseudocyst) at 6 weeks; Group 1: 28/29, Group 2: 23/27; Risk of bias: Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Colonisation by resistant organisms at >6 months; Serious adverse events at >6 months; Colonisation by resistant organisms at <6 months

H.12 Methods of management of infected necrosis in people with acute pancreatitis

Study (subsidiary papers)	Van Santvoort 2010[1102] (Besselink 2006[124])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=88)
Countries and setting	Conducted in Netherlands; Setting: 7 University medical centers and 12 large teaching hospitals of the Dutch Pancreatitis Study Group.
Line of therapy	Unclear
Duration of study	Intervention time: 3 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosed by contrast enhanced CT. Infected necrosis was defined as a positive culture of pancreatic or peripancreatic necrotic tissue obtained by means of fine-needle aspiration or from the first drainage procedure or operation.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients with a confirmed or suspected infected pancreatic or peripancreatic necrosis due for surgical intervention.
Exclusion criteria	A flare-up of chronic pancreatitis, previous exploratory laparotomy during the current episode of pancreatitis, previous drainage or surgery for confirmed or suspected infected necrosis, pancreatitis caused by abdominal surgery, and an acute intraabdominal event (for example, perforation of a visceral organ, bleeding, or the abdominal compartment syndrome)
Recruitment/selection of patients	Patients were admitted to participating hospitals
Age, gender and ethnicity	Age - Mean (SD): MI group: 57.6 (2.1) PON group: 57.4 (2). Gender (M:F): 44:38. Ethnicity: Not reported

Further population details	1. Severity of infection: Not stated / Unclear 2. Severity of pancreatitis: Severe pancreatitis
Extra comments	MI group Etiology: Gallstones - 60%, Alcohol - 7%, Other - 33%; BMI (median): 28; CT severity index (median): 8 PON group Etiology: Gallstones - 64%, Alcohol - 11%, Other - 24%; BMI (median): 27; CT severity index (median): 8
Indirectness of population	No indirectness
Interventions	(n=43) Intervention 1: Minimally invasive surgery - Percutaneous. The first step in the step-up approach was percutaneous or endoscopic transgastric drainage. The preferred route was through the left retroperitoneum. If there was no clinical improvement after 72 hours and if the position of the drain was inadequate or other fluid collections could be drained, a second drainage procedure was performed. If this was not possible, or if there was no clinical improvement after an additional 72 hours, the second step, video -assisted retroperitoneal debridement with postoperative lavage was performed.. Duration During admission. Concurrent medication/care: Postoperative management included the following: Continuous postoperative lavage with normal saline or peritoneal dialysis fluid was started. On the third postoperative day, the lavage amounted to at least 10 L per 24 hourse. CECT was performed 1 week after every drain placement and surgical intervention. Catheters were removed if collapse of the cavity was shown through CECT. Further details: 1. Procalcitonin-led antibiotic treatment: Not stated / Unclear 2. Type of minimally invasive surgery : Systematic review: mixed (n=45) Intervention 2: Open surgery. Laparotomy through a bilateral subcostal incision. After blunt removal of all necrotic tissue, 2 large-bore drains for post-operative lavage were inserted, and the abdomen was closed.. Duration During admission. Concurrent medication/care: Postoperative management included the following: Continuous postoperative lavage with normal saline or peritoneal dialysis fluid was started. On the third postoperative day, the lavage amounted to at least 10 L per 24 hours. CECT was performed 1 week after every drain placement and surgical intervention. Catheters were removed if collapse of the cavity was shown through CECT. Further details: 1. Procalcitonin-led antibiotic treatment: Not stated / Unclear 2. Type of minimally invasive surgery : Not applicable
Funding	Academic or government funding (Supported by a grant from the Dutch Organisation for Health Research and Development)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PERCUTANEOUS OR ENDOSCOPIC DRAINAGE versus OPEN SURGERY Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year - Actual outcome: Days in CCU at During admission; Other: Median; Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: Days in hospital at During admission; Other: Median; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 2: Mortality at <1 year - Actual outcome: Mortality at During admission; Group 1: 8/43, Group 2: 7/45; Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 3: Number of procedures (repeated procedures) at <1 year - Actual outcome: Total number of operations at During admission; Other: Median; Risk of bias: Low; Indirectness of outcome: No indirectness - Actual outcome: Total number of drainage procedures at During admission; Other: Median; Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 4: Complications (for example, bleeding, fistulae) at <1 year - Actual outcome: New onset multiple organ failure at During admission; Group 1: 5/43, Group 2: 19/45; Risk of bias: Low; Indirectness of outcome: No indirectness - Actual outcome: Multiple organ failure at During admission; Group 1: 5/43, Group 2: 18/45; Risk of bias: Low; Indirectness of outcome: No indirectness - Actual outcome: Multiple systemic complications at During admission; Group 1: 0/43, Group 2: 1/45; Risk of bias: Low; Indirectness of outcome: No indirectness - Actual outcome: Intraabdominal bleeding requiring intervention at During admission; Group 1: 7/43, Group 2: 10/45; Risk of bias: Low; Indirectness of outcome: No indirectness - Actual outcome: Enterocutaneous fistula or perforation of a visceral organ requiring intervention at During admission; Group 1: 6/43, Group 2: 10/45; Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 5: Pancreatic function (for example, development of diabetes) at <1 year - Actual outcome: New onset diabetes at During admission; Group 1: 7/43, Group 2: 17/45; Risk of bias: Low; Indirectness of outcome: No indirectness - Actual outcome: Use of pancreatic enzymes at During admission; Group 1: 3/43, Group 2: 15/45; Risk of bias: Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Recurrence of infection at <1 year

Study	Besselink 2006[123]
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=106)
Countries and setting	Conducted in Netherlands
Line of therapy	1st line
Duration of study	Intervention and follow-up: 3 years (2000-2003)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: The diagnosis of necrotising pancreatitis was accepted when confirmed by contrast-enhanced CT or during surgery
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	All consecutive patients undergoing surgical treatment for infected necrotising pancreatitis between 1 October 2000 and 1 October 2003. Indications for intervention were persistent sepsis despite maximal conservative therapy or clinical deterioration after initial clinical improvement (suspected infection), documented infection of peri-pancreatic necrosis by FNA, air collections in (peri)pancreatic necrosis on contrast-enhanced CT images, suspected bowel perforation or active bleeding.
Exclusion criteria	Patients younger than 18 years, those with acute flare-up of chronic pancreatitis and patients undergoing elective surgery for pancreatic pseudocysts were excluded.
Recruitment/selection of patients	Computer database search for acute pancreatitis operation codes
Age, gender and ethnicity	Age - Median (range): 59 (20-81). Gender (M:F): 76/30. Ethnicity: not stated
Further population details	1. Severity of infection: Not stated / Unclear 2. Severity of pancreatitis: Not stated / Unclear

Extra comments	Etiology: biliary n=34, ERCP n=13, alcoholic n=11, idiopathic n=29, other n=19.
Indirectness of population	No indirectness
Interventions	(n=23) Intervention 1: Open surgery. Open abdomen strategy (OAS): the abdomen was left open following the first laparotomy for debridement; planned relaparotomy or relaparotomy on demand were both possible after the first laparotomy. . Duration unclear. Concurrent medication/care: not stated Further details: 1. Procalcitonin-led antibiotic treatment: Not applicable 2. Type of minimally invasive surgery : Not applicable (n=53) Intervention 2: Open surgery. Continuous postoperative lavage (CPL): rinsing of the necrosectomy areas after debridement for INP, followed by closure of the abdomen and continuous postoperative local or locoregional lavage with liberal amounts of fluids . Duration unclear. Concurrent medication/care: not stated Further details: 1. Procalcitonin-led antibiotic treatment: Not applicable 2. Type of minimally invasive surgery : Not applicable (n=18) Intervention 3: Minimally invasive surgery - Percutaneous. Minimally invasive procedures (MIP): open or videoscopically assisted retroperitoneal debridement, followed by closure of the abdomen and continuous local or locoregional lavage with liberal amounts of fluids. The preferred route was straight into the retroperitoneum through a small left-sided lumbar incision. If this was not possible, an anterior transabdominal laparoscopic approach was used. . Duration unclear. Concurrent medication/care: not stated Further details: 1. Procalcitonin-led antibiotic treatment: Not applicable 2. Type of minimally invasive surgery : Not applicable (n=12) Intervention 4: Open surgery. Laparotomy with primary abdominal closure (PAC): laparotomy and blunt debridement of necrotic tissue, followed by abdominal closure with no postoperative lavage system in place. . Duration unclear. Concurrent medication/care: not stated Further details: 1. Procalcitonin-led antibiotic treatment: Not applicable 2. Type of minimally invasive surgery : Not applicable
Funding	Academic or government funding (Senter, an agency of the Dutch Ministry of Economic Affairs)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: OPEN SURGERY (OPEN ABDOMEN STRATEGY) versus MINIMALLY INVASIVE SURGERY (RETROPERITONEAL DEBRIDEMENT)

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome: Postop. CCU stay in survivors at unclear; Mean (Median (range) for OAS and MIP, respectively: 16 (0-68); 2 (0-83)); Risk of bias: Very high; Indirectness of outcome: No indirectness
- Actual outcome: Postop. hospital stay in survivors at unclear; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality at <1 year
- Actual outcome: In-hospital deaths at unclear; Group 1: 16/23, Group 2: 2/18; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 3: Number of procedures (repeated procedures) at <1 year
- Actual outcome: Reintervention at unclear; Group 1: 23/23, Group 2: 12/18; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 4: Complications (for example, bleeding, fistulae) at <1 year
- Actual outcome: Bowel perforation at unclear; Group 1: 7/23, Group 2: 3/18; Risk of bias: Very high; Indirectness of outcome: No indirectness
- Actual outcome: Bleeding (transfusion) at unclear; Group 1: 11/23, Group 2: 3/18; Risk of bias: Very high; Indirectness of outcome: No indirectness

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: OPEN SURGERY (CONTINUOUS POSTOPERATIVE LAVAGE) versus MINIMALLY INVASIVE SURGERY (RETROPERITONEAL DEBRIDEMENT)

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome: Postop. CCU stay in survivors at unclear; Risk of bias: Very high; Indirectness of outcome: No indirectness
- Actual outcome: Postop. hospital stay in survivors at unclear; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality at <1 year
- Actual outcome: In-hospital deaths at unclear; Group 1: 13/53, Group 2: 2/18; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 3: Number of procedures (repeated procedures) at <1 year
- Actual outcome: Reintervention at unclear; Group 1: 39/53, Group 2: 12/18; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 4: Complications (for example, bleeding, fistulae) at <1 year
- Actual outcome: Bowel perforation at unclear; Group 1: 11/53, Group 2: 3/18; Risk of bias: Very high; Indirectness of outcome: No indirectness
- Actual outcome: Bleeding (transfusion) at unclear; Group 1: 17/53, Group 2: 3/18; Risk of bias: Very high; Indirectness of outcome: No indirectness

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: OPEN SURGERY (LAPAROTOMY WITH PRIMARY ABDOMINAL CLOSURE) versus MINIMALLY

INVASIVE SURGERY (RETROPERITONEAL DEBRIDEMENT) Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year - Actual outcome: Postop. CCU stay in survivors at unclear; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome: Postop. hospital stay in survivors at unclear; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 2: Mortality at <1 year - Actual outcome: In-hospital deaths at unclear; Group 1: 5/12, Group 2: 2/18; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 3: Number of procedures (repeated procedures) at <1 year - Actual outcome: Reintervention at unclear; Group 1: 2/12, Group 2: 12/18; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 4: Complications (for example, bleeding, fistulae) at <1 year - Actual outcome: Bowel perforation at unclear; Group 1: 0/0, Group 2: 3/18; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome: Bleeding (transfusion) at unclear; Group 1: 2/12, Group 2: 3/18; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Pancreatic function (for example, development of diabetes) at <1 year; Recurrence of infection at <1 year

Study	Garg 2010[391]
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=80)
Countries and setting	Conducted in India; Setting: tertiary care academic centre
Line of therapy	1st line
Duration of study	Other: 1997-2006
Method of assessment of guideline condition	--: Diagnosis of AP was made in the presence of suggestive clinical deatures, increased serum amilase levels (>3 times the upper limit of normal), and evidence of AP on imaging studies. Diagnosis of IPN was made when pancreatic necrotic tissue obtained by FNA showed presence of bacteria on Gram stain or when it grew an organism on culture. In pts with suspected IPN, presence of extraintestinal gas in the pancreatic bed on a CT scan was taken as another evidence of infected necrosis.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	All consecutive patients with AP admitted to the hospital were included in the study. Patients with IPN formed the study group.
Exclusion criteria	Define
Recruitment/selection of patients	consecutive patients
Age, gender and ethnicity	Age – not stated: . Gender (M:F): 52/28. Ethnicity: not reported
Further population details	1. Severity of infection: Not stated / Unclear 2. Severity of pancreatitis: Not stated / Unclear

Extra comments	Etiology: gallstone n=48, alcohol n=10, others n=22..
Indirectness of population	--
Interventions	(n=30) Intervention 1: Open surgery. Surgical necrosectomy, lavage and drainage. Initial surgical treatment included debridement (necrosectomy) and if required (for example, intraoperative bleeding necessitating packing or inadequate necrosectomy), planned re-explorations after 48 hours. When intraoperative assessment was considered satisfactory regarding hemostasis/necrosectomy, the abdomen was closed, multiple drains were placed, and perioperative lavage was carried out. . Duration 1997-2002. Concurrent medication/care: not stated Further details: 1. Procalcitonin-led antibiotic treatment: 2. Type of minimally invasive surgery : (n=50) Intervention 2: Combination of intervention techniques - Step-up approach. Primary conservative medical treatment: aggressive medical management that included combination antibiotics, organ support, intensive nutritional support and percutaneous drainage if required (for IPN that had become organised and walled off, under US or CT guidance). If clinical improvement was noted, the patient was continued on conservative treatment and antibiotics were given for 4 weeks. If no improvement, the patient was subjected to surgery. . Duration 2003-2006. Concurrent medication/care: not stated Further details: 1. Procalcitonin-led antibiotic treatment: 2. Type of minimally invasive surgery :
Funding	Funding not stated (No conflict of interest declared)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: OPEN SURGERY (NECROSECTOMY) versus STEP-UP APPROACH Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year - Actual outcome: Hospital stay.; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Recurrence of infection at <1 year; Number of procedures (repeated procedures) at <1 year; Complications (for example, bleeding, fistulae) at <1 year; Pancreatic function (for example, development of diabetes) at <1 year; Mortality at <1 year

Study	Gluck 2012[406]
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=102)
Countries and setting	Conducted in USA; Setting: The Digestive Disease Institute, Virginia Mason Medical Center
Line of therapy	Unclear
Duration of study	Intervention time: 5 years
Method of assessment of guideline condition	Unclear method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Define
Exclusion criteria	Define
Recruitment/selection of patients	All patients had been admitted to the hospital.
Age, gender and ethnicity	Age - Mean (SD): SPD: 53.5 DMD: 55.9. Gender (M:F): Define. Ethnicity: Not reported
Further population details	1. Severity of infection: Not stated / Unclear 2. Severity of pancreatitis: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=50) Intervention 1: Minimally invasive surgery - Endoscopic. CT-guided percutaneous drains were placed as in SPD cohort, but only 10 mL of fluid was aspirated. The patient was then rapidly transferred to a fluoroscopically equipped endoscopy suite at which time the WOPN was accessed either transgastrically or transduodenally. Endoscopic

	ultrasound was used if there was an inconclusive luminal bulge.. Duration During admission. Concurrent medication/care: All patients received culture directed antibiotics, and all patients were managed by critical care specialists or hospitalists. Further details: 1. Procalcitonin-led antibiotic treatment: Not stated / Unclear 2. Type of minimally invasive surgery : Percutaneous (n=52) Intervention 2: Percutaneous drainage (radiological). Symptomatic SAP patients has percutaneous drainage catheters placed into areas of WOPN.. Duration During admission. Concurrent medication/care: All patients received culture directed antibiotics, and all patients were managed by critical care specialists or hospitalists. Further details: 1. Procalcitonin-led antibiotic treatment: Not stated / Unclear 2. Type of minimally invasive surgery : Not applicable
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ENDOSCOPY versus PERCUTANEOUS DRAINAGE (RADIOLOGICAL) Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year - Actual outcome: Length of stay in hospital at During admission; Group 1: mean 24 days (SD 23); n=49, Group 2: mean 54 days (SD 41); n=45; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 2: Mortality at <1 year - Actual outcome: Mortality at During admission; Group 1: 2/49, Group 2: 3/45; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 3: Complications (for example, bleeding, fistulae) at <1 year - Actual outcome: Pseudoaneurysm bleeding at During admission; Group 1: 0/49, Group 2: 5/45; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Number of procedures (repeated procedures) at <1 year; Pancreatic function (for example, development of diabetes) at <1 year; Recurrence of infection at <1 year

Study	**He 2017[449]**

Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=26)
Countries and setting	Conducted in China; Setting: Hospital
Line of therapy	Adjunctive to current care
Duration of study	Intervention and follow-up: 1 year
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Acute pancreatitis was its severity are defined by the revision of the Atlanta classification
Stratum	Overall
Subgroup analysis within study	Not applicable:
Inclusion criteria	Patients aged 18-70 years admitted or transferred to hospital with suspected infected pancreatic necrosis, and an indication for intervention. IPN was defined as extraluminal gas in the pancreatic and/or peripancreatic tissues on CECT, or when percutaneous, image-guided, fine-needle aspiration is positive for bacteria and/or fungi on a Gram stain and culture
Exclusion criteria	Serious heart, lung, liver, or brain disease, coagulation dysfunction and patients who could not tolerate endoscopic treatment or CT-guided percutaneous catheter drainage. Pregnant or lactating women and patients who did not sign the consent were excluded from the study.
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Median (IQR): ETN group 48 (27-55); PCD group 48 (43-59). Gender (M:F): 12:12. Ethnicity: Not reported
Further population details	1. Severity of infection: Not stated / Unclear 2. Severity of pancreatitis: Not stated / Unclear
Indirectness of population	No indirectness

Interventions	(n=13) Intervention 1: Minimally invasive surgery - Endoscopic. The initial session of endoscopic transluminal drainage consists of an endoscopic ultrasound-guided puncture and placing 2 double-pigtail stents and a nasocystic catheter in the necrotic collection. EUS was used to visualise the extent of the necrosis and obvious blood vessels. The necrotic cavity was punctured under EUS guidance using a 19 guage needle. The content of the necrotic collection was aspirated to confirm the correct position. Then zebra guidewire was inserted through the 19 gauge needle to the necrotic cavity. The outer sheath of a 10F cycstogastrostomy was advanced into the stomach wall followed by balloon dilation of the tract up to 1cm. Two double-pigtail plastic stents and a 6F nasocystic catheter were placed in the collection. The cavity was irrigated with 1L of normal saline per 24 hours by nasocystic catheter. Clinical improvement as CECT were observed 3-5 days later after ETD. Patients with clinical improvement would continue to be observed to see if symptoms reappear again or whether the necrotic cavity did not decrease after 2 weeks, in which case they would also receive ETN. The second session of ETN consisted of removing the necrotic tissue from the necrotic cavity under endoscopic observation. The ETN was repeated in those with no clinical improvement in the subsequent 3-5 days. Duration During admission. Concurrent medication/care: All patients received enteral nutrition, mainly through the nasojejunal tube, and an oral diet was restored if oral feeding was tolerated. If the required caloric intake would not be reached, the patient would receive additional parenteral nutrition. All patients received intravenous antibiotics which were adjusted according to the culture results or stopped if there was clinical improvement Further details: 1. Procalcitonin-led antibiotic treatment: 2. Type of minimally invasive surgery : (n=13) Intervention 2: Minimally invasive surgery - Percutaneous. The initial session of PCD consists of CT or ultrasound-guided percutaneous placement of 12-16F catheters in the pancreatic or peripancreatic collection using the Seldinger technique. The preferred route includes the retroperitoneum and/or transperitoneal. If possible, each necrotic area is given at least 2 catheters to achieve sufficient convection and drainage. Drains are kept open by flushing with 0.9% saline solution every 8 hours. The clinical improvement and CECT were also observed 3-5 days after PCD. If a patient does not have clinical improvement, or changes in pancreatic necrosis after 3-5 days, 1 or more catheters were changed to double-catheterisation cannulas; then double-catheterisation cannulas were continuously flushed with saline and continuous negative pressure drainage. In the case of clinical improvement, irrigation is continued. If patients failed to improver for another 5 days, they were converted to open surgery. Duration During admission. Concurrent medication/care: All patients received enteral nutrition, mainly through the nasojejunal tube, and an oral diet was restored if oral feeding was tolerated. If the required caloric intake would not be reached, the patient would receive additional parenteral nutrition. All patients received intravenous antibiotics which were adjusted according to the culture results or stopped if there was clinical improvement Further details: 1. Procalcitonin-led antibiotic treatment: 2. Type of minimally invasive surgery :
Funding	Academic or government funding (Supported by the NAtional clinical key specialty construction project, Jiangxi

	Provincial Science and Technology Project and Science and Technology project of Health and Family Planning Commission of Jiangxi Province)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ENDOSCOPIC versus PERCUTANEOUS

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome: Length of stay in hospital at During admisson; Group 1: mean 40 Days (SD 25); n=11, Group 2: mean 66 Days (SD 37); n=13
Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in number of patients with alcohol abuse (36.4% versus 15.4%), number of patients with organ failure (18.2% versus 46.2%); Group 1 Number missing: 2, Reason: 1 transferred to surgery due to ACS and septic shock, 1 withdrew to receive self expanding metal stent drainage; Group 2 Number missing: 0
- Actual outcome: Length of stay in CCU at During admisson; Group 1: mean 17 Days (SD 13); n=11, Group 2: mean 25 Days (SD 18); n=13
Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in number of patients with alcohol abuse (36.4% versus 15.4%), number of patients with organ failure (18.2% versus 46.2%); Group 1 Number missing: 2, Reason: 1 transferred to surgery due to ACS and septic shock, 1 withdrew to receive self expanding metal stent drainage; Group 2 Number missing: 0

Protocol outcome 2: Mortality at <1 year
- Actual outcome: Mortality at 1 year; Group 1: 3/11, Group 2: 3/13
Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in number of patients with alcohol abuse (36.4% versus 15.4%), number of patients with organ failure (18.2% versus 46.2%); Group 1 Number missing: 2, Reason: 1 transferred to surgery due to ACS and septic shock, 1 withdrew to receive self expanding metal stent drainage; Group 2 Number missing: 0

Protocol outcome 3: Complications (eg bleeding, fistulae) at <1 year
- Actual outcome: Upper gastrointestinal bleeding at 1 year; Group 1: 1/11, Group 2: 0/13
Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in number of patients with alcohol abuse (36.4% versus 15.4%), number of patients with organ failure (18.2% versus 46.2%); Group 1 Number missing: 2, Reason: 1 transferred to surgery due to ACS and septic shock, 1 withdrew to receive self expanding metal stent drainage; Group 2 Number missing: 0
- Actual outcome: Intraabdominal bleeding requiring intervention at 1 year; Group 1: 1/11, Group 2: 2/13
Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in number of patients with alcohol abuse (36.4% versus 15.4%), number of patients with organ failure (18.2% versus 46.2%); Group 1 Number missing: 2, Reason: 1 transferred to surgery due to ACS and septic shock, 1 withdrew to receive self expanding metal stent drainage; Group 2 Number missing: 0

- Actual outcome: Enterocutaneous fistula or perforation at 1 year; Group 1: 1/11, Group 2: 5/13 Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in number of patients with alcohol abuse (36.4% versus 15.4%), number of patients with organ failure (18.2% versus 46.2%); Group 1 Number missing: 2, Reason: 1 transferred to surgery due to ACS and septic shock, 1 withdrew to receive self expanding metal stent drainage; Group 2 Number missing: 0 - Actual outcome: Pancreatic fistula at 1 year; Group 1: 0/11, Group 2: 1/13 Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in number of patients with alcohol abuse (36.4% versus 15.4%), number of patients with organ failure (18.2% versus 46.2%); Group 1 Number missing: 2, Reason: 1 transferred to surgery due to ACS and septic shock, 1 withdrew to receive self expanding metal stent drainage; Group 2 Number missing: 0 - Actual outcome: New onset organ failure at 1 year; Group 1: 2/11, Group 2: 2/13 Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in number of patients with alcohol abuse (36.4% versus 15.4%), number of patients with organ failure (18.2% versus 46.2%); Group 1 Number missing: 2, Reason: 1 transferred to surgery due to ACS and septic shock, 1 withdrew to receive self expanding metal stent drainage; Group 2 Number missing: 0 - Actual outcome: Multiple organ failure at 1 year; Group 1: 1/11, Group 2: 0/13 Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in number of patients with alcohol abuse (36.4% versus 15.4%), number of patients with organ failure (18.2% versus 46.2%); Group 1 Number missing: 2, Reason: 1 transferred to surgery due to ACS and septic shock, 1 withdrew to receive self expanding metal stent drainage; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Quality of life at <1 year; Number of procedures (repeated procedures) at <1 year; Pancreatic function (eg development of diabetes) at <1 year; Recurrence of infection at <1 year

Study	Kumar 2014[622]
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=24)
Countries and setting	Conducted in USA; Setting: The center for Pancreatic Disease, Division of Gastroenterology, Hepatology and Endoscopy, Brigham and Women's Hospital, Boston, MA.
Line of therapy	Unclear
Duration of study	Not clear: 1 year
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: All patients had CT of the abdomen and pelvis within 5 days before the procedure.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Fever, leukocytosis, positive fluid aspirate Gram stain, and/or positive blood cultures.
Exclusion criteria	Patients with other prior intervention for WOPN were excluded.
Recruitment/selection of patients	Patients were admitted to hospital.
Age, gender and ethnicity	Age - Mean (SD): DEN: 58.9 (3.9) SUA: 53.3 (3). Gender (M:F): 17:7. Ethnicity:
Further population details	1. Severity of infection: Not stated / Unclear 2. Severity of pancreatitis: Not stated / Unclear
Extra comments	DEN - Etiology: Alcohol - 3, Gallstone - 7, Unknown - 2; APACHE-II: 10.1 (1.1); TPN use: 3; CT severity index: 8.3 (0.8) SUA - Etiology: Alcohol - 3, Gallstone - 5, Hypertriglyceridemia: 1, Post-ERCP: 1, Unknown - 2; APACHE-II: 9.4 (1.2); TPN use: 2; CT severity index: 7.8 (0.8)

Indirectness of population	No indirectness
Interventions	(n=12) Intervention 1: Minimally invasive surgery - Endoscopic. All procedures were performed by a single endoscopist using a standardised technique. Linear endoscopic ultrasound was employed to localise the site of WOPN entry and avoid vascular injury. Walled off pancreatic necrosis contents were aspirated and sent for Gram stain and culture. . Duration During admission. Concurrent medication/care: Not reported Further details: 1. Procalcitonin-led antibiotic treatment: 2. Type of minimally invasive surgery : (n=12) Intervention 2: Combination of intervention techniques - Step-up approach. With the use of cross-sectional imaging to avoid injury to vasculature and organs, a percutaneous needle was placed into the necrotic collection. Fluid was aspirated and sent for Gram stain and culture. The collection was followed with repeat cross-sectional imaging. If the collection size was no longer decreasing with irrigation, the drains were repositioned or additional drains were placed at the discretion of the radiologist. Those patients with lack of response to drainage or with clinical signs or symptoms of infection or abdominal pain were taken to surgery at the discretion of the surgical team. Surgical technique was at the discretion of the attending surgeon and included both open and minimally invasive approaches.. Duration During admission. Concurrent medication/care: Not reported Further details: 1. Procalcitonin-led antibiotic treatment: Not stated / Unclear 2. Type of minimally invasive surgery : Not stated / Unclear
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DIRECT ENDOSCOPIC NECROSECTOMY versus STEP-UP APPROACH

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome: Floor length of stay at During admission; Group 1: mean 5.3 days (SD 1.4); n=12, Group 2: mean 23.6 days (SD 6.5); n=12; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 2: Number of procedures (repeated procedures) at <1 year
- Actual outcome: Number of procedures at During admission; Group 1: mean 1.5 (SD 0.3); n=12, Group 2: mean 2.8 (SD 0.2); n=12; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 3: Complications (for example, bleeding, fistulae) at <1 year
- Actual outcome: Complications at During admission; Group 1: 1/12, Group 2: 8/12; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 4: Pancreatic function (for example, development of diabetes) at <1 year - Actual outcome: New exocrine insufficiency at During admission; Group 1: 3/12, Group 2: 5/12; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome: New endocrine insufficiency at During admission; Group 1: 0/12, Group 2: 7/12; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 4: Morality at <1 year - Actual outcome: Mortality at During admission; Group 1: 0/12, Group 2: 0/12; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Recurrence of infection at <1 year; Mortality at <1 year

Study	Pupelis 2015[884]
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=70)
Countries and setting	Conducted in Latvia; Setting: Riga East Clinical University
Line of therapy	Unclear
Duration of study	Intervention time: 10 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: New or first episodes of acute pancreatitis were confirmed by CECT after the acute phase (first week) from the onset of disease.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients who were treated at Riga East hospital with acute necrotising pancreatitis and were operated on due to the infected necrosis were prospectively included.
Exclusion criteria	Not reported
Recruitment/selection of patients	Patients were admitted to hospital
Age, gender and ethnicity	Age - Median (IQR): FOCUSED OPEN NECROSECTOMY: 52 (46-64) CONVENTIONAL:: 47 (41-62). Gender (M:F): 54:16. Ethnicity: Not reported
Further population details	1. Severity of infection: Not stated / Unclear 2. Severity of pancreatitis: Not stated / Unclear
Indirectness of population	No indirectness

Interventions	(n=31) Intervention 1: Minimally invasive surgery - Percutaneous. Ultrasound-guided percutaneous acute necrotic collections (ANC) drainage was performed under local anaesthesia. Ultrasound-guided surgery included a provision of intraoperative ultrasound and ultrasound-guided minimally invasive interventions. The main intraoperative ultrasound steps were as follows: stereotypical diagnostics ensuring the recognition of anatomical structures and its relation to ANC and necrotic tissue; intraoperative navigation - precise definition of the surgical access; intraoperative monitoring - ultrasonography in real time during the surgical manipulation in reaching deep collections through the avascular zone; controlled drain provision; precise definition of necroses and assistance in focused necrosectomy.. Duration During admission. Concurrent medication/care: All patients received conservative treatment during the early phase of the disease. Further details: 1. Procalcitonin-led antibiotic treatment: Not stated / Unclear 2. Type of minimally invasive surgery : Percutaneous (n=39) Intervention 2: Open surgery. Conventional open necrosectomy was performed using the longitudinal midline or bilateral subcostal trand-peritoneal approach, adhering to the semi-opened or closed drainage principles. The laparotomy was executed providing examination of the abdominal cavity, peripancreatic and paracolic spaces and providing proper necrosectomy using blunt finger dissection combined with a suction and drainage. Once the necrosectomy was finished, 2 large bore drains for postoperative lavage were inserted, and the abdomen was closed in cases when completeness of necrosectomy was achieved. . Duration During admission. Concurrent medication/care: All patients received conservative treatment during the early phase of the disease. Further details: 1. Procalcitonin-led antibiotic treatment: 2. Type of minimally invasive surgery :
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRASOUND-GUIDED FOCUSED OPEN NECROSECTOMY versus OPEN SURGERY

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome: Length of stay in hospital at During admission; Other: Median; Risk of bias: Very high; Indirectness of outcome: No indirectness
- Actual outcome: Length of stay in CCU at During admission; Other: Median; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality at <1 year
- Actual outcome: Mortality at During admission; Group 1: 2/31, Group 2: 5/39; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 3: Number of procedures (repeated procedures) at <1 year

- Actual outcome: Repeat necrosectomy at During admission; Group 1: 8/31, Group 2: 18/39; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 4: Complications (for example, bleeding, fistulae) at <1 year - Actual outcome: Pancreatic fistulae at During admission; Group 1: 4/31, Group 2: 5/39; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome: Intestinal fistulae at During admission; Group 1: 4/31, Group 2: 3/39; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Pancreatic function (for example, development of diabetes) at <1 year; Recurrence of infection at <1 year

Study	Rasch 2016[901]
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=220)
Countries and setting	Conducted in Germany; Setting: 7 tertiary referral centers and 3 secondary hospitals in Germany
Line of therapy	Unclear
Duration of study	Intervention time: 6 years
Method of assessment of guideline condition	Unclear method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients with necrotising pancreatitis requiring treatment (percutaneous and/or transgastric/transduodenal drainage, surgical/percutaneous and/or endoscopic necrosectomy) in the late phase of pancreatitis (>10 days after onset of symptoms) were included in the study.
Exclusion criteria	Not reported
Recruitment/selection of patients	Patients were admitted to hospital.
Age, gender and ethnicity	Age - Range: 18-88. Gender (M:F): 2.6:1. Ethnicity: Not reported
Further population details	1. Severity of infection: Not stated / Unclear 2. Severity of pancreatitis: Not stated / Unclear
Extra comments	All patients: Etiology - Biliary: 41.4%, Alcoholic: 29.1%, Iatrogen: 13.6%, Drug induced: 2.7%, Hypertriglyceridemia: 1.8%

Indirectness of population	No indirectness
Interventions	(n=30) Intervention 1: Open surgery. Primary open surgical necrosectomy was performed in 30/220. 36/190 patients in the step-up group needed open surgical intervention later in the course of disease.. Duration During admission. Concurrent medication/care: Not reported Further details: 1. Procalcitonin-led antibiotic treatment: Not stated / Unclear 2. Type of minimally invasive surgery : Not stated / Unclear (n=190) Intervention 2: Minimally invasive surgery - Percutaneous. 190/220 patients were treated according to a step-up approach.. Duration During admission. Concurrent medication/care: Not reported Further details: 1. Procalcitonin-led antibiotic treatment: Not stated / Unclear 2. Type of minimally invasive surgery : Percutaneous Comments: 197/220 recieved percutaneous drainage, transgastric drainage or both. Without further intervention 50.8% of these patients recovered and 49.2% underwent minimally invasive necrosectomy.
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: STEP-UP APPROACH versus OPEN SURGERY

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome: Length of stay in hospital at During admission ; Other: Median; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality at <1 year
- Actual outcome: Mortality at During admission or within 4 weeks of discharge; Group 1: 20/190, Group 2: 10/30; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 3: Complications (for example, bleeding, fistulae) at <1 year
- Actual outcome: Severe complication (sepsis, persistent MODS or erosion bleeding) at During admission; Group 1: 85/190, Group 2: 25/30; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 4: Pancreatic function (for example, development of diabetes) at <1 year
- Actual outcome: Emergence of type 4c diabetes at During admission ; Group 1: 9/190, Group 2: 10/30; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcomes not reported by the study	Quality of life at <1 year; Number of procedures (repeated procedures) at <1 year; Recurrence of infection at <1 year

Study	Szeliga 2014[1051]
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=34)
Countries and setting	Conducted in Poland; Setting: Department of general, gastroenterological and oncological surgery, Collegium Medicum, Nicolaus Copernicus University, Torun
Line of therapy	Unclear
Duration of study	Other: data collection 2007-2010
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients with diagnosis of severe acute pancreatitis on the basis of Atlanta criteria. All patients had a post-inflammatory, infected focus or foci within the pancreas and/or pancreatic region. The diagnosis of necrosis infection was not based only on typical clinical symptoms but also on CT results and in 27 cases on microbiological examination.
Exclusion criteria	not stated
Recruitment/selection of patients	All patients with severe acute pancreatitis treated at Nicolaus Copernicus University, Torun
Age, gender and ethnicity	Age - Mean (range): 52(28-78). Gender (M:F): 21/13. Ethnicity: not stated
Further population details	1. Severity of infection: Not stated / Unclear 2. Severity of pancreatitis: Severe pancreatitis
Extra comments	Aetiology: n=14 biliary; n=18 alcohol, n=2 other.

Indirectness of population	No indirectness
Interventions	(n=7) Intervention 1: Combination of intervention techniques - Combined approach upfront. Type 1: laparotomy + necrosectomy + passive drainage (scheduled repeated laparotomies) + targeted antibiotic therapy. Duration unclear. Concurrent medication/care: not stated Further details: 1. Procalcitonin-led antibiotic treatment: 2. Type of minimally invasive surgery : (n=5) Intervention 2: Combination of intervention techniques - Combined approach upfront. Type 2: laparotomy + necrosectomy + active drainage + targeted antibiotic therapy. Duration unclear. Concurrent medication/care: not stated Further details: 1. Procalcitonin-led antibiotic treatment: 2. Type of minimally invasive surgery : (n=12) Intervention 3: Combination of intervention techniques - Step-up approach. Type 3: video-assisted retroperitoneal debridement. For patients in whom an attempt of percutaneous drainage to collect fluid or foci of pancreatic necrosis had been made, but no satisfactory clinical outcomes were observed after such a procedure. Approx. 5-cm incision in the left lumbar area was made at the site of a drain to be introduced, or after determination during an ultrasound examination so that it would not interfere with significant anatomical structures (for example, large vessels) and would be at the lowest distance in relation to the targetspace indicated for drainage. After integuments were dissected, the peripancreatic space was reached bluntly, most frequently with a dinger and under ultrasound supervision, so to achieve free flow of infected, necrotic tissues. then a laparoscopic camera was introduced and under video supervision necrotic tissues were flushed out using a suction-flushing device. No attempt was undertaken to remove fragments of necrotic pancreas that were not demarcated; they were left for subsequently placed active flushing gravitational drainage covering the bed after necrosectomy. . Duration unclear. Concurrent medication/care: After the procedure the patient was supervised at the CCU, having basic signal signs monitored, with compensated nutrition and water-electrolyte balance. Further details: 1. Procalcitonin-led antibiotic treatment: 2. Type of minimally invasive surgery : (n=10) Intervention 4: Percutaneous drainage (radiological). Type 4: Percutaneous drainage (12 to 20 F drains) of necrotic and suppurative cisterns from the pancreatic area. Duration unclear. Concurrent medication/care: not stated Further details: 1. Procalcitonin-led antibiotic treatment: 2. Type of minimally invasive surgery :
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINED APPROACH UPFRONT (LAPAROTOMY+NECROSECTOMY+PASSIVE DRAINAGE) versus STEP-UP APPROACH (PERCUTANEOUS DRAINAGE+VARD)

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome: Duration of hospitalisation (days) at perioperative; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality at <1 year
- Actual outcome: Deaths at perioperative; Group 1: 5/7, Group 2: 2/12; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 3: Complications (for example, bleeding, fistulae) at <1 year
- Actual outcome: N of patients with complications (wound infection, haemorrage at surgical site, pancreatic fistula, intestinal fistula) at perioperative; Group 1: 7/7, Group 2: 6/12; Risk of bias: Very high; Indirectness of outcome: No indirectness

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINED APPROACH UPFRONT (LAPAROTOMY+NECROSECTOMY+PASSIVE DRAINAGE) versus PERCUTANEOUS DRAINAGE (RADIOLOGICAL)

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome: Duration of hospitalisation (days) at perioperative; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality at <1 year
- Actual outcome: Deaths at perioperative; Group 1: 5/7, Group 2: 1/10; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 3: Complications (for example, bleeding, fistulae) at <1 year
- Actual outcome: N of patients with complications (wound infection, haemorrage at surgical site, pancreatic fistula, intestinal fistula) at perioperative; Group 1: 7/7, Group 2: 2/10; Risk of bias: Very high; Indirectness of outcome: No indirectness

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINED APPROACH UPFRONT (LAPAROTOMY+NECROSECTOMY+ACTIVE DRAINAGE) versus COMBINED APPROACH UPFRONT (LAPAROTOMY+NECROSECTOMY+PASSIVE DRAINAGE)

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome: Duration of hospitalisation (days) at perioperative; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality at <1 year
- Actual outcome: Deaths at perioperative; Group 1: 1/5, Group 2: 5/7; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 3: Complications (for example, bleeding, fistulae) at <1 year

- Actual outcome: N of patients with complications (wound infection, haemorrage at surgical site, pancreatic fistula, intestinal fistula) at perioperative; Group 1: 5/5, Group 2: 7/7; Risk of bias: Very high; Indirectness of outcome: No indirectness

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINED APPROACH UPFRONT (LAPAROTOMY+NECROSECTOMY+ACTIVE DRAINAGE) versus STEP-UP APPROACH (PERCUTANEOUS DRAINAGE+VARD)

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome: Duration of hospitalisation (days) at perioperative; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality at <1 year
- Actual outcome: Deaths at perioperative; Group 1: 1/5, Group 2: 2/12; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 3: Complications (for example, bleeding, fistulae) at <1 year
- Actual outcome: N of patients with complications (wound infection, haemorrage at surgical site, pancreatic fistula, intestinal fistula) at perioperative; Group 1: 5/5, Group 2: 6/12; Risk of bias: Very high; Indirectness of outcome: No indirectness

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINED APPROACH UPFRONT (LAPAROTOMY+NECROSECTOMY+ACTIVE DRAINAGE) versus PERCUTANEOUS DRAINAGE (RADIOLOGICAL)

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome: Duration of hospitalisation (days) at perioperative; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality at <1 year
- Actual outcome: Deaths at perioperative; Group 1: 1/5, Group 2: 1/10; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 3: Complications (for example, bleeding, fistulae) at <1 year
- Actual outcome: N of patients with complications (wound infection, haemorrage at surgical site, pancreatic fistula, intestinal fistula) at perioperative; Group 1: 5/5, Group 2: 2/10; Risk of bias: Very high; Indirectness of outcome: No indirectness

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: STEP-UP APPROACH (PERCUTANEOUS DRAINAGE+VARD) versus PERCUTANEOUS DRAINAGE (RADIOLOGICAL)

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome: Duration of hospitalisation (days) at perioperative; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality at <1 year

- Actual outcome: Deaths at perioperative; Group 1: 2/12, Group 2: 1/10; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 3: Complications (for example, bleeding, fistulae) at <1 year - Actual outcome: N of patients with complications (wound infection, haemorrage at surgical site, pancreatic fistula, intestinal fistula) at perioperative; Group 1: 6/12, Group 2: 2/10; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Number of procedures (repeated procedures) at <1 year; Pancreatic function (for example, development of diabetes) at <1 year; Recurrence of infection at <1 year

Study	Van brunschot 2017[1096]
Study type	Systematic Review
Number of studies (number of participants)	15 (n=1485 (in infected necrosis subgroup))

Countries and setting	Conducted in Brazil, Canada, Germany, Hungary, India, Netherlands, United Kingdom, USA; Setting: Not stated
Line of therapy	Unclear
Duration of study	Not clear:
Method of assessment of guideline condition	Method of assessment /diagnosis not stated
Stratum	Overall
Subgroup analysis within study	Sys review – pre-specified in protocol: Infected pancreatic necrosis
Inclusion criteria	1. Observational cohort studies (both retrospective and prospective) or randomised trials reporting on the outcome of patients undergoing surgical necrosectomy or endoscopic necrosectomy for infected or sterile pancreatic and/or peripancreatic necrosis. 2. Cohorts with a sample size of ≥ 30 patients.
Exclusion criteria	1. Cohorts which included patients with chronic pancreatitis. 2. No data available for 1 or more of these variables: sex, age, method of necrosectomy, median time from hospital admission to necrosectomy, sterile or infected necrosis, and mortality.
Recruitment/selection of patients	Not stated
Age, gender and ethnicity	Age - Mean (SD): Minimally invasive: 45 (11); open (MI matched): 46 (14); endoscopic: 41 (14); open (endoscopic matched): 42 (10). Gender (M:F): 70/30% in minimally invasive cohort; 60/40% in endoscopic cohort. Ethnicity: Not stated

Further population details	1. Severity of infection: Systematic review: mixed 2. Severity of pancreatitis: Systematic review: mixed
Indirectness of population	No indirectness
Interventions	(n=127) Intervention 1: Minimally invasive surgery - Endoscopic. Endoscopic pancreatic necrosectomy is performed following endoscopic ultrasound-guided transgastric or transduodenal drainage of the pancreatic necrotic cavity. Usually, the drainage canal is created using electrocautery and balloon dilation. For endoscopic necrosectomy, further balloon dilation is needed in order to allow entrance of necrosectomy instruments (for example, snares, baskets, grasping forceps). Postprocedural lavage and re-necrosectomy was performed at the treating physician's discretion. . Duration Unclear. Concurrent medication/care: Unclear. Indirectness: No indirectness Further details: 1. Procalcitonin-led antibiotic treatment: Not applicable 2. Type of minimally invasive surgery : Endoscopic (n=335) Intervention 2: Minimally invasive surgery - Percutaneous. Minimally invasive surgical pancreatic necrosectomy is usually preceded radiologic catheter drainage, the drain being preferably placed in the left retroperitoneum. A small incision close to the drain entrance allows the surgeon to follow the drain tract into the necrotic cavity. Subsequent pancreatic necrosectomy can be performed under direct vision or videoscopic guidance using basic surgical instruments. Post-operative lavage and re-necrosectomy was performed at the treating surgeon's discretion. . Duration Unclear. Concurrent medication/care: Unclear. Indirectness: No indirectness Further details: 1. Procalcitonin-led antibiotic treatment: Not applicable 2. Type of minimally invasive surgery : Percutaneous (n=127) Intervention 3: Open surgery. Pancreatic necrosectomy performed through a bilateral subcostal incision with blunt and/or surgical removal of necrotic tissue. Post-operative lavage and re-necrosectomy was performed at the treating surgeon's discretion. «. Duration Unclear. Concurrent medication/care: Unclear. Indirectness: No indirectness

	Further details: 1. Procalcitonin-led antibiotic treatment: Not applicable 2. Type of minimally invasive surgery : Not applicable (n=335) Intervention 4: Open surgery. Pancreatic necrosectomy performed through a bilateral subcostal incision with blunt and/or surgical removal of necrotic tissue. Post-operative lavage and re-necrosectomy was performed at the treating surgeon's discretion. . Duration Unclear. Concurrent medication/care: Unclear. Indirectness: No indirectness Further details: 1. Procalcitonin-led antibiotic treatment: Not applicable 2. Type of minimally invasive surgery : Not applicable
Funding	Study funded by industry
Protocol outcomes not reported by the study	Quality of life at <1 year; Recurrence of infection at <1 year; Number of procedures (repeated procedures) at <1 year; Complications (eg bleeding, fistulae) at <1 year; Pancreatic function (eg development of diabetes) at <1 year; Length of stay (in intensive therapy unit or hospital) at <1 year

Study	**Van Brunschot 2017[1097]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=98)
Countries and setting	Conducted in Netherlands; Setting: 7 university medical centers and 12 teaching hospitals of the Dutch Pancreatitis Study Group
Line of therapy	1st line
Duration of study	Intervention and follow-up: 6 months' follow-up

Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Acute pancreatitis defined as having at least 2 of: upper abdominal pain; serum lipase or amylase levels >3-times the ULN; characteristic finding of acute pancreatitis on cross-sectional abdominal imaging
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Adults with a high suspicion or evidence of infected necrosis with an indication for invasive intervention and for whom both the endoscopic and surgical step-up approach were deemed feasible.
Exclusion criteria	Previous invasive interventions for necrotising pancreatitis, an acute flare of chronic pancreatitis, recurrent acute pancreatitis and an indication for emergency laparotomy
Age, gender and ethnicity	Age - Mean (SD): Endoscopic: 63 (14); surgical: 60 (11) years. Gender (M:F): 64/36%. Ethnicity: Not stated
Further population details	1. Severity of infection: Not stated / Unclear (Apporixmately 50% had <30% pancreatic necrosis). 2. Severity of pancreatitis: Severe pancreatitis (Averge APACHEII score 9-10).
Extra comments	71% had complete encapsulation of the necrotic collection; 28% had single organ failure and 16% had multiple organ failure at baseline. Infected necrosis was defined as a positive culture obtained by FNA or the presence of gas within necrotic collections on contrast-enhanced CT. Infected necrosis was suspected in necrotising pancreatitis patients with clinical signs of persistent sepsis or progressive clinical deterioration despite maximal CCU support without other causes for infection.
Indirectness of population	No indirectness
Interventions	(n=51) Intervention 1: Combination of intervention techniques - Step-up approach. Endoscopic ultrasound-guided transluminal (transgastric or transduodenal) drainage with placement of 2 doube pigtail stents and 1 nasocystic catheter. If drainage alone did not lead to considerable clinical improvement endoscopic transluminal necrosectomy was performed.. Duration N/A. Concurrent medication/care: Additional

	endoscopic/percutaneous drainage and endoscopic or surgical necrosectomies were allowed. Indirectness: No indirectness Further details: 1. Procalcitonin-led antibiotic treatment: Not applicable 2. Type of minimally invasive surgery : Endoscopic (n=47) Intervention 2: Combination of intervention techniques - Step-up approach. Radiological CT-guided or ultrsound-guided percutaneous catheter drainage, preferably through the left retroperitoneum with the catheter as guidance for video-assisted retroperitoneal debridement (VARD) if needed. If drainage was not successful a VARD procedure was performed.. Duration N/A. Concurrent medication/care: Additional endoscopic/percutaneous drainage and endoscopic or surgical necrosectomies were allowed. Indirectness: No indirectness Further details: 1. Procalcitonin-led antibiotic treatment: Not applicable 2. Type of minimally invasive surgery : Percutaneous
Funding	Academic or government funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ENDOSCOPIC STEP-UP APPROACH versus SURGICAL STEP-UP APPROACH

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome: Days in hospital at 6 months ; Group 1: mean 53 (SD 47); n=51, Group 2: mean 69 (SD 38); n=47; Comments: Median (IQR): 35 (19-85); 65 (40-90)
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: 1 spontaneous improvement; 2 treated in surgery group; Group 2 Number missing: 1, Reason: 1 spontaneous improvement

Protocol outcome 2: Mortality at <1 year
- Actual outcome: Mortality at 6 months; Group 1: 9/51, Group 2: 6/47; Comments: Most common causes of death were multiorgan failure or progressive sepsis
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: 1 spontaneous improvement; 2 treated in surgery group; Group 2

Number missing: 1, Reason: 1 spontaneous improvement

Protocol outcome 3: Number of procedures (repeated procedures) at <1 year
- Actual outcome: Median number of drainage procedures at 6 months ; ;
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: 1 spontaneous improvement; 2 treated in surgery group; Group 2 Number missing: 1, Reason: 1 spontaneous improvement

Protocol outcome 4: Complications (eg bleeding, fistulae) at <1 year
- Actual outcome: Bleeding requiring intervention at 6 months; Group 1: 11/51, Group 2: 10/47
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: 1 spontaneous improvement; 2 treated in surgery group; Group 2 Number missing: 1, Reason: 1 spontaneous improvement
- Actual outcome: Perforation of visceral organ or enterocutaneous fistula requiring intervention at 6 months; Group 1: 4/51, Group 2: 8/47
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: 1 spontaneous improvement; 2 treated in surgery group; Group 2 Number missing: 1, Reason: 1 spontaneous improvement
- Actual outcome: Pancreatic fistula at 6 months (excluding those who had died); Group 1: 2/42, Group 2: 13/41
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: 1 spontaneous improvement; 2 treated in surgery group; Group 2 Number missing: 1, Reason: 1 spontaneous improvement
- Actual outcome: New onset single organ failure at 6 months; Group 1: 7/51, Group 2: 13/47
Risk of bias: All domain - ; Indirectness of outcome: No indirectness
- Actual outcome: New onset multiple organ failure at 6 months; Group 1: 2/51, Group 2: 6/47
Risk of bias: All domain - ; Indirectness of outcome: No indirectness

Protocol outcome 5: Pancreatic function (eg development of diabetes) at <1 year
- Actual outcome: Exocrine insufficiency (fecal elastase <200 mg/g) at 6 months (excluding those who had died); Group 1: 22/42, Group 2: 19/41; Comments: Also reports N using enzymes and N with steatorrhoea
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: 1 spontaneous improvement; 2 treated in surgery group; Group 2 Number missing: 1, Reason: 1 spontaneous improvement

- Actual outcome: Endocrine insufficiency at 6 months (excluding those who had died); Group 1: 10/42, Group 2: 9/41 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: 1 spontaneous improvement; 2 treated in surgery group; Group 2 Number missing: 1, Reason: 1 spontaneous improvement	
Protocol outcomes not reported by the study	Quality of life at <1 year; Recurrence of infection at <1 year

Study	**Van Santvoort 2007[1103]**
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=30)
Countries and setting	Conducted in Netherlands; Setting: Department of surgery, University Medical Center Utrecht
Line of therapy	Unclear
Duration of study	Intervention time: 10 years
Method of assessment of guideline condition	Unclear method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients admitted to the hospital who underwent primary pancreatic necrosectomy were eligible for inclusion.
Exclusion criteria	Not reported
Recruitment/selection of patients	Participants had been admitted to hospital

Age, gender and ethnicity	Age - Median (range): Retroperitoneal: 52 (34-66) Laparotomy: 53 (39-75). Gender (M:F): 22:8. Ethnicity: Not reported
Further population details	1. Severity of infection: Not stated / Unclear 2. Severity of pancreatitis: Not stated / Unclear
Extra comments	Retro group: Etiology - Biliary: 8, Alcohol: 3, Post-ERCP: 1, Other/Unknown: 3; CT severity index - 4-6: 4, 8-10: 11; APACHE II score 24h preoperatively: 9 (5-18) Lap group: Etiology - Biliary: 5, Alcohol: 2, Post-ERCP: 2, Other/Unknown: 6; CT severity index - 4-6: 5, 8-10: 10; APACHE II score 24h preoperatively: 9 (5-20)
Indirectness of population	No indirectness
Interventions	(n=15) Intervention 1: Open surgery. After a bilateral subcostal or median incision, the lesser sac is entered through the gastrocolic omentum. Blunt debridement of all necrotic tissue is performed. Two double-lumen catheters are inserted through separate incisions and positioned in the retroperitoneal space. Six patients received pre-operative PCD.. Duration During admission. Concurrent medication/care: Not reported Further details: 1. Procalcitonin-led antibiotic treatment: Not stated / Unclear 2. Type of minimally invasive surgery : Not stated / Unclear (n=15) Intervention 2: Minimally invasive surgery - Percutaneous. As the first step, a 12F to 14F percutaneous drain is placed in the collection through the left retroperitoneum. If drainage does not lead to clinical improvement (combined normalisation of body temperature and decreased WBC count and CRP level) within the next days, the patient is operated on.. Duration During admission. Concurrent medication/care: Not reported Further details: 1. Procalcitonin-led antibiotic treatment: Not stated / Unclear 2. Type of minimally invasive surgery : Not stated / Unclear
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PERCUTANEOUS DRAINAGE versus OPEN SURGERY

Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at <1 year
- Actual outcome: Postoperative hospital stay at During admission; Other: Median (range); Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality at <1 year - Actual outcome: Mortality at During admission; Group 1: 1/15, Group 2: 6/15; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 3: Number of procedures (repeated procedures) at <1 year - Actual outcome: Further necrosectomy at During admission; Group 1: 11/15, Group 2: 13/15; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 4: Complications (for example, bleeding, fistulae) at <1 year - Actual outcome: Bowel perforation at During admission; Group 1: 1/15, Group 2: 2/15; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome: Bleeding at During admission; Group 1: 4/15, Group 2: 1/15; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome: GI fistulas at During admission; Group 1: 1/15, Group 2: 3/15; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome: Pancreatic fistulas at During admission; Group 1: 2/15, Group 2: 0/15; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at <1 year; Pancreatic function (for example, development of diabetes) at <1 year; Recurrence of infection at <1 year

H.13 Timing of management of infected necrosis in people with acute pancreatitis

Study	**Guo 2014[422]**
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=223)
Countries and setting	Conducted in China; Setting: West China Hospital, Sichuan University
Line of therapy	Unclear
Duration of study	Intervention + follow up: Unclear
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis was confirmed by CECT
Stratum	Adults >16 years
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients diagnosed with acute pancreatitis with pancreatic necrosis or peripancreatic necrosis were included.
Exclusion criteria	Not reported

Recruitment/selection of patients	Patients were admitted to hospital
Age, gender and ethnicity	Age - Median (range): 47 (22-74). Gender (M:F): 136:87. Ethnicity: Not reported
Further population details	1. Severity of infection: Not stated / Unclear 2. Severity of pancreatitis: Not stated / Unclear
Extra comments	Early group: Aetiology: Biliary - 67/136, Alcohol - 13/136, Others - 56/136; BMI (Median (Range)) - 27(30-33); APACHE II score (Median (Range)) - 10 (2-32) Late group: Aetiology: Biliary - 41/87, Alcohol - 11/87, Others - 35/87; BMI (Median (Range)) - 31 (22-34); APACHE II score (Median (Range)) - 6 (2-30)
Indirectness of population	No indirectness
Interventions	(n=87) Intervention 1: Late intervention (as defined by studies) - Late combination of interventions. Intervention was postponed until approximately 4 weeks after the onset of disease, whenever possible. Open pancreatic necrosectomy, retroperitoneal pancreatic necrosectomy, or primary percutaneous catheter drainage with pigtail plastic stents were the possible types of intervention.. Duration Unclear. Concurrent medication/care: Cultures were taken during all primary procedures to confirm the diagnosis of infected necrosis. Further details: 1. Procalcitonin-led antibiotic treatment: Not stated / Unclear 2. Type of minimally intervention: Systematic review: mixed (n=136) Intervention 2: Early intervention (as defined by studies) - Early combination of interventions. Intervention was postponed until approximately 4 weeks after the onset of disease, whenever possible. However, when severe clinical deterioration persisted, a prompt intervention was performed. Open pancreatic necrosectomy, retroperitoneal pancreatic necrosectomy, or primary percutaneous catheter drainage with pigtail plastic stents were the possible types of intervention.. Duration Unclear. Concurrent medication/care: Cultures were taken during all primary procedures to confirm the diagnosis of infected necrosis. Further details: 1. Procalcitonin-led antibiotic treatment: 2. Type of minimally intervention:
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LATE COMBINATION OF INTERVENTIONS versus EARLY COMBINATION OF INTERVENTIONS

Protocol outcome 1: Mortality at <1 year
- Actual outcome for Adults >16 years: OF: Mortality at Unclear; Group 1: 3/21, Group 2: 23/61
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults >16 years: NOF: Mortality at Unclear; Group 1: 6/66, Group 2: 5/75

Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Number of procedures (repeated procedures) at <1 year - Actual outcome for Adults >16 years: OF: Re-intervention at Unclear; Group 1: 2/21, Group 2: 17/61 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults >16 years: NOF: Re-intervention at Unclear; Group 1: 3/66, Group 2: 7/75 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Complications (for example, bleeding, fistulae) at <1 year - Actual outcome for Adults >16 years: OF: Intra-abdominal bleeding at Unclear; Group 1: 5/21, Group 2: 24/61 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults >16 years: OF: Enterocutaneous fistula at Unclear; Group 1: 3/21, Group 2: 6/61 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults >16 years: OF: New-onset organ failure at Unclear; Group 1: 6/21, Group 2: 16/61 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults >16 years: NOF: Intra-abdominal bleeding at Unclear; Group 1: 3/66, Group 2: 3/75 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults >16 years: NOF: Enterocutaneous fistula at Unclear; Group 1: 9/66, Group 2: 6/75 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults >16 years: NOF: New-onset organ failure at Unclear; Group 1: 1/66, Group 2: 4/75 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life at <1 year; Recurrence of infection at <1 year; Pancreatic function (for example, development of diabetes) at <1 year; Length of stay (in intensive therapy unit or hospital) at <1 year

H.14 Management of pain in people with chronic pancreatitis

Study (subsidiary papers)	Ahmed 2014[14] (Banks 1997[85]; Bhardwaj 2009[127]; Durgaprasad 2005[323]; Jarosz 2010[524]; Kirk 2006[601]; Siriwardena 2012[1001]; Uden 1990[1084, 1086])
Study type	Systematic Review
Number of studies (number of participants)	8 (n=503)
Countries and setting	Conducted in multiple countries; Setting: Systematic review: mixed
Line of therapy	Unclear
Duration of study	Systematic review: mixed
Method of assessment of guideline condition	Systematic review: method of assessment mixed
Stratum	Adults >16 years
Subgroup analysis within study	Not applicable
Inclusion criteria	Randomised trials evaluating antioxidant for treatment of pain in chronic pancreatitis, all adult patients with established chronic pancreatitis according to the criteria of at least one international guideline. Patients must have had some degree of pain, described as constant or recurrent pain attacks
Exclusion criteria	Quasi-randomised trials
Recruitment/selection of patients	Systematic review: mixed
Age, gender and ethnicity	Age - Range: 21–91 years. Gender (M:F) 231:81 (not reported for 91 participants). Ethnicity: Not reported
Further population details	
Indirectness of population	Serious indirectness: Includes some acute pancreatitis patients
Interventions	Systematic review: see study characteristics
Funding	No funding

RESULTS
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ANTIOXIDANT versus CONTROL
Banks 1997
Protocol outcome 1: quality of life
- Actual outcome: activities of daily living at 10 weeks; MD; 3.3 (95%CI 10.3 to -3.7) ADL 0-120 Top=High is good outcome;
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness

Protocol outcome 2: pain
- Actual outcome: pain VAS at 10 weeks: MD; -2.8 (95%CI 2.2 to -7.7) VAS 0-100 Top=High is poor outcome;
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness
Protocol outcome 2: adverse events
- Actual outcome: adverse events: Group 1:1/13, Group 2: 1/13
Risk of bias: All domain – Very high, Selection - High, Blinding - Low, Incomplete outcome data - high, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness

Bhardwaj 2009
Protocol outcome 1: pain
- Actual outcome: reduction in painful days per month: Group 1: mean 7.37 (SD 6.75); n=66, Group 2: mean 3.21 (SD 3.99); n=53
- Actual outcome: reduction in pain medication – oral analgesic tablets/month: Group 1: mean 10.51 (SD 11.77); n=71, Group 2: mean 4.36 (SD 5.78); n=56
- Actual outcome: reduction in pain medication – parenteral analgesic injections/month: Group 1: mean 2.59 (SD 3.88); n=71, Group 2: mean 1.89 (SD 3.01); n=56
- Actual outcome: pain free participants: Group 1: 23/71, Group 2: 7/56
Risk of bias: All domain - high, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low,
Indirectness of outcome: No indirectness ; Group 1 Number missing: 15; Group 2 Number missing: 5
Protocol outcome 2: adverse events
- Actual outcome: adverse events: Group 1: 12/71, Group 2: 3/56
Risk of bias: All domain - high, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low,
Indirectness of outcome: No indirectness ; Group 1 Number missing: 15; Group 2 Number missing: 5
Protocol outcome: mortality
- Actual outcome: mortality: Group 1: 0/71, Group 2: 0/56
Risk of bias: All domain - high, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low,
Indirectness of outcome: No indirectness ; Group 1 Number missing: 15; Group 2 Number missing: 5

Durgaprasad 2005
Protocol outcome 1: pain
- Actual outcome: pain VAS: Group 1: mean 5.81 (SD 2.09); n=8, Group 2: mean 6.57 (SD 1.38); n=7, VAS 0-10 Top=High is poor outcome
Risk of bias: All domain – Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Number missing overall 5/20
Protocol outcome 2: adverse events
- Actual outcome: adverse events: Group 1: 0/8, Group 2: 0/7
Ri Risk of bias: All domain – Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Number missing overall 5/20

Jarosz 2010
Protocol outcome 1: pain
- Actual outcome: number of pain free participants: Group 1: 22/32, Group 2: 11/35
Risk of bias: All domain – Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Number missing overall 24/91

Kirk 2006
Protocol outcome 1: adverse events
- Actual outcome: adverse events: Group 1: 1/19, Group 2: 1/19
Risk of bias: All domain – Very high, Selection - high, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - High;
Indirectness of outcome: No indirectness ; Number missing overall 17/36

Siriwardena 2012
Protocol outcome 1: pain
- Actual outcome: daily NRS average: Group 1: mean 2.93 (SD 1.96); n=33, Group 2: mean 3.05 (SD 1.96); n=37: NRS 0-10 Top=High is poor outcome
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: unclear; Group 2 Number missing: unclear
Protocol outcome 2: Quality of life
- Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: EORTC-QLQ-PAN28 overall: MD; -4.1 (95%CI -8.5 to 0.2) EORTC QLQ-PAN28 30-126 Top=High is good outcome;
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: unclear; Group 2 Number missing: unclear
- Actual outcome: EORTC-QLQ-PAN28 pancreatic pain: MD; -0.08 (95%CI -1.05 to 0.90) EORTC QLQ-C30 30-126 Top=High is good outcome;
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: unclear; Group 2 Number missing: unclear
- Actual outcome: EQ-5D: MD; 0.04 (95%CI -0.10 to 0.19) EQ-5D 0-1 Top=High is good outcome
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: unclear; Group 2 Number missing: unclear
- Actual outcome: EQ-5D VAS: MD; 2.3 (95%CI -6.5 to 11.1) EQ-5D VAS 0-100 Top=High is good outcome
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: unclear; Group 2 Number missing: unclear

Protocol outcome 3: Adverse events
- Actual outcome: adverse events: Group 1: 8/33, Group 2: 1/37
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low;

Indirectness of outcome: No indirectness ; Group 1 Number missing: unclear; Group 2 Number missing: unclear **Uden 1990** Protocol outcome 1: adverse events - Actual outcome: adverse events: Group 1: 0/20, Group 2: 0/20 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - High; Indirectness of outcome: No indirectness ; Group 1 Number missing:4; Group 2 Number missing: 1 Protocol outcome 2: pain - Actual outcome: pain/distress at 10 weeks: Median difference 0.26 (95%CI -0.06 to 0.84) 0-10 Top=High is poor outcome Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 4); Group 2 Number missing: 1	
Protocol outcomes not reported by the study	Serious adverse events at 1 year or under; Return to usual activities ; Pancreatic function (endocrine and exocrine)

Study	**Malesci 1995[704]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=24)
Countries and setting	Conducted in Denmark; Setting: Not reported
Line of therapy	Unclear
Duration of study	Intervention time: 8 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: presence of ductal changes at endoscopic retrograde cholangiopancreatography; pancreatic calcifications; abnormalities at ultrasonography scan; pancreatic insufficiency at the secretin-cerulein test.
Stratum	Adults over 16
Subgroup analysis within study	Not applicable
Inclusion criteria	all patients had complained of typical recurrent pancreatic pain and had had at least one episode of long-lasting pain (>12h) with concomitant elevation of serum pancreatic enzyme levels
Exclusion criteria	exclusion criteria included pancreatic pseudocysts, ductal changes typical of "advanced pancreatitis", steatorrhoea with passage of more than 20 g fat/day, previous pancreatic surgery, concomitant peptic ulcer, or cholethiasis.
Recruitment/selection of patients	Not reported

Study	Malesci 1995[704]
Age, gender and ethnicity	Age - Range: 21-70. Gender (M:F): 19:3. Ethnicity: Not reported
Further population details	1. Severity of pain: Not stated / Unclear 2. Types of nerve blocks: Not applicable
Indirectness of population	No indirectness
Interventions	(n=24) Intervention 1: Enzyme replacement therapy. Participants were given pancreatic extract (Pancrex-Duo, Samil-Sandoz, Italy) as capsules of enteric-coated microspheres, each capsule containing 34,376 USP units of protease, 13,000 USP units of lipase, and 43, 570 USP units of amylase. The dose given was four times daily (at meals and bedtime).. Duration 4 months. Concurrent medication/care: Strict alcohol abstinence was strongly recommended to all the recruited patients at least one year before the entered the study. Patients were allowed to consume analgesics: the drug and manner of administration were the patients' choice in accordance with pre-study habits. Further details: 1. Types of surgery: Not applicable (n=24) Intervention 2: Enzyme replacement therapy. Participants were given placebo four times daily (at meals and bedtime). Duration 4 months. Concurrent medication/care: Strict alcohol abstinence was strongly recommended to all the recruited patients at least one year before the entered the study. Patients were allowed to consume analgesics: the drug and manner of administration were the patients' choice in accordance with pre-study habits. Further details: 1. Types of surgery: Not applicable
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PANCREX-DUO versus PLACEBO Protocol outcome 1: Pain (duration of pain, reduction in pain, medication reduction) - Actual outcome for Adults over 16: Pain (People experiencing long-lasting (>12h) pain attacks) at 4 months; Group 1: 14/22, Group 2: 11/22 Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2; Group 2 Number missing: 2 - Actual outcome for Adults over 16: Pain (Use of analgesics) at 4 months; Group 1: 10/22, Group 2: 5/22 Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2; Group 2 Number missing: 2	
Protocol outcomes not reported by the study	Quality of life ; Mortality ; Pain (duration of pain, reduction in pain, medication reduction) ; Serious adverse events at 1 year or under; Adverse events at 1 year or under; Return to usual activities ; Return to usual activities ; Pancreatic function (endocrine and exocrine)

Study	Mossner 1992[763]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=47)
Countries and setting	Conducted in Germany; Setting: Not reported
Line of therapy	Unclear
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: CP documented by typical duct abnormalities at ERCP or calcifications on plain X-ray films or typical signs in CT or sonography (calcifications, duct abnormalities, organ enlargement)
Stratum	Adults over 16
Subgroup analysis within study	Not applicable
Inclusion criteria	Acute or chronic abdominal pain most likely due to chronic pancreatitis, activity of the disease not so severe as to need treatment by parenteral nutrition or intensive care, CP documented by typical duct abnormalities at ERCP or calcifications on plain X-ray films or typical signs in CT or sonography (calcifications, duct abnormalities, organ enlargement), quantitative fecal fat below 30g/day, age range between 20 and 60, history of CP of more than 50 months
Exclusion criteria	History of gastric resections or vagotomy, history of pancreatic resections included Whipple operation, pancreas divisum, complications of CP such as pseudocysts, kidney abnormalities in sonography, bilirubin above 1.5 mg/dl, cholesterol above 500 mg/dl, triglycerides above 1000 mg/dl
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - --: Not reported. Gender (M:F): 41:6. Ethnicity: Not reported
Further population details	1. Severity of pain: Not stated / Unclear 2. Types of nerve blocks: Not applicable
Indirectness of population	No indirectness
Interventions	(n=47) Intervention 1: Enzyme replacement therapy. Patients received either placebo or pancreatic extracts in double-blind randomised manner for 14 days. This was followed by crossover treatment for another 14 days with either verum or placebo. A new preparation of acid-protected commercially available porcine pancreatic enzymes was applied together with meals in a higher dosage that commonly used for treatment of pancreatic insufficiency (5x2 capsules a day; Panzytrat 20,000, Nordmark Arzneimittel, Uetersen, FRG; capsules with microtablets, containing per capsule according to the information provided by the manufacturer, triaglycerol lipase 20,000 Pharmacopoea europaea units, (Ph Eur U), amylase 20,000 Ph Eur U, proteases 1000 Ph Eur U). This dosage ensured the application of 10,000 Ph Eur U of proteases/day.. Duration 14 days. Concurrent medication/care: Not reported

Study	Mossner 1992[763]
	Further details: 1. Types of surgery: Not applicable (n=47) Intervention 2: Enzyme replacement therapy. Patients received either placebo or pancreatic extracts in double-blind randomised manner for 14 days. This was followed by crossover treatment for another 14 days with either verum or placebo. . Duration 14 days. Concurrent medication/care: Not reported Further details: 1. Types of surgery: Not applicable
Funding	Study funded by industry (The study was supported by a grant from Nordmark Arzneimittel, Uetersen, FRG.)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PANZYTRAT versus PLACEBO Protocol outcome 1: Pain (duration of pain, reduction in pain, medication reduction) - Actual outcome for Adults over 16: Pain (Pain score) at 2 weeks; Group 1: mean 1.08 (SD 0.87); n=47, Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: 4; Group 2 Number missing: 4	
Protocol outcomes not reported by the study	Quality of life ; Mortality ; Pain (duration of pain, reduction in pain, medication reduction) ; Serious adverse events at 1 year or under; Adverse events at 1 year or under; Return to usual activities ; Return to usual activities ; Pancreatic function (endocrine and exocrine)

H.15 Management of pancreatic duct obstruction in people with chronic pancreatitis

Study (subsidiary papers)	Cahen 2007[182] (Cahen 2011[181])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=39)
Countries and setting	Conducted in Netherlands; Setting: The Hepato-Pancreatico-Biliary outpatient clinic of the study hospital

Line of therapy	Unclear
Duration of study	Intervention plus follow up: 2 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Based on clinical symptoms and morphological changes detected by imaging studies; pancreatic insufficiency or both.
Stratum	Adults over 16
Subgroup analysis within study	Not applicable
Inclusion criteria	Diagnosis of chronic pancreatitis, based on clinical symptoms and morphological changes detected by imaging studies; pancreatic insufficiency or both, obstruction of the pancreatic duct due to stenosis, intraductal stones, or both located left of the spine, with dilation of the duct by at least 5 mm proximal to the obstruction, as determined by magnetic resonance cholangiopancreatography, abdominal computed tomography, or both, severe recurrent pancreatic pain insufficiently relieved by non-narcotic analgesics or requiring opiates.
Exclusion criteria	Age <18 or >80, enlargement of the pancreatic head >4 cm, contraindications to surgery (American Society of Anesthesiologists class IV, severe portal hypertension), contraindications to endoscopic treatment (gastrectomy with Billroth II reconstruction, other pancreatitis-related complications requiring surgery), previous pancreatic surgery, suspected pancreatic cancer, life expectancy <2 years, pregnancy.
Recruitment/selection of patients	Patients were invited to participate after attending the clinic
Age, gender and ethnicity	Age - Mean (SD): Endo: 52 (9) Surgery: 46 (12). Gender (M:F): 26:13. Ethnicity: Not reported
Further population details	1. Presence of an inflammatory mass: Not stated / Unclear
Extra comments	Endoscopy: Aetiology - Alcohol: 9, Idiopathic: 7, Hereditary: 1, Pancreas divisum: 2; Continuous pain: 12, Intermittent pain: 7; Izbicki pain score (Mean (SD)): 73 (12); Duration of symptoms: 16 (14); SF-36 Physical health component: 31 (8), Mental health component: 33 (8) . Surgery: Aetiology - Alcohol: 12, Idiopathic: 5, Hereditary: 1, Pancreas divisum: 0, Other: 2; Continuous pain: 12, Intermittent pain: 9; Izbicki pain score (Mean (SD)): 69 (18); Duration of symptoms: 21 (19); SF-36 Physical health component: 35 (8), Mental health component: 37 (12)

Indirectness of population	No indirectness
Interventions	(n=19) Intervention 1: Combination of techniques - eg ESWL plus pancreatic endotherapy. Endoscopic treatment was performed by experienced endoscopists who had each performed more than 1000 ERCPs. The procedure was performed with the patient under conscious sedation or, if endoscopy was preceded by shock-wave lithotripsy, with the patient under general anaesthesia with propofol. If one or more intraductal stones more than 7 mm in diameter were identified by imaging studies, the patient was referred for lithotripsy. After lithotripsy, stone fragments were removed during a consecutive endoscopic transampullary drainage procedure with a balloon or Dormia basket and the use of the "rotation-perfusion" technique.If stone removal was incomplete, a 6-French nasopancreatic catheter was left in place, and lavage with saline (1L per 24h) was performed until the next treatment.If obstruction of the main duct could not be completely resolved, one or two endoprostheses were placed during the last endoscopic procedure. If an endoprosthesis had been inserted, an elective endoscopic pancreatogram was scheduled for every 3 months. When complete runoff of contrast material was observed after removal of the stent and an extraction balloon could be passed through the pancreatic duct, endoscopic treatment was terminated. Persistent strictures were treated by repeated dilation and sequential insertion of multiple stents. (16 people underwent lithotripsy). Duration 2 years. Concurrent medication/care: In patients with persistent or recurrent pain, imagine studies were repeated and evaluated by a multidisciplinary team of gastroenterologists, surgeons and radiologists. If a recurrent pancreatic duct obstruction was seen in a patient who had completed endoscopic treatment, stent therapy was resumed. Further details: 1. Types of endotherapy: Not stated / Unclear 2. Types of surgery: Not applicable (n=20) Intervention 2: Surgery - Resection and/or surgical drainage procedure. Surgery was performed 4 weeks after randomisation by experienced hepatobiliary surgeons. A pancreaticojejunostomy was performed by the method of Partington and Rochelle. The pancreatic duct was incised over the full length up to 2 cm from the ampulla. When retrieval of concretions from the head area required further opening of the duct toward the ampulla, a limited wedge resection of pancreatic tissue was performed. The patency of the anastamosis was evaluated by means of magnetic resonance cholangiopancreatography 3 months after the procedure and again if symptoms recurred. . Duration 2 years. Concurrent medication/care: In patients with persistent or recurrent pain, imagine studies were repeated and evaluated by a multidisciplinary team of gastroenterologists, surgeons and radiologists. If a recurrent pancreatic duct obstruction was seen in a patient who had completed endoscopic treatment, stent therapy was resumed. Further details: 1. Types of endotherapy: Not applicable 2. Types of surgery: Surgical drainage
Funding	Study funded by industry (Supported by an unrestricted grant from AstraZeneca, the Netherlands)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ESWL PLUS PANCREATIC ENDOTHERAPY versus SURGICAL DRAINAGE

Protocol outcome 1: Quality of life
- Actual outcome for Adults over 16: QoL (SF-36; Physical health component) at 2 years; Group 1: mean 38 (SD 9); n=19, Group 2: mean 47 (SD 7); n=20; SF-36 0-100 Top=High is good outcome
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 1
- Actual outcome for Adults over 16: QoL (SF-36; Mental health component) at 2 years; Group 1: mean 40 (SD 9); n=19, Group 2: mean 45 (SD 9); n=20; SF-36 0-100 Top=High is good outcome
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 1
- Actual outcome for Adults over 16: QoL (SF-36; Physical health component) at 7 years; Group 1: mean 43 (SD 11); n=16, Group 2: mean 48 (SD 9); n=15; SF-36 0-100 Top=High is good outcome
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3; Group 2 Number missing: 5
- Actual outcome for Adults over 16: QoL (SF-36; Mental health component) at 7 years; Group 1: mean 46 (SD 9); n=16, Group 2: mean 48 (SD 10); n=15; SF-36 0-100 Top=High is good outcome
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3; Group 2 Number missing: 5

Protocol outcome 2: Mortality
- Actual outcome for Adults over 16: Mortality at 2 years; Group 1: 1/19, Group 2: 0/20
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 1

Protocol outcome 3: Pain (duration of pain, reduction in pain, medication reduction)
- Actual outcome for Adults over 16: Pain (Izbicki pain score) at 2 years; Group 1: mean 51 (SD 23); n=19, Group 2: mean 25 (SD 15); n=20
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 1
- Actual outcome for Adults over 16: Pain (Pain relief) at 2 years; Group 1: 6/19, Group 2: 15/20
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 1
- Actual outcome for Adults over 16: Pain (Izbicki pain score) at 7 years; Group 1: mean 39 (SD 28); n=16, Group 2: mean 22 (SD 31); n=15; Izbicki pain score 0-100 Top=High is poor outcome
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3; Group 2 Number missing: 5

- Actual outcome for Adults over 16: Pain (Pain relief) at 7 years; Group 1: 6/16, Group 2: 12/15
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 3; Group 2 Number missing: 5

Protocol outcome 4: Length of stay (in critical care or hospital) at 1 year or under
- Actual outcome for Adults over 16: Hospital stay at 2 years; Mean; , Comments: Endoscopy (Median (range)): 8 (0-128)
Surgery (Median (range)): 11 (5-59) ;
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 1

Protocol outcome 5: Repeated procedures
- Actual outcome for Adults over 16: Number of procedures at 2 years; Mean; , Comments: Endoscopy (Median (range)): 8 (1-21)
Surgery (Median (range)): 3 (1-9);
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 1

Protocol outcome 6: Pancreatic function (endocrine and exocrine)
- Actual outcome for Adults over 16: Pancreatic function (Exocrine insufficiency persisted) at 2 years; Group 1: 11/19, Group 2: 13/20
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 1
- Actual outcome for Adults over 16: Pancreatic function (Exocrine insufficiency developed) at 2 years; Group 1: 6/19, Group 2: 1/20
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 1
- Actual outcome for Adults over 16: Pancreatic function (Endocrine insufficiency developed) at 2 years; Group 1: 3/19, Group 2: 1/20
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 1
- Actual outcome for Adults over 16: Pancreatic function (Endocrine insufficiency persisted) at 2 years; Group 1: 3/19, Group 2: 4/20
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 1
- Actual outcome for Adults over 16: Pancreatic function (Exocrine insufficiency persisted) at 7 years; Group 1: 10/16, Group 2: 11/15
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 3; Group 2 Number missing: 5
- Actual outcome for Adults over 16: Pancreatic function (Exocrine insufficiency developed) at 7 years; Group 1: 6/16, Group 2: 2/15
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: 3; Group 2 Number missing: 5
- Actual outcome for Adults over 16: Pancreatic function (Endocrine insufficiency developed) at 7 years; Group 1: 7/16, Group 2: 3/15

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3; Group 2 Number missing: 5 - Actual outcome for Adults over 16: Pancreatic function (Endocrine insufficiency persisted) at 7 years; Group 1: 4/16, Group 2: 4/15 Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3; Group 2 Number missing: 5	
Protocol outcomes not reported by the study	Complications at 1 year or under; Pain (duration of pain, reduction in pain, medication reduction)

Study	**Dite 2003[299]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=72)
Countries and setting	Conducted in Czech Republic; Setting: Not reported
Line of therapy	Unclear
Duration of study	Intervention plus follow up: 5 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Established by imaging methods such as ultrasound, ERCP, computed tomography, and endosonography
Stratum	Adults over 16
Subgroup analysis within study	Not applicable
Inclusion criteria	Age 18-70, a diagnosis of chronic pancreatitis established by imaging methods such as ultrasound, ERCP, computed tomography, and endosonography, an obsrtuctive form of chronic pancreatitis, with a pain score of more than 3 on Melzack's score, failure of conservative management during the previous 3 years, duration of clinical disease over 5 years, indication for interventional treatment (with both surgery and endoscopy being possible therapeutic alternatives in order for the patient to be included), established in consensus by a consulting gastroenterologist and surgeon.

Exclusion criteria	Aged under 18 or over 70 years, pregnancy, previous interventional therapy for chronic pancreatitis, such as celiac plexus blockade, pancreatic endotherapy, or pancreatic surgery for chronic pancreatitis, suspected pancreatic malignancy, refusal to consent to the study therapies and/or noncompliance with follow-up examinations.
Recruitment/selection of patients	Patients were invited to participate.
Age, gender and ethnicity	Age - Range: 26-53. Gender (M:F): Not reported. Ethnicity: Not reported
Further population details	1. Presence of an inflammatory mass: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=36) Intervention 1: Pancreatic endotherapy - Endoscopic techniques – pancreatic stent (plastic or metal), pancreatic sphincterotomy, drainage. Endotherapy was carried out by two experienced therapeutic endoscopists (who had each performed over 200 therapeutic ERCPs prior to the start of the study). Endotherapy consisted of pancreatic sphincterotomy, dilation or bougienage of strictures, stenting in case of strictures that could not be resolved by sphincterotomy alone, and/or stone extraction, after mechanical lithotripsy when appropriate; extracorporeal shock-wave lithotripsy (ESWL) was not included in the treatment protocol. Stenting was planned for 12-24 months, with stent exchanges being performed every 2-4 months. After the initial treatment period, consisting of either stone extraction and/or long-term stenting over several months, further endoscopic treatment was not carried out.. Duration 5 years. Concurrent medication/care: Not reported Further details: 1. Types of endotherapy: Not stated / Unclear 2. Types of surgery: Not applicable (n=36) Intervention 2: Surgery - Resection and/or surgical drainage procedure. Surgery was carried out by one experienced abdominal surgeon (who had performed 90 pancreatic operations before the start of the study). The surgical therapy was tailored to the individuals situation and included resection procedures for localised disease and drainage procedures for diffuse disease with ductaldilation. In patients in whom chronic pancreatitis was limited predominantly to the pancreatic head, either duodenum-preserving pancreatic head resection or - if the duodenum and/or bile duct were also involved and stenosed - pancreatoduodenectomy (Whipple's resection) were performed. Chronic pancreatitis predominantly affecting the pancreatic tail was treated surgically by left pancreatic resection. Partington-Rochelle pancreatojejunal anastomosis (a drainage procedure) was used in patients with absence of focal pancreatic enlargement, grossly dilated pancreatic duct, and chronic pancreatic pseudocysts if present.. Duration 5 years. Concurrent medication/care: Not reported Further details: 1. Types of endotherapy: Not applicable 2. Types of surgery: Systematic review: mixed

Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ENDOTHERAPY versus RESECTION AND/OR SURGICAL DRAINAGE PROCEDURE Protocol outcome 1: Pain (duration of pain, reduction in pain, medication reduction) - Actual outcome for Adults over 16: Pain (Complete absence of abdominal pain) at 5 years; Group 1: 5/36, Group 2: 12/36 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults over 16: Pain (Partial relief of abdominal pain) at 5 years; Group 1: 17/36, Group 2: 19/36 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Pancreatic function (endocrine and exocrine) - Actual outcome for Adults over 16: Pancreatic function (New onset diabetes) at 5 years; Group 1: 12/36, Group 2: 14/36 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Mortality ; Complications at 1 year or under; Pain (duration of pain, reduction in pain, medication reduction) ; Length of stay (in critical care or hospital) at 1 year or under; Repeated procedures

Study	**Dumonceau 2007[319]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=55)
Countries and setting	Conducted in Switzerland; Setting: Not reported
Line of therapy	Unclear

Duration of study	Intervention plus follow up: 2 years
Method of assessment of guideline condition	Unclear method of assessment/diagnosis
Stratum	Adults over 16
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients were considered eligible if they had painful chronic pancreatitis with at least one calcification >4 mm in the pancreatic head or body with upstream dilation of the MPD and no previous intervention on the pancreas.
Exclusion criteria	The presence of a pancreatic fluid collection >2 cm, serum alkaline phosphatases greater than twice the normal value or cholangitis, age <18 years or pregnancy or lactation, and unwillingness to participate.
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): ESWL alone: 51.8 (12.3) ESWL with endoscopy: 49 (10.1). Gender (M:F): 43:12. Ethnicity: Not reported
Further population details	1. Presence of an inflammatory mass: Not stated / Unclear
Extra comments	ESWL group: Alcoholism: 19, N of pain episodes in the last year: 2.5, Intensity of pain: 7.2, Pain present at inclusion: 11, Continuous pain: 10, diabetes: 6 ESWL plus endotherapy group: Alcoholism: 20, N of pain episodes in the last year: 3, Intensity of pain: 7.3, Pain present at inclusion: 20, Continuous pain: 8, diabetes: 4
Indirectness of population	No indirectness
Interventions	(n=26) Intervention 1: Pancreatic ESWL - Extracorporeal Shock wave lithotripsy – with or without ERCP. One or more sessions of ESWL were performed in all patients using the Lithostar Plus until the obstructive stones were broken into fragments <2 mm, as measured by x-ray.. Duration 2 years. Concurrent medication/care: Follow-up consisted clinical examination 1 month after treatment (supplemented with secretin-enhanced magnetic resonance cholangio-pancreatography in centre 1), and every 6 months thereafter. Further details: 1. Types of endotherapy: Different types of endotherapy 2. Types of surgery: Not applicable

	(n=29) Intervention 2: Pancreatic ESWL - Extracorporeal Shock wave lithotripsy – with or without ERCP. One or more sessions of ESWL were performed in all patients using the Lithostar Plus until the obstructive stones were broken into fragments <2 mm, as measured by x-ray. In addition to this, the patients in the ESWL combined with endoscopy group underwent an endoscopic retrograde pancreatography immediately after the last ESWL session with attempted extraction of stone fragments and insertion of 10-French plastic pancreatic stents if pancreatic strictures were identified.. Duration 2 years. Concurrent medication/care: Follow-up consisted clinical examination 1 month after treatment (supplemented with secretin-enhanced magnetic resonance cholangio-pancreatography in centre 1), and every 6 months thereafter. Further details: 1. Types of endotherapy: Different types of endotherapy 2. Types of surgery: Not applicable
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY versus EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY WITH ERP Protocol outcome 1: Pain (duration of pain, reduction in pain, medication reduction) - Actual outcome for Adults over 16: Pain (Pain relapse at 2 years) at 2 years; Group 1: 10/24, Group 2: 13/24 Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2; Group 2 Number missing: 5 - Actual outcome for Adults over 16: Pain (Pain intensity) at 2 years; Group 1: mean 5.7 (SD 2.1); n=24, Group 2: mean 5.7 (SD 1.3); n=24; VAS pain score 1-10 Top=High is poor outcome Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2; Group 2 Number missing: 5 Protocol outcome 2: Length of stay (in critical care or hospital) at 1 year or under - Actual outcome for Adults over 16: Length of hospital stay at 2 years; Group 1: mean 3.1 days (SD 5.3); n=24, Group 2: mean 8.6 days (SD 16.5); n=24 Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2; Group 2 Number missing: 5	
Protocol outcomes not reported by the study	Quality of life ; Mortality ; Complications at 1 year or under; Pain (duration of pain, reduction in pain, medication reduction) ; Repeated procedures ; Pancreatic function (endocrine and exocrine)

H.16 Management of small-duct disease in people with chronic pancreatitis

Study	Basinski 2005[93]
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=48)
Countries and setting	Conducted in Poland; Setting: Not reported
Line of therapy	Unclear
Duration of study	Not clear:
Method of assessment of guideline condition	Unclear method of assessment/diagnosis
Stratum	Adults over 16
Subgroup analysis within study	Not applicable
Inclusion criteria	Chronic pancreatitis diagnosed by CT scan and endoscopic retrograde cholangiopancreatography, persistent pain for at least 3 months, scoring at least 66.7% on the pain visual analog scale.
Exclusion criteria	Patients with pancreatic inflammatory tumors or pseudocysts were excluded from the study.
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): NCPB: 49.9 (7.8) VSPL: 47.3 (%). Gender (M:F): NCPB: 3.01, VSPL: 3.51. Ethnicity: Not reported
Further population details	

Indirectness of population	No indirectness
Interventions	(n=18) Intervention 1: Surgery - Partial or total resection and drainage operation. Because unilateral (preferably left-sided) splanchnicectomy was reported to be adequate in control of the intractable pancreatic pain, all patients were given a left-sided intervention. General anaesthesia was administered with single bronchus intubation in every case. The patient was placed in the right lateral decubitus position with the left are elevated at a 90· angle, and fixed with support-arms and bandages, and the table was then tilted 30 degrees anteriorly in the longitudinal axis. After desufflation of the lung, two trocars were inserted into the thorax. After identification of the splanchnic nerve, situated above the aorta on the left or above the azygos vein on the right, the parietal pleura was incised and the nerve together with its minor connecting branches, was prepared to a distance of 5-8 cm and then excised. After insufflation of the lung, the trocars were removed, a single chest tube was placed, and the wounds were closed according to surgical standards. Duration During admission. Concurrent medication/care: Not reported. Indirectness: No indirectness Further details: 1. Types of endotherapy: Not applicable 2. Types of surgery: Not stated / Unclear (n=30) Intervention 2: Endoscopic treatment. Patients were fixed in the prone position with a slight bending forward. The lower margin of the 12th rib was marked on both sides of the body. After the superficial anaesthesia with 1% lignocaine, the 20-G needle pierced into the point located 5-7 cm laterally from the midline on both sides just under the lower margin of the 12th rib, at the angle of 30-45 towards the trunk of L1 and TH12 vertebrae or the space between L1 and TH12 vertebrae. The canal of the needle was then additionally anesthetised with further 6-10 ml of 1% lignocaine. The needle was pierced into until the resistance of bone was met.. Duration During admission. Concurrent medication/care: Not reported. Indirectness: No indirectness Further details: 1. Types of endotherapy: Not stated / Unclear 2. Types of surgery: Not stated / Unclear
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: VSPL versus NCPB

Protocol outcome 1: Pain (duration of pain, reduction in pain, medication reduction)
- Actual outcome for Adults over 16: Pain (Use of opioids) at Unclear; Group 1: 11/18, Group 2: 17/30
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life ; Mortality ; Complications at 1 year or under; Pain (duration of pain, reduction in pain, medication reduction) ; Length of stay (in critical care or hospital) at 1 year or under; Repeated procedures ; Pancreatic function (endocrine and exocrine)

H.17 Management of pseudocysts

Study	**Akshintala 2014[20]**
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=81)
Countries and setting	Conducted in USA; Setting: academic centre
Line of therapy	1st line
Duration of study	Intervention + follow up: 19 year
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults over 16
Subgroup analysis within study	Not applicable
Inclusion criteria	Adult patients with symptomatic pseudocysts within <1 cm of the gastric or duodenal wall who underwent ED (endoscopic drainage) or PD (percutaneous drainage). Only those pseudocysts within 1cm of the gastric or duodenal wall were included in this study because these would allow for either percutaneous drainage or endoscopic drainage.
Exclusion criteria	Patients were excluded if they had acute fluid collections or walled-off pancreatic necrosis (WOPN) as determined by a history of acute necrotising pancreatitis, with a CT scan of the abdomen demonstrating necrosis of >30% of the pancreas, with anassociated post-necrotic peripancreatic fluid collection. Pseudocysts that could be drained by only one approach were excluded. Patients with cystic neoplasms as diagnosed by fine-needle aspiration cytology or subsequent surgical resection histopathology were also excluded.
Recruitment/selection of patients	Patients who underwent endoscopic or percutaneous drainage for symptomatic pseudocysts between January 1993 and December 2011 were identified from an institutional claims database.
Age, gender and ethnicity	Age - Mean (SD): ED- 47.1 (14.9); PD- 52.7 (12.68). Gender (M:F): Male: ED- 28 (68.3%); 26 (65%) . Ethnicity:
Further population details	1. Presence of pain: 2. Type of pancreatitis:

Extra comments	. A total of 32 patients (78%) in the endoscopic drainage group and 38 patients (95%) in the percutaneous drainage group underwent their index procedures as inpatients. However, all patients undergoing endoscopic drainage or percutaneous drainage as outpatients were subsequently admitted after their index procedures. Pseudocysts, n(%): single: ED 31 (75.6%); 22 (55%);multiple- 10 (24.4%); 18 (45%)
Indirectness of population	--
Interventions	(n=41) Intervention 1: Endoscopic drainage. Endoscopic drainage was performed by using monitored sedation after appropriate antibiotic prophylaxis. The conventional transmural approach by using a duodenoscope or therapeutic upper GI endoscope was performed only if a visible gastric or duodenal bulge from a pseudocyst was appreciated by the endopscopist. The transmural drainage approach of using EUS guidance, was performed by using linear array echo endoscopes.. Duration during admission. Concurrent medication/care: not stated . Indirectness: No indirectness Further details: 1. Type of stent: 2. Type of surgery: Comments: 909 days follow-up (n=40) Intervention 2: Percutaneous drainage . Percutaneous drainage was performed under CT guidance and/or US and fluoroscopic guidance. The pseudocyst was identified, and a suitable route for catheter drainage was chosen. Using a real-time imaging guidance,a site for needle insertion was chosen that would avoid the spleen, interposed bowel, and blood vessels. The site was marked on the skin. The skin and subcutaneous tissue were anaesthetised with a subcutaneous injection of 1% lidocaine solution. The pseudocyst was first punctured under CT/US guidance with an 18guage single-wall needle and a small aliquot of fluid was obtained for Gram stain, culture, and fluid amylase levels.. Duration during admission. Concurrent medication/care: not stated . Indirectness: No indirectness Further details: 1. Type of stent: 2. Type of surgery: Comments: 671 days follow-up
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ENDOSCOPIC DRAINAGE versus PERCUTANEOUS DRAINAGE

Protocol outcome 1: Mortality at 1 year or under
- Actual outcome: Mortality at end of follow-up ; Group 1: 0/41, Group 2: 0/40
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Complications
- Actual outcome: Procedural adverse events at end of follow-up ; Group 1: 6/41, Group 2: 6/40

Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Length of stay (in critical care or hospital) at 1 year or under - Actual outcome: length of stay in hospital at end of follow-up ; Group 1: mean 6.5 (SD 6.7); n=41, Group 2: mean 14.8 (SD 14.4); n=40 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Repeated procedures - Actual outcome: Re-intervention at end of follow-up ; Group 1: 4/41, Group 2: 17/40 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Resolution of presenting symptoms (e.g. Pain, nutritional status, gastric outlet obstruction) ; Resolution or recurrence of pseudocysts ; Length of stay (in critical care or hospital) at 1 year or under

Study	**Andersson 2006[40]**
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=44)
Countries and setting	Conducted in Sweden; Setting: Hospital
Line of therapy	1st line
Duration of study	Intervention + follow up: 10 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults over 16
Subgroup analysis within study	Not applicable:
Inclusion criteria	Patients >15 years of age with pancreatic pseudocysts.
Exclusion criteria	Patients primarily treated at another hospital were excluded.
Recruitment/selection of patients	All patients >15 years of age admitted to the department of surgery, University Hospital of Lund, Sweden, between January 1994 and December 2003 were identified from the hospital records, aided by a computer search.

Age, gender and ethnicity	Age - Mean (SD): 55 (14). Gender (M:F): Male- 29 (66%). Ethnicity:
Further population details	1. Presence of pain: Not stated / Unclear 2. Type of pancreatitis: Acute pancreatitis (77% acute; 23% chronic).
Extra comments	34 patients had acute pancreatitis and 10 chronic pancreatitis. Ultrasonography was performed in 93% and CT examination in 91% of patients.
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Percutaneous drainage . Percutaneous puncture and drainage procedures were performed under US or CT guidance.. Duration during admission. Concurrent medication/care: not stated Further details: 1. Type of stent: 2. Type of surgery: (n=21) Intervention 2: Standard treatment. conservative treatment. Duration during admission. Concurrent medication/care: not stated . Indirectness: No indirectness Further details: 1. Type of stent: 2. Type of surgery: (n=3) Intervention 3: Open Surgery - Drainage or resection. surgery (e.g. internal drainage with cystogastrostomy or external drainage). No further details. . Duration during admission . Concurrent medication/care: not stated . Indirectness: No indirectness Further details: 1. Type of stent: 2. Type of surgery:
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PERCUTANEOUS DRAINAGE versus STANDARD TREATMENT

Protocol outcome 1: Complications
- Actual outcome: complications at 10 years; Group 1: 4/20, Group 2: 0/21
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Resolution or recurrence of pseudocysts
- Actual outcome: recurrences at 10 years; Group 1: 14/20, Group 2: 11/21
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PERCUTANEOUS DRAINAGE versus DRAINAGE OR RESECTION

	Protocol outcome 1: Resolution or recurrence of pseudocysts - Actual outcome: recurrences at 10 years; Group 1: 15/20, Group 2: 1/3 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DRAINAGE OR RESECTION versus STANDARD TREATMENT Protocol outcome 1: Complications - Actual outcome: Length of hospital stay at 10 years; Mean; Interventional treatment: 14 (2-60) days; conservative treatment: 10 (0-141) days; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Resolution or recurrence of pseudocysts - Actual outcome: recurrences at 10 years; Group 1: 1/3, Group 2: 11/21 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
Protocol outcomes not reported by the study	Quality of life ; Mortality at 1 year or under; Resolution of presenting symptoms (e.g. Pain, nutritional status, gastric outlet obstruction) ; Length of stay (in critical care or hospital) at 1 year or under; Length of stay (in critical care or hospital) at 1 year or under; Repeated procedures

Study	**Bhasin 2011[129]**
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=11)
Countries and setting	Conducted in India; Setting: Not reported.
Line of therapy	1st line
Duration of study	Intervention time: 8 weeks
Method of assessment of guideline condition	Unclear method of assessment/diagnosis
Stratum	Adults over 16:
Subgroup analysis within study	Not applicable:

Inclusion criteria	Patients with symptomatic large (>6cm) pseudocysts of pancreas located at tail region of pancreas.
Exclusion criteria	Patients with pancreatic mass, pregancy, age less than 18 years, presence of chronic cardiac, renal or pulmonary failure, or patients not giving informed consent were excluded.
Recruitment/selection of patients	Not reported.
Age, gender and ethnicity	Age - Mean (SD): 41+/- 9 years. Gender (M:F): 9/2. Ethnicity: Not reported
Further population details	1. Presence of pain: Not stated / Unclear 2. Type of pancreatitis: Not stated / Unclear
Extra comments	. Patients were told the pros and cons of both methods and the stent or NPD was placed as per the patients' choice.
Indirectness of population	No indirectness
Interventions	(n=5) Intervention 1: Endoscopic drainage. Endoscopic transpapillary nasopancreatic drainage. All patients were symptomatic, had pseudocysts of the pancreas at tail end of pancreas and all had documented persistence of pseudocysts for 6 weeks or more. Initially, an attempt was made for contrast-free pancreatic duct cannulation and if that was not possible, minimal contrast was injected. Once cannulated, minimal contrast was injected to confirm pancreatic duct (PD) disruption, defined by free extravasation of contrast outside the pancreatic ductal system as seen on fluoroscopy. PD disruption was defined as complete when the main duct upstream to the disruption was not opacified and as partial when the main duct was visualised upstream from the site of disruption. After confirming the ductal disruption, a 5-Fr NPD was placed across the papilla in to the PD by advancing it over a 0.025 or 0.035 in. hydrophilic guide wire. An attempt was made to place the NPD across the area of the disruption and if that was not possible, it was placed as close as possible to the disruption. . Duration 6 weeks. Concurrent medication/care: Intravenous ciproflaxin was administered for antibiotic prophylaxis. Further details: 1. Type of stent: 2. Type of surgery: (n=6) Intervention 2: Pancreatic endoscopic stent. Endoscopic retrograde cholangiopancreatography (ERCP), using a standard technique using a TJF 145 or TJF 160 side-viewing duodenoscope under conscious sedation by intravenous midazolam and hyoscine butylbromide to inhibit duodenal contractions. Initially, an attempt was made for contrast-free pancreatic duct cannulation and if that was not possible, minimal contrast was injected. Once cannulated, minimal contrast was injected to confirm pancreatic duct (PD) disruption, defined by free extravasation of contrast outside the pancreatic ductal system as seen on fluoroscopy. PD disruption was defined as complete when the main duct upstream to the disruption was not opacified and as partial when the main duct was visualised upstream from the site of disruption. After confirming the ductal disruption, a 5-Fr stent was placed across the papilla in to the PD by advancing it over a 0.025 or 0.035 in. hydrophilic guide wire. . Duration After the procedure all cases were admitted and kept under observation for 48 to 72 hours. Concurrent medication/care: Intravenous ciprofloxacin was administered for antibiotic prophylaxis Indirectness: No indirectness

	Further details: 1. Type of stent: 2. Type of surgery:
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ENDOSCOPIC TRANSPAILLARY NASOPANCREATIC DRAINAGE versus PANCREATIC ENDOSCOPIC STENT

Protocol outcome 1: Complications
- Actual outcome: Significant complications at 3-10 days (after insertion of stent); Group 1: 0/4, Group 2: 4/6
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: It should be noted that the patients who developed complications in the ERP arm are also included in the resolution of pseudocysts; Baseline details: No significant difference in the size of the pseudocysts between the two groups. ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Resolution or recurrence of pseudocysts
- Actual outcome: Resolution of pseudocysts at 4-8 weeks; Group 1: 4/4, Group 2: 2/6; Comments: One patient in the NPD group is not included as deep cannulation could not be achieved.
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: No significant difference in the size of the pseudocysts between the two groups. ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome: Recurrence of pseudocysts at 16.4+/-11.4 months; Group 1: 0/4, Group 2: 0/2
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: The ERP group required additional percutaneous drainage and antibiotics for successful outcomes therefore only one patient is included for this arm. ; Baseline details: No significant difference in the size of the pseudocysts between the two groups. ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life ; Mortality at 1 year or under; Resolution of presenting symptoms (e.g. Pain, nutritional status, gastric outlet obstruction) ; Length of stay (in critical care or hospital) at 1 year or under; Length of stay (in critical care or hospital) at 1 year or under; Repeated procedures

Study	**Davila-cervantes 2004[269]**
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=16)

Countries and setting	Conducted in Mexico; Setting: Hospital
Line of therapy	1st line
Duration of study	Other: Retrospective collection of data from between March 1996 and November 2003. Median follow up 22 months (range 1-72 months)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: All cases originated in a well-documented episode of acute pancreatitis. Diagnosis of pancreatic pseudocysts was confirmed by ultrasonography and CT scan.
Stratum	Overall:
Subgroup analysis within study	Not applicable:
Inclusion criteria	Patients presented with mature pseudocysts developed after a documented episode of acute pancreatitis.
Exclusion criteria	NR
Recruitment/selection of patients	10 patients undergoing laproscopic surgical management at one institution from March 1996 to November 2003, compared to 6 patients who underwent conventional open drainage at the same institution during the same time period.
Age, gender and ethnicity	Age - Mean (range): Laparoscopic 42 (17-68) years; open surgery 36 (18-54) years. Gender (M:F): 11/5. Ethnicity: NR
Further population details	1. Presence of pain: Not stated / Unclear (Indication for drainage was abdominal pain in 7/16 people). 2. Type of pancreatitis: Acute pancreatitis
Extra comments	None of the patients had evidence of chronic alcoholic pancreatitis. Etiology of pancreatitis was alcoholic in 8 people, biliary in 5, toxic in 2 and associated with systemic lupus erythematous in 1. Indications for drainage were abdominal pain in 7 people, abdominal mass unresponsive to conservative management in 7 people and food intolerance in 2 people.. 3 patients in the laproscopic group and all patients in the open surgery group had previous abdominal operations (appendectomy, cesarean section, cholecystectomy, pancreatic necrosectomy)
Indirectness of population	No indirectness
Interventions	(n=10) Intervention 1: Laparscopic drainage - Laparoscopic drainage. Type of drainage chosen according to the size and location of the pseudocyst (4 people had Roux-en-Y cystojejunostomy, 4 had extraluminal cystogastrostomy and 2 had intraluminal cystogastrostomy). Closed drains used in all cases.. Duration N/A. Concurrent medication/care: All procedures performed under general anaesthesia. In 6 patients, intraoperative ultrasound was used at the beginning of the procedure to confirm the position of the pseudocyst and after drainage to rule out non-communicated persistent collections. Diet initiated 48 hours after surgery.. Indirectness: No indirectness Further details: 1. Type of stent: Not applicable 2. Type of surgery: Not applicable

	(n=6) Intervention 2: Open Surgery - Drainage or resection. Conventional open drainage (3 people had cystojejunostomy and 3 had cystogastrostomy). Duration N/A. Concurrent medication/care: NR. Indirectness: No indirectness Further details: 1. Type of stent: Not applicable 2. Type of surgery: Not applicable
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LAPAROSCOPIC DRAINAGE versus DRAINAGE OR RESECTION

Protocol outcome 1: Mortality at 1 year or under
- Actual outcome for Adults over 16: All-cause mortality at median 22 months (range 1-72); Group 1: 1/10, Group 2: 0/6
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Complications
- Actual outcome for Adults over 16: Upper gastrointestinal bleeding at NR; Group 1: 1/10, Group 2: 0/6
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults over 16: Post-operative abscess at NR; Group 1: 1/10, Group 2: 0/6
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults over 16: Small bowel obstruction secondary to an internal hernia (requiring reoperation) at NR; Group 1: 0/10, Group 2: 1/6
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults over 16: Pneumonia at NR; Group 1: 0/10, Group 2: 1/6
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults over 16: Overall complications at NR; Group 1: 2/10, Group 2: 2/6
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Resolution of presenting symptoms (e.g. Pain, nutritional status, gastric outlet obstruction)
- Actual outcome for Adults over 16: Asymptomatic with no evidence of recurrent disease by CT scan at median 22 months; Group 1: 10/10, Group 2: 6/6
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Resolution or recurrence of pseudocysts - Actual outcome for Adults over 16: Presented with residual pseudocyst at NR; Group 1: 1/10, Group 2: 1/6 Risk of bias: All domain - ; Indirectness of outcome: No indirectness Protocol outcome 5: Length of stay (in CCU or hospital) at 1 year or under - Actual outcome for Adults over 16: Length of hospital stay (reported as median, range) at NR; Median (range): laproscopic: 7 (4-15); open surgery: 14 (8-21) days); Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Length of stay (in CCU or hospital) at 1 year or under; Repeated procedures

Study	**Heider 1999[451]**
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=173)
Countries and setting	Conducted in USA; Setting: Hospital
Line of therapy	Not applicable
Duration of study	Other: Retrospective collection of data from between December 1984 and May 1995
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Well-documented pancreatic pseudocyst
Stratum	Adults over 16:
Subgroup analysis within study	Not applicable
Inclusion criteria	Well-documented pancreatic pseudocyst (definition of pancreatic pseudocyst by the Atlantic International Symposium applied retrospectively to CT and US reports for a uniform definition)
Exclusion criteria	Transfer from other hospitals with insufficient information, incomplete data, or a misdiagnosis of pancreatic pseudocyst.
Recruitment/selection of patients	Computerised index search of the University of North Carolina Hospitals medical records from December 1984 to May 1995 using the key word pseudocyst
Age, gender and ethnicity	Age - Mean (SD): 45 ± 1 years. Gender (M:F): 112/61. Ethnicity: NR
Further population details	1. Presence of pain: Not stated / Unclear (71% presented with abdominal pain). 2. Type of pancreatitis: Not stated / Unclear (27% had documented chronic pancreatitis).

Extra comments	27% had documented chronic pancreatitis. Etiology was alcohol in 61%, gallstones in 10%, and miscellaneous causes in 29%.
Indirectness of population	No indirectness
Interventions	(n=66) Intervention 1: Percutaneous drainage . Defined as non-operative, US- or CT- guided percutaneous placement of a catheter for pseudocyst drainage. Duration N/A. Concurrent medication/care: NR. Indirectness: No indirectness Further details: 1. Type of stent: Not applicable 2. Type of surgery: Not applicable (n=66) Intervention 2: Open Surgery - Drainage or resection. Surgical treatment included internal or external drainage, longitudinal pancreaticojejunostomy, or distal pancreatectomy. Duration N/A. Concurrent medication/care: NR. Indirectness: No indirectness Further details: 1. Type of stent: Not applicable 2. Type of surgery: Not applicable (n=41) Intervention 3: Standard treatment. Observation (defined by lack of intervention other than fluid management and pain control). Duration N/A. Concurrent medication/care: NR. Indirectness: No indirectness Further details: 1. Type of stent: Not applicable 2. Type of surgery: Not applicable
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PERCUTANEOUS DRAINAGE versus DRAINAGE OR RESECTION

Protocol outcome 1: Mortality at 1 year or under
- Actual outcome for Adults over 16: Mortality at NR; Group 1: 6/66, Group 2: 0/66
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Complications
- Actual outcome for Adults over 16: Bleeding at NR; Group 1: 6/66, Group 2: 3/66
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults over 16: Infection at NR; Group 1: 30/66, Group 2: 10/66
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults over 16: Fistula at NR; Group 1: 5/66, Group 2: 4/66
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;

Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults over 16: Number of people without late sequelae (after hospital discharge; defined as recurrent cyst, recurrent pancreatitis, fistula, infection) at After hosptial discharge; Group 1: 33/66, Group 2: 45/66
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Resolution or recurrence of pseudocysts
- Actual outcome for Adults over 16: Failure (defined as radiographic persistence of a symptomatic pseudocyst in the observed group and a persistent symptomatic pseudocyst requiring a further procedure in the intervention groups) at NR; Group 1: 38/66, Group 2: 8/66
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Length of stay (in CCU or hospital) at 1 year or under
- Actual outcome for Adults over 16: Length of hospital stay at NR; Group 1: mean 45 days (SD 5); n=66, Group 2: mean 18 days (SD 2); n=66
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PERCUTANEOUS DRAINAGE versus STANDARD TREATMENT

Protocol outcome 1: Mortality at 1 year or under
- Actual outcome for Adults over 16: Mortality at NR; Group 1: 6/66, Group 2: 0/41
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Complications
- Actual outcome for Adults over 16: Bleeding at NR; Group 1: 6/66, Group 2: 1/41
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults over 16: Infection at NR; Group 1: 30/66, Group 2: 3/41
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults over 16: Fistula at NR; Group 1: 5/66, Group 2: 1/41
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults over 16: Number of people without late sequelae (after hospital discharge; defined as recurrent cyst, recurrent pancreatitis, fistula, infection) at After hosptial discharge; Group 1: 33/66, Group 2: 28/41

Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Resolution or recurrence of pseudocysts
- Actual outcome for Adults over 16: Failure (defined as radiographic persistence of a symptomatic pseudocyst in the observed group and a persistent symptomatic pseudocyst requiring a further procedure in the intervention groups) at NR; Group 1: 38/66, Group 2: 3/41
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DRAINAGE OR RESECTION versus STANDARD TREATMENT

Protocol outcome 1: Mortality at 1 year or under
- Actual outcome for Adults over 16: Mortality at NR; Group 1: 0/66, Group 2: 0/41
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Complications
- Actual outcome for Adults over 16: Bleeding at NR; Group 1: 3/66, Group 2: 1/41
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults over 16: Infection at NR; Group 1: 10/66, Group 2: 3/41
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults over 16: Fistula at NR; Group 1: 4/66, Group 2: 1/41
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults over 16: Number of people without late sequelae (after hospital discharge; defined as recurrent cyst, recurrent pancreatitis, fistula, infection) at After hosptial discharge; Group 1: 45/66, Group 2: 28/41
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Resolution or recurrence of pseudocysts
- Actual outcome for Adults over 16: Failure (defined as radiographic persistence of a symptomatic pseudocyst in the observed group and a persistent symptomatic pseudocyst requiring a further procedure in the intervention groups) at NR; Group 1: 8/66, Group 2: 3/41
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life ; Resolution of presenting symptoms (e.g. Pain, nutritional status, gastric outlet obstruction) ; Length of stay (in CCU or hospital) at 1 year or under; Repeated procedures

Study	**Johnson 2009[547]**
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=54)
Countries and setting	Conducted in USA; Setting: Department of General surgery and Gastroenterology, Cleveland Clinic
Line of therapy	Unclear
Duration of study	Not clear:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: CP was diagnosed in the setting of recurrent episodes of documented pancreatitis supplemented by evidence of exocrine and/or endocrine insufficiency when appropriate.
Stratum	Adults over 16
Subgroup analysis within study	Not applicable
Inclusion criteria	Participants included were those who had undergone an intervention for a diagnosed pancreatic pseudocyst.
Exclusion criteria	Not reported
Recruitment/selection of patients	Participants had been treated at the Cleveland Clinic
Age, gender and ethnicity	Age - Mean (SD): Surgery: 49, Endoscopy: 52. Gender (M:F): Not reported. Ethnicity: Not reported
Further population details	1. Presence of pain: Not stated / Unclear 2. Type of pancreatitis: Systematic review: mixed
Extra comments	Surgery: Pseudocyst diameter: 9.1 cm; Aetiology: Alcohol - 8, Biliary - 8, Postoperative - 1, Idiopathic - 11, Other - 2; Multiple pseudocysts - 12 Surgery: Pseudocyst diameter: 9.5 cm; Aetiology: Alcohol - 8, Biliary - 8, Postoperative - 5, Idiopathic - 5, Other - 1; Multiple pseudocysts - 5
Indirectness of population	No indirectness
Interventions	(n=30) Intervention 1: Open Surgery - Drainage or resection. Surgical treatment consisted of pseudocyst drainage and also additional pancreatobiliary procedures in certain cases as deemed necessary by the surgeon at the time of operation. Cholecystectomy was performed when there was a question of gallstones either contributing to, or

	potentially complicating pancreatitis. Longitudinal pancreaticojejunostomy was performed when feasible in the presence of chronic pancreatitis. Splenectomy and gastric drainage procedures were selectively performed by the operating surgeon in the presence of splenic vein thrombosis and gastric outlet obstruction, respectively. . Duration During admission. Concurrent medication/care: Not reported. Indirectness: No indirectness Further details: 1. Type of stent: Not applicable 2. Type of surgery: Different types of surgery (n=24) Intervention 2: Endoscopic drainage. Endoscopic drainage was performed using monitored sedation and consisted of transmural drainage through the gastric wall with or without transpapillary drainage. Transmural drainage was performed if a visible bulge was appreciated by the endoscopist. Using Seldinger technique, the tract was balloon-dilated and stented with either 1 or 2 double pigtail stents at the discretion of the endoscopist. A pancreatic duct sphincterotomy was performed and pancreatic duct stent was placed unless technical reasons prevented access to the pancreatic duct. . Duration During admission. Concurrent medication/care: Not reported. Indirectness: No indirectness Further details: 1. Type of stent: Not applicable 2. Type of surgery: Not applicable
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ENDOSCOPIC DRAINAGE/PANCREATIC ENDOSCOPIC STENT versus SURGERY

Protocol outcome 1: Mortality at 1 year or under
- Actual outcome for Adults over 16: Mortality at Unclear; Group 1: 0/24, Group 2: 0/30
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Complications
- Actual outcome for Adults over 16: Complications at Unclear; Group 1: 5/24, Group 2: 6/30; Comments: Endoscopic: 2 technical failures, 2 episodes of post-procedure heamorrhage and 1 stent malfunction leading to pseudocyst infection; surgery group: 3 incisional hernias, 1 post-op deep vein thrombosis, 1 heamorrhage into a pseudocyst from a splenic artery pseudoaneurysm and 1 pancreatic fistula.
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Resolution or recurrence of pseudocysts
- Actual outcome for Adults over 16: Resolution of pseudocysts at Unclear; Group 1: 21/24, Group 2: 28/30
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life ; Resolution of presenting symptoms (e.g. Pain, nutritional status, gastric outlet obstruction) ; Length of stay (in CCU or hospital) at 1 year or under; Length of stay (in CCU or hospital) at 1 year or under; Repeated procedures

Study	**Melman 2009[734]**
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=83)

Countries and setting	Conducted in USA; Setting: Barnes-Jewish Hospital, Washington University Medical Center
Line of therapy	Unclear
Duration of study	Intervention + follow up: 16 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: The diagnosis of a pancreatic pseudocyst was established by abdominal computed tomography scan, magnetic resonance cholangiopancreatogram, endoscopic ultrasound, or abdominal ultrasound.
Stratum	Adults over 16
Subgroup analysis within study	Not applicable
Inclusion criteria	Data was collected on patients who underwent transgastric pancreatic pseudocyst drainage.
Exclusion criteria	Not reported
Recruitment/selection of patients	Data was collected retrospectively
Age, gender and ethnicity	Age - Mean (SD): Endo: 51.8 (1.9), Lap: 46.5 (3.6), Open: 52 (3.8). Gender (M:F): Unclear. Ethnicity: Not reported
Further population details	1. Presence of pain: Not stated / Unclear 2. Type of pancreatitis: Not stated / Unclear
Extra comments	Gallstone pancreatitis: Endo: 51.7%, Lap: 50%, Open: 59.1%; Pseudocyst size (cm): Endo: 9.1±0.4, Lap: 10.4±0.5, Open: 9.5±0.8
Indirectness of population	No indirectness
Interventions	(n=45) Intervention 1: Endoscopic drainage. Endoscopic cases were managed in a dedicated endoscopy suite with the patient under procedural sedation by an anesthetist. Endoscopic ultrasound was used selectively. All cases were managed using a transmural approach. Endoscopic retrograde cholangiopancreatography was performed before endoscopic pancreatic cystgastrostomy. The pancreatic cystgastrostomy was created by puncturing the cyst through the posterior gastric wall, introducing a guidewire through the needle into the pancreatic cyst, and dilating the tract with a balloon. Double pigtail catheters were exchanged over the wire.. Duration During admission . Concurrent medication/care: Not reported. Indirectness: No indirectness Further details: 1. Type of stent: Not applicable 2. Type of surgery: Not applicable (n=22) Intervention 2: Open Surgery - Drainage or resection. Open cyst gastrostomy usually was achieved through a midline or bilateral subcostal incision. After an exploration through the lesser sac, an anterior gastrotomy was performed at the position overlying the area in which the cyst was adherent to the posterior wall of the stomach. An 8- to 10-cm posterior gastrotomy was extended through the cyst wall, and the pancreatic pseudocyst was aspirated and debrided of its contents. A biopsy of the cyst wall was performed. The cystgastrotomy was performed with a running

	suture between the gastric and cyst walls to complete the anastomosis. The anterior gastrotomy then was closed.. Duration During admission. Concurrent medication/care: Not reported. Indirectness: No indirectness Further details: 1. Type of stent: Not applicable 2. Type of surgery: Different types of surgery (n=16) Intervention 3: Laparscopic drainage - Laparoscopic drainage. The laparoscopic transgastric technique was similar to the open surgery technique, except that the pancreatic cystgastrostomy was accomplished using a linear endoscopic stapler to create the cystenteric anastomosis. . Duration During admission. Concurrent medication/care: Not reported. Indirectness: No indirectness Further details: 1. Type of stent: Not applicable 2. Type of surgery: Not applicable
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ENDOSCOPIC DRAINAGE versus OPEN SURGERY

Protocol outcome 1: Complications
- Actual outcome for Adults over 16: Complications (Grade 2 or greater complications) at 16 months; Group 1: 7/45, Group 2: 5/22
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Resolution of presenting symptoms (e.g. Pain, nutritional status, gastric outlet obstruction)
- Actual outcome for Adults over 16: Resolution (Primary success rate) at 16 months; Group 1: 16/45, Group 2: 18/22
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults over 16: Resolution (Overall success rate) at 16 months; Group 1: 38/45, Group 2: 20/22
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ENDOSCOPIC DRAINAGE versus LAPAROSCOPIC DRAINAGE

Protocol outcome 1: Complications
- Actual outcome for Adults over 16: Complications (Grade 2 or greater complications) at 16 months; Group 1: 7/45, Group 2: 4/16
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Resolution of presenting symptoms (e.g. Pain, nutritional status, gastric outlet obstruction)

- Actual outcome for Adults over 16: Resolution (Primary success rate) at 16 months; Group 1: 16/45, Group 2: 14/16 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults over 16: Resolution (Overall success rate) at 16 months; Group 1: 38/45, Group 2: 15/16 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LAPAROSCOPIC DRAINAGE versus OPEN SURGERY Protocol outcome 1: Complications - Actual outcome for Adults over 16: Complications (Grade 2 or greater complications) at 16 months; Group 1: 4/16, Group 2: 5/22 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Resolution of presenting symptoms (e.g. Pain, nutritional status, gastric outlet obstruction) - Actual outcome for Adults over 16: Resolution (Primary success rate) at 16 months; Group 1: 14/16, Group 2: 18/22 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults over 16: Resolution (Overall success rate) at 16 months; Group 1: 15/16, Group 2: 20/22 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Mortality at 1 year or under; Resolution or recurrence of pseudocysts ; Length of stay (in CCU or hospital) at 1 year or under; Length of stay (in CCU or hospital) at 1 year or under; Repeated procedures

Study	**Morton 2005[761]**
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=14,914)
Countries and setting	
Line of therapy	1st line
Duration of study	Intervention + follow up: 4 years

Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults over 16
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients >17 years of age. Cases were identified byInternational Classification of Diseases, Ninth Revision (ICD-9) diagnosis code for pancreatic pseudocysts (PP), 577.2, and by procedure code 52.01 for percutaneous drainage (PD) and codes 52.4 and 52.96 for surgical drainage (SD)of pseudocysts. No specific ICD-9 code exists for endoscopic drainage.
Exclusion criteria	To ensure homogeneity of the two comparison cohorts, cases with ICD-9 diagnoses codes for gastrointestinal malignancies were excluded . Cases that had procedure codes for both SD and PD were excluded because primary treatment could not be established temporarily.
Recruitment/selection of patients	The period studies was from January 1, 1997 through December 31,2001.
Age, gender and ethnicity	Age - Mean (SD): PD- 53 (16); SD- 51 (15). Gender (M:F): Male- PD- 58%; SD-59%. Ethnicity:
Further population details	1. Presence of pain: Not stated / Unclear 2. Type of pancreatitis: mixed
Extra comments	Surgically treated patients had significantly less frequent diagnoses of acute pancreatitis, both acute and chronic pancreatitis, diabetes, and cirrhosis but had significantly more frequent diagnoses of chronic pancreatitis, biliary tract disorders, and other pancreatic disorders.
Indirectness of population	No indirectness
Interventions	(n=8121) Intervention 1: Percutaneous drainage . no details . Duration during admission. Concurrent medication/care: not stated . Indirectness: No indirectness Further details: 1. Type of stent: 2. Type of surgery: (n=6409) Intervention 2: Open Surgery - Drainage or resection. no details . Duration during admission. Concurrent medication/care: not stated . Indirectness: No indirectness Further details: 1. Type of stent: 2. Type of surgery:
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PERCUTANEOUS DRAINAGE versus SURGICAL DRAINAGE

Protocol outcome 1: Mortality at 1 year or under
- Actual outcome: Mortality at end of follow-up ; Group 1: 479/8121, Group 2: 179/6409
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low,

Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Complications - Actual outcome: complications (Intra-abdominal abcess and bleeding requiring transfusion) at end of follow-up ; Group 1: 1335/8121, Group 2: 864/6409 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Length of stay (in CCU or hospital) at 1 year or under - Actual outcome: Length of stay in hospital at end of follow-up ; Group 1: mean 21 (SD 22); n=8121, Group 2: mean 15 (SD 15); n=6409 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Resolution of presenting symptoms (e.g. Pain, nutritional status, gastric outlet obstruction) ; Resolution or recurrence of pseudocysts ; Length of stay (in CCU or hospital) at 1 year or under; Repeated procedures

Study	**Rasch 2017[900]**
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=129)
Countries and setting	Conducted in Germany; Setting: Tertiary referral centre
Line of therapy	Unclear
Duration of study	Intervention + follow up: Median follow-up 4.7 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: International Classification of Diseases (ICD)-10 code K85 and K86
Stratum	Adults over 16
Subgroup analysis within study	Not applicable

Inclusion criteria	Patients with pancreatic pseudocysts larger than 10 mm who presented more than one time
Exclusion criteria	Patients with cysts suspicious of dysplasia or walled of necrosis
Recruitment/selection of patients	Consecutive
Age, gender and ethnicity	Age - Mean (SD): 52 (14.9). Gender (M:F): 1:2. Ethnicity: Not stated
Further population details	1. Presence of pain: People presenting with pain (Majority (63.6%) presented with abdominal pain). 2. Type of pancreatitis: Chronic pancreatitis (Majority (65.1%) chronic; 14.7% acute; 16.3% idiopathic; 3.9% iatrogenic or trauma).
Extra comments	17.8% had pancreatic duct obstruction and 13.2% had bile duct obstruction.
Indirectness of population	No indirectness
Interventions	(n=44) Intervention 1: Standard treatment. Unclear. Duration Unclear. Concurrent medication/care: Not stated. Indirectness: No indirectness Further details: 1. Type of stent: Not applicable 2. Type of surgery: Not applicable (n=41) Intervention 2: Endoscopic drainage - EUS-guided. All endoscopic drainage procedures were performed under endosonographic guidance by a linear scanner. Duration Unclear. Concurrent medication/care: Not stated. Indirectness: No indirectness Further details: 1. Type of stent: Not applicable 2. Type of surgery: Not applicable (n=8) Intervention 3: Percutaneous drainage . Pig tail catheters were placed by Seldinger's technique under sonographic or computertomographic guidance. Duration Unclear. Concurrent medication/care: Not stated. Indirectness: No indirectness Further details: 1. Type of stent: Not applicable 2. Type of surgery: Not applicable (n=21) Intervention 4: Open Surgery - Drainage or resection. A gastro- or duodenocystostomy was carried out with a cystostome, fluid specimen were obtained by aspiration and 1–3 double pig tails were placed via a guide wire. All surgical drainage procedures were cystojejunostomies with a Roux-en-Y reconstruction.. Duration Unclear. Concurrent medication/care: Not stated. Indirectness: No indirectness Further details: 1. Type of stent: Not applicable 2. Type of surgery: Different types of surgery (Drainage or resection).

Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EUS-GUIDED versus STANDARD TREATMENT

Protocol outcome 1: Complications
- Actual outcome for Adults over 16: Complications at Unclear; Group 1: 9/41, Group 2: 0/44
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Resolution of presenting symptoms (e.g. Pain, nutritional status, gastric outlet obstruction)
- Actual outcome for Adults over 16: Improvement of symptoms at Unclear; Group 1: 32/41, Group 2: 24/44
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Repeated procedures
- Actual outcome for Adults over 16: Re-intervention at Unclear; Group 1: 9/41, Group 2: 0/44
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EUS-GUIDED versus PERCUTANEOUS DRAINAGE

Protocol outcome 1: Complications
- Actual outcome for Adults over 16: Complications at Unclear; Group 1: 9/41, Group 2: 1/8
Risk of bias: All domain - ; Indirectness of outcome: No indirectness

Protocol outcome 2: Resolution of presenting symptoms (e.g. Pain, nutritional status, gastric outlet obstruction)
- Actual outcome for Adults over 16: Improvement of symptoms at Unclear; Group 1: 32/41, Group 2: 7/8
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Repeated procedures
- Actual outcome for Adults over 16: Re-intervention at Unclear; Group 1: 9/41, Group 2: 4/8

Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EUS-GUIDED versus DRAINAGE OR RESECTION

Protocol outcome 1: Complications
- Actual outcome for Adults over 16: Complications at Unclear; Group 1: 9/41, Group 2: 6/21; Comments: Most commonly stent occlusion or haemorrhage in endoscopic and infection in surgical
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Resolution of presenting symptoms (e.g. Pain, nutritional status, gastric outlet obstruction)
- Actual outcome for Adults over 16: Improvement of symptoms at Unclear; Group 1: 32/41, Group 2: 17/21
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Repeated procedures
- Actual outcome for Adults over 16: Re-intervention at Unclear; Group 1: 9/41, Group 2: 0/21
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PERCUTANEOUS DRAINAGE versus STANDARD TREATMENT

Protocol outcome 1: Complications
- Actual outcome for Adults over 16: Complications at Unclear; Group 1: 1/8, Group 2: 0/44; Comments: 1 haemorrhage
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Resolution of presenting symptoms (e.g. Pain, nutritional status, gastric outlet obstruction)
- Actual outcome for Adults over 16: Improvement of symptoms at Unclear; Group 1: 7/8, Group 2: 25/44
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Repeated procedures
- Actual outcome for Adults over 16: Re-intervention at Unclear; Group 1: 4/8, Group 2: 0/44
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;

Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PERCUTANEOUS DRAINAGE versus DRAINAGE OR RESECTION

Protocol outcome 1: Complications
- Actual outcome for Adults over 16: Complications at Unclear; Group 1: 1/8, Group 2: 6/21
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Resolution of presenting symptoms (e.g. Pain, nutritional status, gastric outlet obstruction)
- Actual outcome for Adults over 16: Improvement of symptoms at Unclear; Group 1: 7/8, Group 2: 17/21
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Repeated procedures
- Actual outcome for Adults over 16: Re-intervention at Unclear; Group 1: 4/8, Group 2: 0/21
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DRAINAGE OR RESECTION versus STANDARD TREATMENT

Protocol outcome 1: Mortality at 1 year or under
- Actual outcome for Adults over 16: Mortality at Unclear; ;
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Complications
- Actual outcome for Adults over 16: Complications at Unclear; Group 1: 6/21, Group 2: 0/44; Comments: 6 infections with resection
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Resolution of presenting symptoms (e.g. Pain, nutritional status, gastric outlet obstruction)
- Actual outcome for Adults over 16: Improvement of symptoms at Unclear; Group 1: 17/21, Group 2: 25/44
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Repeated procedures - Actual outcome for Adults over 16: Re-intervention at Unclear; Group 1: 0/21, Group 2: 0/44 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults over 16: Length of hospital stay (days) at Unclear; ; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Resolution or recurrence of pseudocysts ; Length of stay (in CCU or hospital) at 1 year or under; Length of stay (in CCU or hospital) at 1 year or under

Study	**Saul 2016[954]**
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=61)
Countries and setting	Conducted in Mexico; Setting: Hospital
Line of therapy	1st line
Duration of study	Other: Retrospective analysis of data obtained between the years 2000 to 2012.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Pancreatic pseudocyst defined as a fluid collection in the pancreatic or peripancreatic area that had a well-defined wall and contained no solid debris or recognisable parachymal necrosis.
Stratum	Overall:
Subgroup analysis within study	Not applicable
Inclusion criteria	People with pancreatic pseudocysts treated with endoscopic or surgical treatment
Exclusion criteria	People treated outside the hospital
Recruitment/selection of patients	Retrospective analysis of paper and electronic records of people with pancreatic pseudocysts treated with endoscopic or surgical treatment from 2000 to 2012.
Age, gender and ethnicity	Age - Mean (SD): 41.5 (13.8) years. Gender (M:F): 39/22 . Ethnicity:

Further population details	1. Presence of pain: Not stated / Unclear 2. Type of pancreatitis: Not stated / Unclear
Extra comments	Cause of pancreatitis was gallstones in 25, alcoholic in 9, hypertriglyceridemia in 3, idiopathic in 9 and unspecified in 18.
Indirectness of population	No indirectness
Interventions	(n=21) Intervention 1: Endoscopic drainage. Intubated and received 1g I.V. of ceftazidime 30 minutes before the procedure. A convex linear-array echoendoscope was used, and once the pseudocysts was identified, it was accessed using a 19-gauge needle, and a 0.035-inch guidewire was inserted through the needle into the pseudocysts with fluoroscopic guidance. After removal of the needles, a needle knife was inserted over the guidewire to create a bigger fistula. The gastric wall was dilated up to 15mm using a wire-guided balloon and two double pigtail plastic stents (7F and 4cm) were deployed for drainage. Transgastric in 16/21 and transduodenal in 5/21.. Duration Procedure length not reported but 8 weeks after the drainage an ERP or MRCP was performed.. Concurrent medication/care: Not reported.. Indirectness: Serious indirectness; Indirectness comment: Number in each group not by patient but by case (n=61 but number of procedures was 64) Further details: 1. Type of stent: Different types of stent (pigtail plastic stents). 2. Type of surgery: Not applicable (n=43) Intervention 2: Combination of techniques. Open and laparoscopic approaches: open drainage, cystogastrostomy, cystojejunostomy, distal pancreatectomy, PPC resection and pancreato-jejunostomy. In those patients with an open drainage due to inflammation, a second surgery (distal pancreatectomy or PPC resection) was performed months later. They were considered as different procedures and they were analysed separately. . Duration Not reported. . Concurrent medication/care: Not reported.. Indirectness: Serious indirectness; Indirectness comment: Number in each group not by patient but by case (n=61 but number of procedures was 64) Further details: 1. Type of stent: Not applicable 2. Type of surgery: Different types of surgery (Open and laproscopic approaches. Open drainage 13, cystogastrostomy 10, cystojejunostomy 8, distal pancreatectomy 6, PPC resection 5 and pancreato-jejunostomy 1).
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ENDOSCOPIC DRAINAGE versus COMBINATION OF TECHNIQUES

Protocol outcome 1: Mortality at 1 year or under
- Actual outcome for Adults over 16: Mortality at Median (IQR) follow-up: endoscopic 270 (30-1915); combination 580 (0-4320) days; Group 1: 0/21, Group 2: 1/43; Comments: 1 death due to sepsis
Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Complications - Actual outcome for Adults over 16: Overall complications (included bleeding, infection, stent migration) at Median (IQR) follow-up: endoscopic 270 (30-1915); combination 580 (0-4320) days; Group 1: 5/21, Group 2: 11/43 Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Resolution or recurrence of pseudocysts - Actual outcome for Adults over 16: Clinical success (complete resolution or decrease in the size of pseudocysts to 2cm or smaller on CT with associated resolution of symptoms). at 8 weeks; Group 1: 19/21, Group 2: 39/43 Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults over 16: Recurrence (pancreatic pseudocyst found on CT in association with symptoms after initial resolution) at Median (IQR) follow-up: endoscopic 270 (30-1915); combination 580 (0-4320) days; Group 1: 2/21, Group 2: 2/43 Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Length of stay (in CCU or hospital) at 1 year or under - Actual outcome for Adults over 16: Hospital length of stay (median, range) at Median (IQR) follow-up: endoscopic 270 (30-1915); combination 580 (0-4320) days; Median (range): Endoscopic 0 (0-10); Combination 7 (2-42) days); Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults over 16: CCU stay at Median (IQR) follow-up: endoscopic 270 (30-1915); combination 580 (0-4320) days; Group 1: mean 0.19 days (SD 0.13); n=21, Group 2: mean 1.4 days (SD 0.72); n=43 Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Resolution of presenting symptoms (e.g. Pain, nutritional status, gastric outlet obstruction) ; Length of stay (in CCU or hospital) at 1 year or under; Repeated procedures

Study	Talar-wojnarowska 2010[1055]
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=21)
Countries and setting	Conducted in Poland; Setting: Department of Digestive Tract Diseases of Lodz Medical University
Line of therapy	Unclear
Duration of study	Intervention + follow up: 5 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: The diagnosis of chronic pancreatitis was based on the presence of pancreatic calcifications on CT scan, ultrasound or endoscopic ultrasound or historic confirmation after previous chronic pancreatitis surgical treatment.
Stratum	Adults over 16
Subgroup analysis within study	Not applicable
Inclusion criteria	All people admitted with chronic pancreatitis and pancreatic pseudocysts
Exclusion criteria	Patients with an episode of acute pancreatitis in the preceding 6 weeks.
Recruitment/selection of patients	Participants were treated at the center
Age, gender and ethnicity	Age -47.2 (7.3) years. Gender (M:F): 23:14. Ethnicity: not stated
Further population details	1. Presence of pain: Not stated / Unclear 2. Type of pancreatitis: Chronic pancreatitis
Indirectness of population	No indirectness
Interventions	(n=10) Intervention 1: Endoscopic drainage. No details given. Duration During admission. Concurrent medication/care: Not reported. Indirectness: No indirectness Further details: 1. Type of stent: Not applicable 2. Type of surgery: Not applicable (n=4) Intervention 2: Percutaneous drainage . No details given. Duration During admission. Concurrent medication/care: Not reported. Indirectness: No indirectness Further details: 1. Type of stent: Not applicable 2. Type of surgery: Not applicable (n=7) Intervention 3: Open Surgery - Drainage or resection. No details given. Duration During admission. Concurrent medication/care: Not reported. Indirectness: No indirectness Further details: 1. Type of stent: Not applicable 2. Type of surgery: Different types of surgery

Funding	Academic or government funding (Study supported by Lodz Medical University grant 502-11-718)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ENDOSCOPIC DRAINAGE versus DRAINAGE OR RESECTION

Protocol outcome 1: Complications
- Actual outcome for Adults over 16: Complications at Unclear; Group 1: 1/10, Group 2: 2/7
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Resolution or recurrence of pseudocysts
- Actual outcome for Adults over 16: Recurrence of pseudocysts at 26 months; Group 1: 4/10, Group 2: 1/7
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Length of stay (in CCU or hospital) at 1 year or under
- Actual outcome for Adults over 16: Length of stay in hospital at Unclear; Group 1: mean 7.2 days (SD 3.2); n=10, Group 2: mean 15.4 days (SD 5.7); n=7
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PERCUTANEOUS DRAINAGE versus ENDOSCOPIC DRAINAGE

Protocol outcome 1: Complications
- Actual outcome for Adults over 16: Complications at Unclear; Group 1: 2/4, Group 2: 1/10
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Resolution or recurrence of pseudocysts
- Actual outcome for Adults over 16: Recurrence of pseudocysts at 26 months; Group 1: 3/4, Group 2: 4/10
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Length of stay (in CCU or hospital) at 1 year or under
- Actual outcome for Adults over 16: Length of stay in hospital at Unclear; Group 1: mean 13.2 days (SD 4.2); n=4, Group 2: mean 7.2 days (SD 3.2); n=10
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;

Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PERCUTANEOUS DRAINAGE versus DRAINAGE OR RESECTION Protocol outcome 1: Complications - Actual outcome for Adults over 16: Complications at Unclear; Group 1: 2/4, Group 2: 2/7 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Resolution or recurrence of pseudocysts - Actual outcome for Adults over 16: Recurrence of pseudocysts at 26 months; Group 1: 3/4, Group 2: 1/7 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Length of stay (in CCU or hospital) at 1 year or under - Actual outcome for Adults over 16: Length of stay in hospital at Unclear; Group 1: mean 13.2 days (SD 4.2); n=4, Group 2: mean 15.4 days (SD 3.2); n=7 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Mortality at 1 year or under; Resolution of presenting symptoms (e.g. Pain, nutritional status, gastric outlet obstruction) ; Length of stay (in CCU or hospital) at 1 year or under; Repeated procedures

Study	**Varadarajulu 2008[1107]**
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=30)
Countries and setting	Conducted in USA; Setting: University of Alabama Hospital
Line of therapy	1st line

Duration of study	Intervention + follow up: 4 weeks
Method of assessment of guideline condition	Method of assessment /diagnosis not stated
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients over 18 years of age who had undergone surgical cyst-gastrostomy and EUS-guided cyst-gastrostomy at the tertiary referral centre were included.
Exclusion criteria	Not reported
Recruitment/selection of patients	Participants had been treated at the hospital
Age, gender and ethnicity	Age - Mean (SD): Surgery: 42.3 EUS: 43.1. Gender (M:F): 21:9. Ethnicity: 73% white
Further population details	1. Presence of pain: Not stated / Unclear 2. Type of pancreatitis: Not stated / Unclear
Extra comments	Surgery - Mean pseudocyst size: 6179 mm^2; Location - Head: 20%, Body: 10%, Tail: 40 %, Multiple: 30%; Aetiology - Idiopathic: 60%, Gallstones: 20%, Alcohol: 20% EUS - Mean pseudocyst size: 7588 mm^2; Location - Head: 10%, Body: 15%, Tail: 50 %, Multiple: 25%; Aetiology - Idiopathic: 60%, Gallstones: 20%, Alcohol: 20%
Indirectness of population	No indirectness
Interventions	(n=10) Intervention 1: Open Surgery - Drainage or resection. Patients were placed in the supine position and intravenous cefaxolin was administered before incision. A limited upper midline incision was made, approximately 10 cm in length at the middle third of the distance from the umbilicus to the xiphoid process, to allow access to the abdomen. Cautery was used to create an approximate 5-cm longitudinal gastrostomy near the greater curvature of the fundus. Cautery was used to incise an approximate 2 cm opening in the posterior gastric wall. The pseudocysts were aspirated and irrigated. . Duration During admission. Concurrent medication/care: Patients were discharged from hospital when a soft diet was tolerated and pain control was adequate. . Indirectness: No indirectness Further details: 1. Type of stent: Not applicable 2. Type of surgery: Not stated / Unclear (n=20) Intervention 2: Combination of techniques. After administration of one dose of IV ciprofloxacin (400 mg), an EUS-guided cyst-gastrostomy was performed at the endoscopy suite, with the patient under conscious sedation with a combination of midazolam, meperidine, and ketamine administered by the endoscopist. A sample of the cysts aspirate was sent for assessment of carcinoembryonic antigen, amylase and lipase levels in all patients. An ERCP was routinely attempted in all patients, unless the extrinsic compression caused by the pseudocyst precluded duodenoscope passage to the second portion of the duodenum. . Duration During admission. Concurrent medication/care: Not reported. Indirectness: No indirectness

	Further details: 1. Type of stent: Not applicable 2. Type of surgery: Not applicable
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ERCP AND ENDOSCOPIC DRAINAGE CYST-GASTROSTOMY versus SURGICAL CYST-GASTROSTOMY Protocol outcome 1: Complications - Actual outcome for Adults over 16: Complications at During admission; Group 1: 0/20, Group 2: 0/10 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Resolution or recurrence of pseudocysts - Actual outcome for Adults over 16: Resolution of pseudocysts (Treatment success) at 4-6 weeks; Group 1: 19/20, Group 2: 10/10 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Length of stay (in CCU or hospital) at 1 year or under - Actual outcome for Adults over 16: Length of post-procedure hospital stay at During admission; Mean; , Comments: Surgery: Median (range): 6.5 (4-20) EUS: 2.6 (1-11); Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Repeated procedures - Actual outcome for Adults over 16: Repeated procedures (Reintervention) at During admission; Group 1: 0/20, Group 2: 1/10 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Mortality at 1 year or under; Resolution of presenting symptoms (e.g. Pain, nutritional status, gastric outlet obstruction) ; Length of stay (in CCU or hospital) at 1 year or under

Study	**Varadarajulu 2013[1106]**
Study type	RCT (Patient randomised; Parallel)

Number of studies (number of participants)	1 (n=40)
Countries and setting	Conducted in USA; Setting: Hospital
Line of therapy	1st line
Duration of study	Follow up (post intervention): 24 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: All patients were evaluated with CT.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Diagnosis of pancreatic pseudocyst based on CT criteria; pseudocyst measuring ≥6 cm in size and located adjacent to the stomach; documented history of acute or chronic pancreatitis; persistent pancreatic pain requiring narcotics or analgesics; symptomatic gastric outlet or bile duct obstruction induced by the pseudocyst.
Exclusion criteria	Age <18 or >80 years; contraindications to surgery: ASA class IV, severe portal hypertension; contraindication to endoscopic drainage: gastrectomy with Billroth II reconstruction, gastric bypass surgery, prior surgery for pancreas-related complications; pregnancy; associated pancreatic necrosis on CT; pseudocyst not adjacent to the stomach; multiloculated pseudocyst or multiple pseudocysts
Recruitment/selection of patients	Consecutive patients with pancreatic pseudocysts from the pancreaticobiliary clinic or inpatient ward service
Age, gender and ethnicity	Age - Mean (SD): Endoscopy: 48 (14); Surgery 51 (17). Gender (M:F): 28/12. Ethnicity: NR
Further population details	1. Presence of pain: People presenting with pain (All had persistent pancreatic pain requiring narcotics or analgesics). 2. Type of pancreatitis: Not stated / Unclear
Extra comments	Cause of pancreatitis: alcohol 15, gallstones 16, idiopathic 5, hypertriglyceridemia 1, post-surgery 1 and post-trauma 2.
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Pancreatic endoscopic stent. Endoscopic cystogastrostomy. Performed with EUS guidance and fluoroscopy by 2 endosonographers while the patient was under conscious sedation after administration of IV ciprofloxacin. Two plastic stents deployed to facilitate the drainage of pseudocyst contents into the stomach. Transmural stents removed at 2 months evaluation if the pseudocyst had resolved on CT scan. If the pseudocyst was persistent, additional drainage performed by placement of more stents. If the patient failed one additional intervention by endoscopy they were converted to surgery. Transpapillary pancreatic duct stents were also placed in patients in whom a duct leak was evident at endoscopic retrograde cholangiopancreatogram (ERCP). At follow up an ERCP was repeated to assess for resolution of duct leak and in patients with an unsuccessful first ERCP, an MRCP was performed and a pancreatic duct stent placed in patients in whom leak was evident. If a disconnected duct was noted, the transgastric stents were left in place to decrease likelihood of pseudocyst recurrence.. Duration 24 months. Concurrent

	medication/care: Oral ciprofloxacin 500 mg twice daily for 3 days.. Indirectness: No indirectness Further details: 1. Type of stent: Different types of stent (plastic transmural stent). 2. Type of surgery: Not applicable (n=20) Intervention 2: Open Surgery - Drainage or resection. Surgical cystogastrostomy. Performed by one pancreatic surgeon. After administration of intravenous cefazolin, an incision was made at the middle-third of the distance from the umbilicus to xiphoid process, to allow access to the abdomen. The anterior stomach was exposed and a 2-cm gastrostomy was created with cautery. This small opening allowed adequate access to the posterior stomach and the cyst was palpated. After localizing the pseudocyst where it was adhered to the posterior wall of the stomach, it was aspirated and entered with cautery. Once entry was obtained, an endovascular stapler was used to create at least a 6-cm cystogastrostomy. A nasogastric tube then was left in the stomach and passed into the pseudocyst cavity to allow for intermittent irrigation until postoperative day 1. The anterior gastrostomy was closed and the patient was transferred to the surgical floor after postoperative monitoring. The nasogastric tube was removed on postoperative day 1 and clear liquids were started on day 2. . Duration 24 months. Concurrent medication/care: NR. Indirectness: No indirectness Further details: 1. Type of stent: Not applicable 2. Type of surgery: Not applicable
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PANCREATIC ENDOSCOPIC STENT versus DRAINAGE OR RESECTION

Protocol outcome 1: Quality of life
- Actual outcome for Adults over 16: SF36 physical component score at 24 months; MD; 4.48 (95%CI 0.73 to 8.23, Comments: 4.48 lower in the surgery group than the endoscopic group);
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults over 16: SF36 mental component score at 24 months; MD; 4.41 (95%CI 0.55 to 8.26, Comments: 4.41 lower in the surgery group);
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Complications
- Actual outcome for Adults over 16: Complications (including wound infection and haematemesis) at 24 months; Group 1: 0/20, Group 2: 2/20
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Resolution or recurrence of pseudocysts
- Actual outcome for Adults over 16: Treatment success (resolution of symptoms at 4 weeks for surgery group; resolution or a decrease in the size of the fluid collection to

	2 cm or smaller on CT with resolution of symptoms at 8 weeks) at 8 and 4 weeks in endoscopic and surgery groups, respectively; Group 1: 19/20, Group 2: 20/20 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults over 16: Recurrence (new onset abdominal pain in the presence of a pancreatic fluid collection on CT after resolution of the initial presentation) at 24 months; Group 1: 0/20, Group 2: 1/20 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Length of stay (in CCU or hospital) at 1 year or under - Actual outcome for Adults over 16: Length of hospital stay at 24 months; (95%CI -5 to -3); Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 5: Repeated procedures - Actual outcome for Adults over 16: Reintervention at 24 months; Group 1: 1/20, Group 2: 1/20 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
Protocol outcomes not reported by the study	Mortality at 1 year or under; Resolution of presenting symptoms (e.g. Pain, nutritional status, gastric outlet obstruction) ; Length of stay (in CCU or hospital) at 1 year or under

H.18 Management of pancreatic ascites and pleural effusion secondary to pancreatitis

None.

H.19 Management of biliary obstruction in people with chronic pancreatitis

Study	**Haapamäki 2017[430]**
Study type	RCT (Patient randomised; Parallel)

Number of studies (number of participants)	1 (n=60)
Countries and setting	Conducted in Finland; Setting: Helsinki University Hospital, Turku University Hospital, Oulu University Hospital
Line of therapy	Unclear
Duration of study	Intervention + follow up: 2 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Indication for initial ERCP was suspected biliary obstruction caused by chronic pancreatitis as judged by elevated bilirubin and/or AFOS values.
Stratum	Adults
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients who were suspected to have biliary obstruction caused by chronic pancreatitis were included.
Exclusion criteria	Patients with malignancies, known liver cirrhosis, acute or chronic hepatitis or abnormal hepatic imaging studies, and patients with their first attack of acute pancreatitis.
Recruitment/selection of patients	Patients who were admitted to hospital for endoscopic retrograde cholangiopancreatography.
Age, gender and ethnicity	Age - Median (range): 53 (33-78). Gender (M:F): 54:6. Ethnicity: Not reported
Further population details	
Extra comments	Plastic group: Etiology - Alcohol: 29/60, Biliary: 0/60, Autoimmune: 0/60, Idiopathic: 1/60 Metal group: Etiology - Alcohol: 26/60, Biliary: 1/60, Autoimmune: 1/60, Idiopathic: 2/60
Indirectness of population	No indirectness
Interventions	(n=30) Intervention 1: Metal stent - Fully covered metal stent. Dilation was performed with an 8-mm balloon

	in both groups. The original plastic stent was replaced with a single covered self-expandable metallic stent (cSEMS). At three months, the position and function of the stent were checked by ERCP. In case of stent migration, the stent was replaced with a new cSEMS. At six months after randomisation, all stents were removed.. Duration 6 months. Concurrent medication/care: All patients were prepared and sedated for ERCP according to the standard medical practice at the hospital. At the initial ERCP, an endoscopic sphincterotomy was performed and one 10-Fr plastic stent was inserted for the treatment of cholestasis. CBD dilation was performed only if deemed necessary. Any existing CBD stones above the stricture were removed. Pancreatic stents were inserted if indicated Further details: 1. Type of stent: Fully covered metal stent 2. Type of stent insertion: Endoscopic insertion 3. Type of surgery: Not applicable (n=30) Intervention 2: Plastic stent - Multiple plastic stents. Dilation was performed with an 8-mm balloon in both groups. The original plastic stent was replaced with three plastic stents. At three months, balloon dilation was performed and the number of plastic stents was increased to a maximum of six 10-Fr stents when possible. At six months after randomisation, all stents were removed.. Duration 6 months. Concurrent medication/care: All patients were prepared and sedated for ERCP according to the standard medical practice at the hospital. At the initial ERCP, an endoscopic sphincterotomy was performed and one 10-Fr plastic stent was inserted for the treatment of cholestasis. CBD dilation was performed only if deemed necessary. any existing CBD stones above the stricture were removed. Pancreatic stents were inserted if indicated Further details: 1. Type of stent: Multiple plastic stent 2. Type of stent insertion: Endoscopic insertion 3. Type of surgery: Not applicable
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: FULLY COVERED METAL STENT versus MULTIPLE PLASTIC STENTS Protocol outcome 1: Mortality at <1 year - Actual outcome for Adults: Mortality at 2 years; Group 1: 3/30, Group 2: 1/30; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 2: Complications (eg bleeding, fistulae) at not defined	

- Actual outcome for Adults: Adverse events at 2 years; Group 1: 8/28, Group 2: 7/30; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 3: Recurrence of biliary obstruction, including failed stent (removal and additional stents) at not defined - Actual outcome for Adults: Stricture resolution (as defined by normal liver function tests) - Bilirubin level (4-20µmol/L) at 2 years; Other: Median (Range); Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome for Adults: Recurrent strictures at 2 years; Group 1: 2/22, Group 2: 3/25; Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome for Adults: Stricture resolution (as defined by normal liver function tests) - Alkaline phosphatise level (35-105 U/L) at 2 years; Other: Median (Range); Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at not defined; Biliary infections at not defined; Number of procedures (repeated procedures) at not defined; Length of stay (in intensive therapy unit or hospital) at not defined

Study	**Regimbeau 2012[906]**
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=39)
Countries and setting	Conducted in France; Setting: Amiens University Hospital, France
Line of therapy	Unclear
Duration of study	Intervention + follow up:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: The diagnosis of CP was based on one or more of the following three criteria: 1) at least moderate duct anomalies according to the Cambridge classification, 2) the presence of pancreatic calcification, or 3) fibrosis in histologic specimens. Stricture was defined as a narrowing of the common bile duct (CBD) with prestenosis dilation or delayed runoff of contrast on imaging using MRI, CT, or ERCP.
Stratum	Adults

Subgroup analysis within study	Not applicable
Inclusion criteria	All consecutive patients with CP that were managed in the hospital between 2004 and 2009 were included.
Exclusion criteria	Patients with pancreatic malignancy, cirrhosis, primary sclerosing cholagitis, recent acute pancreatitis (i.e., in the previous three weeks), postsurgical stricture or secondary stenosis caused by gallstones, or pseudocysts were excluded from the study.
Recruitment/selection of patients	Patients were admitted to the hospital.
Age, gender and ethnicity	Age - Median (range): Endoscopy group: 52 (49-55) Surgery: 52 (38-66). Gender (M:F): 35:4. Ethnicity: Not reported
Further population details	
Extra comments	Endoscopy group: Median (range) BMI: 19.9 (18-21), Median time since onset of CP: 6.5 years, Preoperative jaundice: 18/33, Preoperative diabetes: 25/33, preoperative exocrine pancreatic insufficiency: 13/33 Surgery group: Median (range) BMI: 19.9 (16-22), Median time since onset of CP: 5.8 years, Preoperative jaundice: 3/6, Preoperative diabetes: 5/6, preoperative exocrine pancreatic insufficiency: 3/6
Indirectness of population	No indirectness
Interventions	(n=16) Intervention 1: Plastic stent - Single plastic stent. A flexible guidewire was passed through the stricture followed by a guiding catheter. Although the biliary stent's diameter and length were matched to the characteristics of the observed stenosis, the decision to perform sphincterotomy of the CBD stricture and the choice of stent were left to the endoscopist. In the event of an associated, symptomatic pancreatic duct stricture, a plastic pancreatic stent was inserted concomitantly.Oral ciprofloxacin therapy (500 mg twice daily) was started before ERCP and continued 3 days thereafter. The minimum defined time for stent therapy was 12 months (with multiple plastic or metallic stents). Patients with plastic stents had a routine stent exchange in 3 months, whereas patients with metallic stents had a routine stent exchange in 6 months to improve the calibration of the CBD and to decrease the number procedures. At the end of the period defined for ET therapy, the stents were removed. . Duration During admission. Concurrent medication/care: Before biliary drainage all the patients underwent a comprehensive imagine workup (including pancreatic MRI or contrast-enhanced, triple phase CT scan) and a nutritional status evaluation, then received appropriate therapy for diabetes or exocrine pancreatic insufficiency. Further details: 1. Type of stent: plastic. 2. Type of stent insertion: Endoscopic insertion 3. Type of surgery: Not

	applicable (n=23) Intervention 2: Open surgery - Choledocho-jejunostomy. Surgical treatment consisted of choledochoduodenostomy or choledochojejunostomy. For patients with a symptomatic inflammatory cephalic mass (diameter >4cm), surgical biliary drainage consisted of a duodenum-preserving pancreatic head resection (the Frey procedure) with concomitant decompression of the CBD within the head of the pancreas to avoid a biliary bypass. 17 people who were originally in the endoscopy group went on to have surgery.. Duration During admission. Concurrent medication/care: Before biliary drainage all the patients underwent a comprehensive imagine workup (including pancreatic MRI or contrast-enhanced, triple phase CT scan) and a nutritional status evaluation, then received appropriate therapy for diabetes or exocrine pancreatic insufficiency. Further details: 1. Type of stent: Not applicable 2. Type of stent insertion: Not applicable 3. Type of surgery: Choledocho-jejunostomy
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PLASTIC OR METAL STENTS versus CHOLEDOCHO-JEJUNOSTOMY OR CHOLECHODUODENOSTOMY Protocol outcome 1: Length of stay (in intensive therapy unit or hospital) at not defined - Actual outcome for Adults: Length of stay in hospital at Unclear; Other: Median; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 2: Mortality at <1 year - Actual outcome for Adults: Mortality at Unclear; Group 1: 0/16, Group 2: 0/23; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 3: Complications (eg bleeding, fistulae) at not defined - Actual outcome for Adults: Event free survival at Unclear; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 4: Recurrence of biliary obstruction, including failed stent (removal and additional stents) at not defined - Actual outcome for Adults: Successful treatment at Unclear; Group 1: 10/16, Group 2: 20/23; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at not defined; Biliary infections at not defined

H.20 Management of type 3c diabetes secondary to pancreatitis

None.

H.21 Receiving specialist input in people with acute pancreatitis

None.

H.22 Follow-up of pancreatic exocrine function in people with chronic pancreatitis

None.

H.23 Follow-up to identify diabetes in people with chronic pancreatitis

None.

H.24 Follow-up to identify pancreatic cancer in people with chronic pancreatitis

None.

Appendix I: Health economic evidence tables

I.1 Patient information

None.

I.2 Lifestyle interventions: stopping or reducing alcohol consumption

None.

I.3 Aetiology of acute pancreatitis

None.

I.4 Aetiology of chronic pancreatitis

None.

I.5 Diagnosing chronic pancreatitis

None.

I.6 Type of intravenous fluid for resuscitation in people with acute pancreatitis

None.

I.7 Speed of intravenous fluid for resuscitation in people with acute pancreatitis

None

I.8 Route of feeding in people with severe acute pancreatitis

Study	Louie 2005[679]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CCA **Study design:** RCT **Approach to analysis:** Within trial analysis **Perspective:** Canadian hospital or regional health authority **Time horizon**: length of treatment **Discounting:** N/A	**Population:** 18 years and over, with acute pancreatitis, a Ranson's score of 3 or greater and inability to tolerate oral fluids after a maximum time from admission of 96 hours, able to accept enteral nutrition (n=28). **Patient characteristics:** Mean age: 61.3 years Male: 54% **Intervention 1:** Parenteral nutrition: long-term vascular catheters were placed percutaneously and infused with 10% dextrose solution and Intralipid and then increased over 2 days to achieve 100% of the target energy rate (n=18). **Intervention 2:** Enteral nutrition: nasojejunal (NJ) feeding tubes were placed and infused with a semielemental product with low fat content, 25 ml/hour and increased by 10 ml/hour every 6 hours until target rate was	**Total costs (mean per patient):** Intervention 1: £1,338 Intervention 2: £705 Incremental (2−1): −£633 (95% CI: NR; p=NR) **Currency & cost year:** Currency and cost year unclear, assumed to be 2004 Canadian dollars, presented as 2004 UK pounds[(a)] **Cost components incorporated:** Cost of nutrition, production of parenteral nutrition, placement of NJ and catheters, radiology costs, operative costs and general and intensive care costs (applied to length of hospital stay for each non-operative complication).	12 outcome measures reported. Key results: <u>Morbidity secondary to pancreatitis</u> *Infected fluid collections per patient* Intervention 1: 0.22 Intervention 2: 0.1 Incremental (2−1): −0.12 <u>Morbidity secondary to nutritional practices</u> *Infected central lines per patient* Intervention 1: 0.11 Intervention 2: 0 Incremental (2−1): −0.11 *Dislodged or removed NJ tubes per patient* Intervention 1: 0 Intervention 2: 0.9 Incremental (2–1): 0.9 Of all 12 outcomes, 8 favoured enteral nutrition, 2 favoured parenteral nutrition and 2 were	<u>Morbidity secondary to pancreatitis: infected fluid collections</u> Dominant (parenteral nutrition is cheaper and leads to fewer infections) <u>Morbidity secondary to nutritional practices: infected central line:</u> Dominant (parenteral nutrition is cheaper and leads to fewer infections) *Dislodged or removed NJ tubes* 0.9 more dislodged or removed tubes per person but £633 cheaper per person with enteral compared with parenteral nutrition **Analysis of uncertainty:** 2 alternative scenarios were investigated to consider the possible costs of enteral nutrition. If only 1 NJ tube was used due to improved tube placement, the average cost of parenteral nutrition would remain £1,338 compared with a reduced £557 for enteral nutrition (95% CI £84 to £1,478). If, in addition, 1 patient unsuitable for enteral nutrition due to alcohol withdrawal was reallocated to parenteral nutrition, the cost of enteral nutrition would fall to £491 (95% CI £118 to £1,577), significantly different from the cost of parenteral nutrition.

	achieved (n=10).		virtually equal. See clinical evidence table for Louie 2005 for full details.	No sensitivity analysis was conducted on any other key parameters.
Data sources				
Health outcomes: Within trial analysis: single RCT of 28 patients in Canadian hospitals. **Quality-of-life weights:** NA. **Cost sources:** Within trial analysis: Canadian hospitals.				
Comments				
Source of funding: NR. **Limitations:** Canadian health service perspective; outcomes were not valued using QALYs. Data taken from a single study of 28 patients; currency and cost year not stated, costs taken from the Canadian health system; sensitivity analysis not undertaken.				
Overall applicability:(b) Partially applicable **Overall quality**(c) Potentially serious limitations				

Abbreviations: CCA: cost–consequences analysis; 95% CI: 95% confidence interval; NR: not reported;

(a) Converted using 2004 purchasing power parities[824]

(b) Directly applicable / Partially applicable / Not applicable

(c) Minor limitations / Potentially serious limitations / Very serious limitations

I.9 Early versus late nutritional intervention in people with chronic pancreatitis

None.

I.10 Specialist versus non-specialist nutritional assessment in people with chronic pancreatitis

None.

I.11 Prophylactic antimicrobial agents to prevent infection in people with acute pancreatitis

None.

I.12 Methods of management of infected necrosis in people with acute pancreatitis

Study	**Van Santvoort 2010**[150]

Study details	Population & interventions	Costs	Health outcomes	Cost effectiveness
Economic analysis: CCA (health outcomes: death, major complications, length of stay) **Study design:** Randomised control trial **Approach to analysis:** Patients were randomly assigned to either primary open necrosectomy or the minimally invasive step-up approach. Follow-up visits took place 3 and 6 months after discharge **Perspective:** Dutch NHS **Follow-up** 6 months **Discounting:** n/a	**Population:** Adults with acute pancreatitis and signs of pancreatic necrosis, peri-pancreatic necrosis or both, as detected by CT (n=88) **Patient characteristics:** Mean age: 57.5 years Male: 73% **Intervention 1:** Open surgery (necrosectomy); laparotomy through a bilateral subcostal incision. After blunt removal of all necrotic tissue, 2 large-bore drains for post-operative lavage were inserted, and the abdomen was closed (n=43). **Intervention 2:** Minimally invasive step-up approach; the first step was percutaneous (95%) or endoscopic (5%) transgastric drainage. If there was no clinical improvement a second drainage was performed. The third step was video-assisted retroperitaneal debridement with postoperative lavage (n=43).	**Total costs (mean per patient):** Intervention 1: £56,955 Intervention 2: £51,978 Incremental (2−1): −£4,977 (95% CI: NR; p=NR) **Currency & cost year:** 2008 Euros (presented here as 2008 UK pounds[(b)]) **Cost components incorporated:** Hospital stay, critical care stay, necrosectomies, drainage-radiologic-endoscopic procedures, microbiology, medication, visits to GP, visits to outpatient clinics, physiotherapy, re-admissions to hospital	Over 20 outcome measures were reported. See clinical evidence table for Van Santvoort 2010 for full details. Key results: **Death** Intervention 1: 16% Intervention 2: 19% Incremental (2−1): +3.0% (95% CI: NR; p=0.70) **Length of stay** <u>Days in CCU</u> Intervention 1: 11 Intervention 2: 9 Incremental (2−1): −2 days (95% CI: NR; p=0.26) <u>Days in hospital</u> Intervention 1: 60 Intervention 2: 50 Incremental (2−1): −10 days (95% CI: NR; p=0.53) **Major complications**[(c)] Intervention 1: 0.87 Intervention 2: 0.42 Incremental (2−1): −0.45 (95% CI: NR; p=NR)	**ICERs:** Death: £163,229 per death averted with open surgery Lengths of stay: Minimally invasive step-up approach dominates open surgery Major complications: Minimally invasive step-up approach dominates open surgery **Analysis of uncertainty:** No sensitivity analysis was conducted

Data sources
Health outcomes: Within trial. **Cost sources:** Resource use (number of procedures) was captured through the trial records. Unit costs relevant to the Dutch healthcare system were applied to the combined resource use.
Comments
Source of funding: Study was supported by a grant from the Dutch organisation for health research and development. **Limitations:** Dutch cohort of patients, the study did not collect quality of life data. The study had a short, 6-month time horizon; unit costs are representable of the Dutch healthcare system.
Overall applicability: partially applicable[(d)] **Overall quality:** potentially serious limitations[(e)]

Abbreviations: CCA: cost–consequences analysis; CCU: critical care unit; CT: computed tomography; 95% CI: 95% confidence interval; ICER: incremental cost-effectiveness ratio; NR: not reported

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

(b) Converted using purchasing power parities[824]

(c) Composite of 'multiple-organ failure', 'multiple systemic complications', 'intraabdominal bleeding requiring intervention' and 'enterocutaneous fistula or perforation of a visceral organ requiring intervention'; number of complications per person

(d) Directly applicable / Partially applicable / Not applicable

(e) Minor limitations / Potentially serious limitations / Very serious limitations

Study	Van Brunschot 2017[146]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CUA (health outcome: QALYs) **Study design:** within-trial analysis (RCT) **Approach to analysis:** outcomes and resource use from same trial **Perspective:** Dutch public health system	**Population:** Adults with acute pancreatitis and a high suspicion or evidence of infected necrosis with an indication for invasive intervention and for whom both the endoscopic and surgical step-up approach were deemed feasible (n=98). **Patient characteristics:** Mean age: 62 Male: 64% **Intervention 1:**	**Total costs:** Intervention 1: £63,391 Intervention 2: £51,674 Incremental (2−1): −£11,717 (95% CI: −£30,725 to £9,305; p=NR)[(a)] [(b)] **Currency & cost year:** 2014 Euros (presented here as 2014 UK pounds[(c)]) **Cost components incorporated:[(c)]**	**QALYs gained:[(d)]** Intervention 1: 0.2656 Intervention 2: 0.2495 Incremental (2−1): −0.0161 (95% CI: −0.0743 to 0.0464; p=NR)	**ICER:** £728,000 per QALY gained (for percutaneous step-up compared with endoscopic step-up). Probability endoscopic step-up is cost effective compared to percutaneous step-up (at a threshold of £42,934): 89%[(e)] **Analysis of uncertainty:** 1000 bootstrapped samples

Follow-up 6 months **Discounting:** n/a	Minimally invasive percutaneous step-up approach: Radiological CT-guided or ultrasound-guided percutaneous catheter drainage, preferably through the left retroperitoneum with the catheter as guidance for video-assisted retroperitoneal debridement (VARD) if needed. If drainage was not successful a VARD procedure was performed. (n=47) **Intervention 2:** Minimally invasive endoscopic step-up approach: Endoscopic ultrasound-guided transluminal (transgastric or transduodenal) drainage with placement of 2 double-pigtail stents and 1 nasocystic catheter. If drainage alone did not lead to considerable clinical improvement endoscopic transluminal necrosectomy was performed. (n=51)	Hospital stay, critical care stay, general ward stay, laboratory, microbiology, conventional radiology, endoscopy, study intervention, other interventions, surgical procedures, outpatient clinic contact, non-hospital medical costs.		were used to calculate the results above. No deterministic sensitivity analyses were conducted.
Data sources				
Health outcomes: Within trial. **Quality of life:** quality of life measured within trial at 3 months and 6 months after start using EQ-5D-3L; utility weights taken from UK population. **Cost sources:** Unit costing based on the 2015 Dutch manual for costing in healthcare research, except for the experimental interventions, which were calculated by the researchers' expert judgement.				
Comments				
Source of funding: Olympus, Netherlands Organisation for Health Research and Development, Dutch Digestive Disease Foundation, Fonds NutsOhra. **Limitations:** The majority (77%) of patients were excluded from the study, so may have limited applicability. The interventions differ in some respects from current UK practice. The study had a short, 6-month time horizon. Quality of life was compared only for surviving patients over the first 6 months; mortality and life expectancy were not included in QALY calculations. Costs are based on the Dutch healthcare system.				
Overall applicability: partially applicable[(f)] **Overall quality:** potentially serious limitations[(g)]				

Abbreviations: CUA: cost–utility analysis; 95% CI: 95% confidence interval; ICER: incremental cost-effectiveness ratio; NR: not reported; QALYs: quality-adjusted life years; RCT: randomised controlled trial

(a) Difference in cost between the primary interventions was +£802, the cost difference is largely driven by a difference of £9,247 for hospital stay (general ward admissions)

(b) Patients' travel expenses also reported; these have been excluded from the total costs for each arm reported here. 95% CI for incremental cost difference between arms reported above is for the incremental difference between the total costs including travel expenses (CI around −£11,717) – however travel expenses only differed by £9 between the 2 arms

(c) Converted using purchasing power parities[824]
(d) QALYs were reported based on utility valuations from both Dutch and UK EQ-5D valuation sets; only UK results are reported here
(e) The probability cost effective was calculated in the paper from the total costs, including travel costs. The result would have been similar without travel costs.
(f) Directly applicable / Partially applicable / Not applicable
(g) Minor limitations / Potentially serious limitations / Very serious limitations

I.13 Timing of management of infected necrosis in people with acute pancreatitis

None.

I.14 Management of pain in people with chronic pancreatitis

None.

I.15 Management of pancreatic duct obstruction in people with chronic pancreatitis

Study	**Dumonceau 2007**[319]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CCA (health outcomes: pain relapse, length of hospital stay, intensity of pain) **Study design:** Randomised control trial **Approach to analysis:** Patients were randomly assigned to either ESWL alone or ESWL in combination with endoscopy. **Perspective:** Belgian public healthcare	**Population:** Patients with uncomplicated painful chronic pancreatitis and calcifications obstructing the main pancreatic duct (n=55). **Patient characteristics:** Age: 50.3 years Male: 78%	**Total costs (mean per patient):** Intervention 1: £9,221 Intervention 2: £3,289 Incremental (2−1): −£5,932 (95% CI: NR; p=0.001) **Currency & cost year:** 2003 Euros (presented here as 2003 UK pounds[(a)])	11 outcome measures reported. Key results: Pain relapse at 2 years (% patients): Intervention 1: 45% Intervention 2: 38% Incremental (2−1): −7% Intensity of relapsing pain (10 point visual analogue scale): Intervention 1: 5.7 Intervention 2: 5.7	Pain relapse: ESWL dominates ESWL in combination with endotherapy Intensity of pain: ESWL is less costly and equally effective compared to ESWL in combination with endotherapy Complications: ESWL dominates ESWL in combination with endotherapy Length of hospital stay: ESWL dominates ESWL in combination with endotherapy

insurance system **Follow-up:** mean 21.5 months **Discounting:** n/a	**Intervention 1:** ESWL in combination with endotherapy (n=29). **Intervention 2:** ESWL (n=26).	**Cost components incorporated:** Initial hospital stay, interventions (ESWL, endoscopy), and procedure-related complications. Follow-up hospital stays and procedures.	Incremental (2−1): 0 <u>Complications (% patients):</u> Intervention 1: 3% Intervention 2: 0% Incremental (2−1): −3% <u>Length of hospital stay (per patient):</u> Intervention 1: 8.6 days Intervention 2: 3.1 days Incremental (2−1): −5.5 days Of all 13 outcomes, 6 favoured ESWL alone, 4 favoured ESWL with endotherapy and 3 were equal. See clinical evidence table for Dumoncaeu 2007 for full details.	**Analysis of uncertainty:** No sensitivity analysis was conducted.
Data sources				
Health outcomes: Within trial analysis. **Cost sources:** Resource use was captured from the trial. Unit costs were based on rates for Belgian public healthcare insurance and applied to resource use.				
Comments				
Source of funding: NR. **Limitations:** Belgian public healthcare insurance perspective. The study did not collect quality of life data. Costs were not discounted. Short follow-up time that may not capture all costs and benefits. Sensitivity analysis not undertaken. **Other:** None.				
Overall applicability: partially applicable[(b)] **Overall quality:** potentially serious limitations[(c)]				

Abbreviations: CCA: cost–consequences analysis; 95% CI: 95% confidence interval; ESWL: extracorporeal shock wave lithotripsy; NR: not reported;

(a) Converted using 2003 purchasing power parities[824]

(b) Directly applicable / Partially applicable / Not applicable

(c) Minor limitations / Potentially serious limitations / Very serious limitations

I.16 Management of small-duct disease in people with chronic pancreatitis

None.

I.17 Management of pseudocysts

None.

I.18 Management of pancreatic ascites and pleural effusion secondary to pancreatitis

None.

I.19 Management of biliary obstruction in people with chronic pancreatitis

None.

I.20 Management of type 3c diabetes secondary to pancreatitis

None.

I.21 Receiving specialist input in people with acute pancreatitis

None.

I.22 Follow-up of pancreatic exocrine function in people with chronic pancreatitis

None.

I.23 Follow-up to identify diabetes in people with chronic pancreatitis

None.

I.24 Follow-up to identify pancreatic cancer in people with chronic pancreatitis

None.

Appendix J: GRADE tables

J.1 Patient information

None.

J.2 Lifestyle interventions: stopping or reducing alcohol consumption

J.2.1 Clinical evidence profile: Structured programme to support people with acute pancreatitis in stopping or reducing alcohol consumption versus usual care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Structured programme to stop alcohol	Usual care	Relative (95% CI)	Absolute		
N of episodes of recurrent AP at 36 months (follow-up 36 months)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	7/39 (17.9%)	31.1%	RR 0.58 (0.26 to 1.28)	131 fewer per 1000 (from 230 fewer to 87 more)	⊕OOO VERY LOW	CRITICAL
Admissions to hospital (n of patients admitted for abdominal complaints fulfilling criteria of recurrent AP) at 2 years (follow-up 2 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	3/39 (7.7%)	20%	RR 0.38 (0.11 to 1.32)	124 fewer per 1000 (from 178 fewer to 64 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

J.3 Aetiology of acute pancreatitis

None

J.4 Aetiology of chronic pancreatitis

None

J.5 Diagnosing chronic pancreatitis

None

J.6 Type of intravenous fluid for resuscitation in people with acute pancreatitis

J.6.1 Clinical evidence profile: Balanced crystalloid (Ringer-lactate) vs normal saline (RCT)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Balanced crystalloid (Ringer-lactate)	Normal saline (RCT)	Relative (95% CI)	Absolute		
Mortality												
2	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	0/38 (0%)	1.19%	Peto OR 0.15 (0.00 to 7.54)	48 fewer per 1000 (from 173 fewer to 78 more)[3]	⊕⊕OO LOW	CRITICAL
Serious adverse events (transfer to critical care)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious	none	1/19 (5.3%)	14.3%	RR 0.37 (0.06 to 2.20)	90 fewer per 1000 (from 134 fewer to 172 more)	⊕OOO VERY LOW	IMPORTANT

Local complications (infection)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/19 (0%)	1/21 (4.8%)	Peto OR 0.15 (0 to 7.54)	40 fewer per 1000 (from 48 fewer to 226 more)	⊕OOO VERY LOW	IMPORTANT
Local complications (necrosis)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/19 (0%)	2/21 (9.5%)	Peto OR 0.14 (0.01 to 2.36)	81 fewer per 1000 (from 94 fewer to 104 more)	⊕OOO VERY LOW	IMPORTANT
Local complications (peri-pancreatic necrosis)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	4/10 (40%)	10/14 (71.4%)	RR 0.56 (0.24 to 1.28)	314 fewer per 1000 (from 543 fewer to 200 more)	⊕⊕OO LOW	IMPORTANT
Systemic complications (renal failure)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/19 (5.3%)	2/21 (9.5%)	RR 0.55 (0.05 to 5.62)	43 fewer per 1000 (from 90 fewer to 440 more)	⊕OOO VERY LOW	IMPORTANT
Systemic complications (respiratory organ failure)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/19 (0%)	1/21 (4.8%)	Peto OR 0.15 (0 to 7.54)	40 fewer per 1000 (from 48 fewer to 226 more)	⊕OOO VERY LOW	IMPORTANT
Systemic complications (shock)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/19 (0%)	1/21 (4.8%)	Peto OR 0.15 (0 to 7.54)	40 fewer per 1000 (from 48 fewer to 226 more)	⊕OOO VERY LOW	IMPORTANT
Systemic complications (persistent organ failure)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	0/19 (0%)	1/21 (4.8%)	Peto OR 0.15 (0 to 7.54)	48 fewer per 1000 (from 173 fewer to 78 more)[3]	⊕⊕OO LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

J.6.2 Clinical evidence profile: Balanced crystalloid (Ringer-lactate) vs normal saline (non-randomised comparative studies)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Balanced crystalloid (Ringer-lactate)	Normal saline (obs)	Relative (95% CI)	Absolute		
Mortality												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	4/68 (5.9%)	21/130 (16.2%)	RR 0.36 (0.13 to 1.02)	104 fewer per 1000 (from 141 fewer to 3 more)	⊕OOO VERY LOW	CRITICAL
Length of stay (in critical care) (Better indicated by lower values)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	68	130	-	MD 2 higher (0.19 to 3.81 higher)	⊕OOO VERY LOW	CRITICAL

[1] Downgraded by 2 increments if the majority of the evidence was from studies with observational/non-randomised study design. Further downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

J.7 Speed of intravenous fluid for resuscitation in people with acute pancreatitis

J.7.1 Clinical evidence profile: Aggressive intravenous fluid resuscitation therapy versus conservative intravenous fluid resuscitation therapy in adults with acute pancreatitis (RCTs)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Aggressive fluid therapy	Conservative fluid therapy	Relative (95% CI)	Absolute		
Mortality												
3	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	14/110 (12.7%)	11.8%	RR 0.90 (0.49 to 1.67)	12 fewer per 1000 (from 60 fewer to 79 more)	⊕OOO VERY LOW	CRITICAL
Length of time in CCU (days) (Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	64	68	-	MD 2 lower (4.23 lower to 0.23 higher)	⊕OOO VERY LOW	CRITICAL
Local complications (infection)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/19 (10.5%)	0%	POR 8.68 (0.52 to 144.35)	105 more per 1000 (from 52 fewer to 263 more)[3]	⊕OOO VERY LOW	IMPORTANT
Local complications (necrosis)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/19 (5.3%)	0%	Peto OR 8.21 (0.16 to 415.76)	52 more per 1000 (from 78 fewer to 183 more)[3]	⊕OOO VERY LOW	IMPORTANT
Systemic complications (Multiple organ dysfunction syndrome)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	18/64 (28.1%)	20/68 (29.4%)	RR 0.96 (0.56 to 1.64)	12 fewer per 1000 (from 129 fewer to 188 more)	⊕OOO VERY LOW	IMPORTANT

Systemic complications (Sepsis)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	36/36 (100%)	13/40 (32.5%)	RR 3 (1.93 to 4.64)	650 more per 1000 (from 302 more to 1000 more)	⊕⊕OO LOW	IMPORTANT
Systemic complications (Abdominal compartment syndrome)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	14/64 (21.9%)	18/68 (26.5%)	RR 0.83 (0.45 to 1.52)	45 fewer per 1000 (from 146 fewer to 138 more)	⊕OOO VERY LOW	IMPORTANT
Systemic complications (renal failure)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/19 (10.5%)	1/21 (4.8%)	RR 2.21 (0.22 to 22.47)	58 more per 1000 (from 37 fewer to 1000 more)	⊕OOO VERY LOW	IMPORTANT
Systemic complications (respiratory failure)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/19 (5.3%)	0%	Peto OR 8.21 (0.16 to 415.76)	52 more per 1000 (from 78 fewer to 183 more)[3]	⊕OOO VERY LOW	IMPORTANT
Systemic complications (shock)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/19 (5.3%)	0%	Peto OR 8.21 (0.16 to 415.76)	52 more per 1000 (from 78 fewer to 183 more)[3]	⊕OOO VERY LOW	IMPORTANT
Serious adverse events (Days using ventilation) (Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	64	68	-	MD 3 lower (4.61 to 1.39 lower)	⊕OOO VERY LOW	IMPORTANT
Serious adverse events (transfer to CCU)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/19 (21.1%)	0%	Peto OR 9.78 (1.27 to 75.43)	210 more per 1000 (from 17 more to 403 more)[3]	⊕OOO VERY LOW	IMPORTANT
Systemic complications (development of SIRS)												

1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/27 (14.8%)	9/33 (27.3%)	RR 0.54 (1.19 to 1.57)	125 fewer per 1000 (from 221 fewer to 155 more)	⊕OOO VERY LOW	IMPORTANT
Systemic complications (persistent SIRS)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/27 (7.4%)	7/33 (21.2%)	RR 0.35 (0.08 to 1.54)	138 fewer per 1000 (from 195 fewer to 115 more)	⊕OOO VERY LOW	IMPORTANT
Serious adverse events (development of severe acute pancreatitis)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/27 (0%)	1/33 (3%)	Peto OR 0.16 (0 to 8.34)	25 fewer per 1000 (from 30 fewer to 222 more)[3]	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs
[3] Peto Odds Ratio

J.7.2 Clinical evidence profile: Aggressive intravenous fluid resuscitation therapy versus conservative intravenous fluid resuscitation therapy in adults with acute pancreatitis (non-randomised comparative studies)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Aggressive fluid therapy**	**Conservative fluid therapy**	**Relative (95% CI)**	**Absolute**		
Mortality												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	0/17 (0%)	5/28 (17.9%)	RR 0.17 (0.03 to 1.14)	148 fewer per 1000 (from 173 fewer to 25 more)	⊕OOO VERY LOW	CRITICAL
Mortality												

1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	4/113 (3.5%)	16/173 (9.2%)	Peto OR 0.38 (0.13 to 1.12)	57 fewer per 1000 (from 80 fewer to 11 more)	⊕OOO VERY LOW	CRITICAL
Mortality - 500-1000ml versus <500ml												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	427	269	OR 0.46 (0.15 to 1.41)	-	⊕OOO VERY LOW	CRITICAL
Mortality - >1000ml versus <500ml												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	314	269	OR 0.64 (0.2 to 2.05)	-	⊕OOO VERY LOW	CRITICAL
Length of hospital stay (Better indicated by lower values)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	17	28	-	MD 3 higher (37.7 lower to 43.7 higher)	⊕OOO VERY LOW	CRITICAL
Local complications (Acute collection) 3100-4100 ml versus >4100ml												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	123	61	OR 1.90 (1.00 to 3.61)	-	⊕OOO VERY LOW	IMPORTANT
Local complications (Acute collection) <3100 ml versus 3100-4100 ml												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	63	123	OR 0.60 (0.30 to 1.20)	-	⊕OOO VERY LOW	IMPORTANT
Local complications (Pancreatic necrosis)												
1	observational	very	no serious	no serious	very serious[2]	none	8/17	11/28	RR 1.20	79 more	⊕OOO	IMPORTANT

	studies	serious[1]	inconsistency	indirectness			(47.1%)	(39.3%)	(0.61 to 2.37)	per 1000 (from 153 fewer to 538 more)	VERY LOW	
Local complications (Pancreatic necrosis)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	26/173 (15%)	8/113 (7.1%)	RR 2.12 (1.00 to 4.52)	79 more per 1000 (from 0 more to 249 more)	⊕OOO VERY LOW	IMPORTANT
Local complications (Pancreatic necrosis) 3100-4100 ml versus >4100ml												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	123	61	OR 1.80 (0.60 to 5.40)	-	⊕OOO VERY LOW	IMPORTANT
Local complications (Pancreatic necrosis) <3100 ml versus 3100-4100 ml												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	63	123	OR 1.50 (0.60 to 3.75)	-	⊕OOO VERY LOW	IMPORTANT
Local complications (Pseudocysts)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	11/17 (64.7%)	20/28 (71.4%)	RR 0.91 (0.59 to 1.38)	64 fewer per 1000 (from 293 fewer to 271 more)	⊕OOO VERY LOW	IMPORTANT
Local complications (acute peripancreatic fluid collections and/or pancreatic necrosis and/or peripancreatic necrosis)) - 500-1000 ml versus <500 ml												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	427	269	OR 0.67 (0.43 to 1.04)	-	⊕OOO VERY LOW	IMPORTANT

Local complications (acute peripancreatic fluid collections and/or pancreatic necrosis and/or peripancreatic necrosis)) - >1000 ml versus <500 ml												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	314	269	OR 1.15 (0.71 to 1.86)	-	⊕OOO VERY LOW	IMPORTANT
Systemic complications (Cardiovascular failure)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/113 (3.5%)	4.1%	RR 0.87 (0.26 to 2.92)	5 fewer per 1000 (from 30 fewer to 79 more)	⊕OOO VERY LOW	IMPORTANT
Systemic complications (Pulmonary failure)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/113 (3.5%)	5.2%	RR 0.68 (0.21 to 2.16)	17 fewer per 1000 (from 41 fewer to 60 more)	⊕OOO VERY LOW	IMPORTANT
Systemic complications (Multisystem organ failure)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	5/113 (4.4%)	10.4%	RR 0.43 (0.16 to 1.11)	59 fewer per 1000 (from 87 fewer to 11 more)	⊕OOO VERY LOW	IMPORTANT
Systemic complications (Respiratory complications)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	21/32 (65.6%)	97.3%	RR 0.67 (0.52 to 0.87)	321 fewer per 1000 (from 126 fewer to 467 fewer)	⊕OOO VERY LOW	IMPORTANT
Systemic complications (Fluid overload)												

1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/32 (0%)	0%	No events	-	⊕OOO VERY LOW	IMPORTANT
Systemic complications (Persistent organ failure)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	6/17 (35.3%)	12/28 (42.9%)	RR 0.82 (0.38 to 1.78)	77 fewer per 1000 (from 266 fewer to 334 more)	⊕OOO VERY LOW	IMPORTANT
Systemic complications (Persistent organ failure) 3100-4100 ml versus <3100ml												
1	observational studies	very serious[2]	no serious inconsistency	no serious indirectness	very serious[2]	none	123	63	OR 2.10 (0.30 to 14.70)	-	⊕OOO VERY LOW	IMPORTANT
Systemic complications (persistent organ failure) - >4100 ml versus 3100-4100 ml												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	61	123	OR 7.70 (1.50 to 39.53)	-	⊕OOO VERY LOW	IMPORTANT
Systemic complications (persistent organ failure) - 500-1000 ml versus <500 ml												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	427	269	OR 0.56 (0.28 to 1.12)	-	⊕OOO VERY LOW	IMPORTANT
Systemic complications (persistent organ failure) - >1000ml versus <500ml												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	314	269	OR 0.50 (0.22 to 1.14)	-	⊕OOO VERY LOW	IMPORTANT
Systemic complications (Renal failure)												

1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	5/113 (4.4%)	5.2%	RR 0.85 (0.29 to 2.47)	8 fewer per 1000 (from 37 fewer to 76 more)	⊕OOO VERY LOW	IMPORTANT
Systemic complications (SIRS)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	15/17 (88.2%)	20/28 (71.4%)	RR 1.24 (0.92 to 1.65)	171 more per 1000 (from 57 fewer to 464 more)	⊕OOO VERY LOW	IMPORTANT
Serious adverse events (pulmonary oedema)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	0/32 (0%)	0/67 (0%)	Not estimable	No events	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 2 increments if the majority of the evidence was from studies with observational/non-randomised study design. Further downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

J.7.3 Clinical evidence profile: Aggressive intravenous fluid resuscitation therapy versus conservative intravenous fluid resuscitation therapy in children with acute pancreatitis (non-randomised comparative studies)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Aggressive fluid therapy**	**Conservative fluid therapy**	**Relative (95% CI)**	**Absolute**		
Serious adverse events (CCU transfer rate)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	5/126 (4%)	14/75 (18.7%)	RR 0.21 (0.08 to	147 fewer per 1000 (from 80 fewer to	⊕OOO VERY	IMPORTANT

									0.57)	172 fewer)	LOW	
Serious adverse events (Readmission rate)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	5/126 (4%)	5/75 (6.7%)	RR 0.6 (0.18 to 1.99)	27 fewer per 1000 (from 55 fewer to 66 more)	⊕OOO VERY LOW	IMPORTANT
Serious adverse events (SAP rate)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	9/126 (7.1%)	16%	RR 0.45 (0.2 to 1.01)	88 fewer per 1000 (from 128 fewer to 2 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 2 increments if the majority of the evidence was from studies with observational/non-randomised study design. Further downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

J.8 Route of feeding in people with severe acute pancreatitis

J.8.1 Clinical evidence profile: Enteral versus parenteral nutrition

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Enteral**	**Parenteral**	**Relative (95% CI)**	**Absolute**		
Mortality (follow-up during hospitalisation)												
8	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	18/186 (9.7%)	17.4%	RR 0.36 (0.22 to 0.59)	111 fewer per 1000 (from 71 fewer to 136 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Length of hospital stay - Overall (follow-up hospitalisation; Better indicated by lower values)												
3	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	55	58	-	MD 2.46 lower (8.45 lower to 3.53 higher)	⊕⊕OO LOW	CRITICAL

Length of hospital stay - Severe (Ranson's criteria >3) (follow-up hospitalisation; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	13	13	-	MD 7.3 lower (9.24 to 5.36 lower)	⊕⊕⊕O MODERATE	CRITICAL
Achieving nutrition - kcal/kg/day (day 5) (follow-up hospitalisation; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	11	11	-	MD 0.71 higher (0.76 lower to 2.18 higher)	⊕⊕OO LOW	CRITICAL
Achieving nutrition - Days to goal (follow-up hospitalisation; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	10	18	-	MD 1.4 higher (0.56 lower to 3.36 higher)	⊕⊕⊕O MODERATE	CRITICAL
Infections - Pancreatic (for example, infected necrosis, abscess) (follow-up hospitalisation)												
5	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	22/127 (17.3%)	22.2%	RR 0.36 (0.24 to 0.54)	142 fewer per 1000 (from 102 fewer to 169 fewer)	⊕⊕⊕O MODERATE	IMPORTANT
Infections - Extra-pancreatic (for example, UTI, pneumonia) (follow-up hospitalisation)												
4	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	9/72 (12.5%)	14.4%	RR 0.73 (0.34 to 1.57)	39 fewer per 1000 (from 95 fewer to 82 more)	⊕OOO VERY LOW	IMPORTANT
Infections - Systemic (for example, central line infection, blood culture) (follow-up hospitalisation)												
6	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	2/108 (1.9%)	19.9%	RR 0.15 (0.06 to 0.41)	169 fewer per 1000 (from 117 fewer to 187 fewer)	⊕⊕⊕O MODERATE	IMPORTANT
Infections – type not specified (follow-up hospitalisation)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	16/25 (64%)	15/25 (60%)	RR 1.07 (0.69 to 1.65)	42 more per 1000 (from 186 fewer to 390 more)	⊕OOO VERY LOW	IMPORTANT
Serious adverse events (follow-up hospitalisation)												
6	randomised trials	no serious risk of bias	very serious[3]	no serious indirectness	serious[2]	none	42/143 (29.4%)	69.4%	RR 0.51 (0.29 to 0.92)	340 fewer per 1000 (from 56 fewer to 493 fewer)	⊕OOO VERY LOW	IMPORTANT

Adverse events - Operative intervention (follow-up during hospitalisation)												
8	randomised trials	serious[1]	serious[3]	no serious indirectness	no serious imprecision	none	43/186 (23.1%)	41.1%	RR 0.5 (0.27 to 0.92)	205 fewer per 1000 (from 33 fewer to 300 fewer)	⊕⊕OO LOW	IMPORTANT
Adverse events - Non-infective pancreatic complications (for example,, necrosis, pseudocyst, fistulae) (follow-up hospitalisation)												
6	randomised trials	serious[1]	serious[3]	no serious indirectness	very serious[2]	none	60/143 (42%)	21.4%	RR 1.09 (0.53 to 2.24)	19 more per 1000 (from 101 fewer to 265 more)	⊕OOO VERY LOW	IMPORTANT
Adverse events - Feeding complications (for example,, tube displacement, hyperglycaemia, diabetes) (follow-up hospitalisation)												
5	randomised trials	serious[1]	very serious[3]	no serious indirectness	very serious[2]	none	24/97 (24.7%)	14.7%	RR 1.03 (0.27 to 3.85)	4 more per 1000 (from 107 fewer to 419 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.
[3] Downgraded by 1 or 2 increments because of heterogeneity, I^2>50%, p<0.04, unexplained by subgroup analysis.

J.8.2 Clinical evidence profile: Enteral (gastric) versus parenteral nutrition

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Enteral (gastric)**	**Parenteral nutrition**	**Relative (95% CI)**	**Absolute**		
Mortality (follow-up 3 months)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	1/23 (4.3%)	0/25 (0%)	Peto OR 8.06 (0.16 to 407.6)	40 more per 1000 (from 70 fewer to 150 more)	⊕OOO VERY LOW	CRITICAL
Achieving nutrition (25 kcal/kg/day) (follow-up 10 days)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	16/24 (66.7%)	17/26 (65.4%)	RR 1.02 (0.68 to 1.52)	13 more per 1000 (from 209 fewer to 340 more)	⊕OOO VERY LOW	CRITICAL
Infections - Pancreatic (e.g. infected necrosis, abscess) (follow-up 3 months)												

1	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	1/23 (4.3%)	0/25 (0%)	Peto OR 8.06 (0.16 to 407.6)	40 more per 1000 (from 70 fewer to 150 more)	⊕OOO VERY LOW	IMPORTANT
Infections - Systemic (e.g. central line infection, blood culture) (follow-up 3 months)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	2/23 (8.7%)	0/25 (0%)	Peto OR 8.43 (0.51 to 139.29)	90 more per 1000 (from 50 fewer to 220 more)	⊕OOO VERY LOW	IMPORTANT
Serious adverse events - Multiple or single organ failure (follow-up 3 months)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	2/23 (8.7%)	2/25 (8%)	RR 1.09 (0.17 to 7.1)	7 more per 1000 (from 66 fewer to 488 more)	⊕OOO VERY LOW	IMPORTANT
Adverse events - General (e.g., pleural effusion) (follow-up 3 months)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	12/23 (52.2%)	7/25 (28%)	RR 1.86 (0.89 to 3.91)	241 more per 1000 (from 31 fewer to 815 more)	⊕OOO VERY LOW	IMPORTANT
Adverse events - Non-infective pancreatic complications (e.g., necrosis, pseudocyst, fistulae) (follow-up 3 months)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	9/23 (39.1%)	4/25 (16%)	RR 2.45 (0.87 to 6.87)	232 more per 1000 (from 21 fewer to 939 more)	⊕OOO VERY LOW	IMPORTANT
Adverse events - Surgical intervention (follow-up 3 months)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	1/24 (4.2%)	1/26 (3.8%)	RR 1.08 (0.07 to 16.38)	3 more per 1000 (from 36 fewer to 592 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment because the majority of evidence was from an indirect population
[3] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.8.3 Clinical evidence profile: Enteral (gastric) versus enteral (jejunal or duodenal) parenteral nutrition

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Gastric**	**Duodenal/jejunal**	**Relative (95% CI)**	**Absolute**		
Mortality (follow-up unclear)												
3	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	14/82 (17.1%)	28.6%	RR 0.69 (0.37 to 1.29)	89 fewer per 1000 (from 180 fewer to 83 more)	⊕⊕OO LOW	CRITICAL
Length of hospital stay (days) (follow-up unclear; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	16	14	-	MD 5.87 lower (20.98 lower to 9.24 higher)	⊕⊕⊕O MODERATE	CRITICAL
Achieving nutrition - Tolerating administration of at least 75% of target within 48 h (follow-up 48 h)												
1	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[1]	none	19/27 (70.4%)	17/22 (77.3%)	RR 0.91 (0.65 to 1.27)	70 fewer per 1000 (from 270 fewer to 209 more)	⊕OOO VERY LOW	CRITICAL
Achieving nutrition - Tolerating administration of at least 75% of target within 60 h (follow-up 60 h)												
1	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[1]	none	21/27 (77.8%)	17/22 (77.3%)	RR 1.01 (0.74 to 1.36)	8 more per 1000 (from 201 fewer to 278 more)	⊕OOO VERY LOW	CRITICAL
Achieving nutrition - Achieving goal nutrient requirement within 3 days (follow-up 3 days)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	39/39 (100%)	39/39 (100%)	RR 1 (0.95 to 1.05)	0 fewer per 1000 (from 50 fewer to 50 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Requiring TPN (follow-up unclear)												
1	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[1]	none	0/27 (0%)	1/22 (4.5%)	Peto OR 0.11 (0 to 5.55)	40 fewer per 1000 (from 45 fewer to 164 more)	⊕OOO VERY LOW	CRITICAL
Infections - Pancreatic (e.g. infected necrosis, abscess) (follow-up unclear)												

2	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	5/55 (9.1%)	17.1%	RR 0.59 (0.21 to 1.67)	70 fewer per 1000 (from 135 fewer to 115 more)	⊕⊕OO LOW	IMPORTANT
Infections - Extrapancreatic (follow-up unclear)												
2	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	4/55 (7.3%)	16.4%	RR 0.36 (0.12 to 1.05)	105 fewer per 1000 (from 144 fewer to 8 more)	⊕⊕⊕O MODERATE	IMPORTANT
Infections - Systemic (e.g. central line infection, blood culture) (follow-up unclear)												
2	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	11/55 (20%)	18.7%	RR 0.97 (0.46 to 2.05)	6 fewer per 1000 (from 101 fewer to 196 more)	⊕⊕OO LOW	IMPORTANT
Serious complications requiring tube removal (follow-up unclear)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/16 (0%)	0/14 (0%)	-	-	⊕⊕⊕⊕ HIGH	CRITICAL
Adverse events - Tube displacement (follow-up unclear)												
2	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[1]	none	2/43 (4.7%)	5.8%	RR 0.84 (0.13 to 5.68)	9 fewer per 1000 (from 50 fewer to 271 more)	⊕OOO VERY LOW	IMPORTANT
Adverse events - Surgical intervention (follow-up unclear)												
2	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	5/55 (9.1%)	9.7%	RR 1.19 (0.34 to 4.17)	18 more per 1000 (from 64 fewer to 307 more)	⊕⊕OO LOW	IMPORTANT

[1] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.
[2] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

J.8.4 Clinical evidence profile: Early versus conventional (delayed) oral 're-feeding'

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Early	Conventional oral re-feeding	Relative (95% CI)	Absolute		
Length of hospital stay (follow-up unclear; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	67	71	-	MD 2 lower (3.94 to 0.06 lower)	⊕⊕OO LOW	CRITICAL
Requiring parenteral nutrition (follow-up unclear)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	65/67 (97%)	69/71 (97.2%)	RR 1 (0.94 to 1.06)	0 fewer per 1000 (from 58 fewer to 58 more)	⊕⊕⊕O MODERATE	CRITICAL
Adverse events (abdominal pain relapse) (follow-up unclear)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	7/67 (10.4%)	10/71 (14.1%)	RR 0.74 (0.3 to 1.84)	37 fewer per 1000 (from 99 fewer to 118 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.8.5 Clinical evidence profile: Early versus on-demand enteral nutrition

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Early	On-demand enteral nurition	Relative (95% CI)	Absolute		
Mortality (follow-up 6 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	11/101 (10.9%)	7/104 (6.7%)	RR 1.62 (0.65 to 4.01)	42 more per 1000 (from 24 fewer to 203 more)	⊕⊕OO LOW	CRITICAL
Requiring parenteral nutrition (follow-up 6 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	5/101 (5%)	10/103 (9.7%)	RR 0.51 (0.18 to 1.44)	48 fewer per 1000 (from 80 fewer to 43 more)	⊕⊕OO LOW	CRITICAL

Infection - Pancreatic (e.g. infected necrosis, abscess) (follow-up 6 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	9/101 (8.9%)	15/104 (14.4%)	RR 0.62 (0.28 to 1.35)	55 fewer per 1000 (from 104 fewer to 50 more)	⊕⊕OO LOW	IMPORTANT
Infection - Extra-pancreatic (e.g. UTI, pneumonia) (follow-up 6 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	12/101 (11.9%)	13/104 (12.5%)	RR 0.95 (0.46 to 1.98)	6 fewer per 1000 (from 67 fewer to 123 more)	⊕⊕OO LOW	IMPORTANT
Infection - Systemic (e.g. central line infection, blood culture) (follow-up 6 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	17/101 (16.8%)	18/104 (17.3%)	RR 0.97 (0.53 to 1.78)	5 fewer per 1000 (from 81 fewer to 135 more)	⊕⊕OO LOW	IMPORTANT
Serious adverse events - Necrosis (follow-up 6 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	64/104 (61.5%)	65/104 (62.5%)	RR 0.98 (0.8 to 1.22)	12 fewer per 1000 (from 125 fewer to 138 more)	⊕⊕⊕⊕ HIGH	IMPORTANT
Serious adverse events - Mutiple or single organ failure (follow-up 6 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	33/67 (49.3%)	37/73 (50.7%)	RR 0.97 (0.7 to 1.35)	15 fewer per 1000 (from 152 fewer to 177 more)	⊕⊕OO LOW	IMPORTANT
Adverse events - Tube displacement (follow-up 6 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	38/99 (38.4%)	14/32 (43.8%)	RR 0.88 (0.55 to 1.4)	53 fewer per 1000 (from 197 fewer to 175 more)	⊕⊕OO LOW	IMPORTANT

[1] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.8.6 Clinical evidence profile: Early versus late enteral nutrition (observational data)

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Early	Delayed enteral nutrition (observational)	Relative (95% CI)	Absolute		
Mortality - adjusted (follow-up unclear)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	3/47 (6.4%)	7/48 (14.6%)	OR 0.46 (0.11 to 1.92)	73 fewer per 1000 (from 127 fewer to 101 more)	⊕OOO VERY LOW	CRITICAL
Mortality (follow-up unclear)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/35 (0%)	1/52 (1.9%)	Peto OR 0.19 (0 to 10.22)	16 fewer per 1000 (from 19 fewer to 148 more)	⊕OOO VERY LOW	CRITICAL
Mortality (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/97 (0%)	9/100 (9%)	Peto OR 0.13 (0.03 to 0.49)	77 fewer per 1000 (from 44 fewer to 87 fewer)	⊕OOO VERY LOW	CRITICAL
Additional parenteral nutrition (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	5/97 (5.2%)	13/100 (13%)	RR 0.4 (0.15 to 1.07)	78 fewer per 1000 (from 110 fewer to 9 more)	⊕OOO VERY LOW	IMPORTANT
Pancreatic infections - adjusted data - Infected pancreatic necrosis (follow-up unclear)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	7/47 (14.9%)	9/48 (18.8%)	OR 0.66 (0.22 to 1.95)	55 fewer per 1000 (from 139 fewer to 123 more)	⊕OOO VERY LOW	IMPORTANT
Pancreatic infections - adjusted data - Infected pancreatic necrosis or infected fluid collection (Copy) (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	4/97 (4.1%)	18/100 (18%)	OR 0.24 (0.07 to 0.86)	Not estimable[3]	⊕OOO VERY LOW	IMPORTANT
Infections - Pancreatic infections (follow-up unclear)												
1	observational	very	no serious	no serious	very serious[2]	none	1/35	6/52	RR 0.25	87 fewer per 1000	⊕OOO	IMPORTANT

	studies	serious[1]	inconsistency	indirectness			(2.9%)	(11.5%)	(0.03 to 1.97)	(from 112 fewer to 112 more)	VERY LOW	
Infections - Extra-pancreatic infections												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	26/97 (26.8%)	39/100 (39%)	RR 0.69 (0.46 to 1.04)	121 fewer per 1000 (from 211 fewer to 16 more)	⊕OOO VERY LOW	IMPORTANT
Infections - Systemic infections (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/97 (2.1%)	4/100 (4%)	RR 0.52 (0.1 to 2.75)	19 fewer per 1000 (from 36 fewer to 70 more)	⊕OOO VERY LOW	IMPORTANT
Infections - Extra-pancreatic or systemic infections (follow-up unclear)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	2/35 (5.7%)	15/52 (28.8%)	RR 0.2 (0.05 to 0.81)	231 fewer per 1000 (from 55 fewer to 274 fewer)	⊕OOO VERY LOW	IMPORTANT
Serious adverse events - Organ failure (follow-up unclear)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	15/47 (31.9%)	24/48 (50%)	OR 0.51 (0.22 to 1.18)	162 fewer per 1000 (from 320 fewer to 41 more)	⊕OOO VERY LOW	IMPORTANT
Serious adverse events -Multi-organ failure (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	9/97 (9.3%)	16/100 (16%)	RR 0.58 (0.27 to 1.25)	67 fewer per 1000 (from 117 fewer to 40 more)	⊕OOO VERY LOW	IMPORTANT
Adverse events - Pancreatic complications (necrosis, pseudocyst, ascites, haemorrhage, fistula) (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	31/35 (88.6%)	50/52 (96.2%)	RR 0.92 (0.81 to 1.05)	77 fewer per 1000 (from 183 fewer to 48 more)	⊕OOO VERY LOW	IMPORTANT
Adverse events - Pancreatic complications (necrosis, pseudocyst, ascites, haemorrhage, fistula) (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	63/97 (64.9%)	86/100 (86%)	RR 0.76 (0.64 to 0.89)	206 fewer per 1000 (from 95 fewer to 310 fewer)	⊕OOO VERY LOW	IMPORTANT

Adverse events - Operative intervention (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	2/35 (5.7%)	11/52 (21.2%)	RR 0.27 (0.06 to 1.15)	154 fewer per 1000 (from 199 fewer to 32 more)	⊕OOO VERY LOW	IMPORTANT
Adverse events - Operative intervention (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	7/97 (7.2%)	11/100 (11%)	RR 0.66 (0.27 to 1.62)	37 fewer per 1000 (from 80 fewer to 68 more)	⊕OOO VERY LOW	IMPORTANT
Adverse events - Feeding complications (abnormal glucose metabolism)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	22/35 (62.9%)	31/52 (59.6%)	RR 1.05 (0.75 to 1.48)	30 more per 1000 (from 149 fewer to 286 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.
[3] Absolute risk difference could not be calculated because adjusted control group event rates were not reported.

J.9 Early versus late nutritional intervention in people with chronic pancreatitis

None

J.10 Specialist versus non-specialist nutritional assessment in people with chronic pancreatitis

None

J.11 Prophylactic antimicrobial agents to prevent infection in people with acute pancreatitis

J.11.1 Clinical evidence profile: Antibiotic prophylaxis versus no therapy

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Antibiotic therapy	No therapy	Relative (95% CI)	Absolute		
Mortality (follow-up 1-6 weeks)												
6	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	13/172 (7.6%)	15%	RR 0.48 (0.26 to 0.91)	78 fewer per 1000 (from 13 fewer to 111 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Mortality (Selective decontamination)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	11/50 (22%)	18/52 (34.6%)	RR 0.64 (0.33 to 1.21)	125 fewer per 1000 (from 232 fewer to 73 more)	⊕⊕⊕O MODERATE	CRITICAL
Length of hospital stay (follow-up 10 days; Better indicated by lower values)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	34	40	-	MD 1.67 higher (4.3 lower to 7.64 higher)	⊕OOO VERY LOW	CRITICAL
Infected necrosis (follow-up 1-6 weeks)												
5	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	23/136 (16.9%)	30.3%	RR 0.54 (0.35 to 0.84)	139 fewer per 1000 (from 48 fewer to 197 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Infected necrosis (Selective decontamination)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	9/50 (18%)	20/52 (38.5%)	RR 0.47 (0.24 to 0.93)	204 fewer per 1000 (from 27 fewer to 292 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Infected necrosis (Peri-pancreatic infection) (follow-up 5-14 days)												
2	randomised trials	serious[1]	serious[2]	no serious indirectness	very serious[3]	none	24/66 (36.4%)	39.5	RR 0.97 (0.66 to 1.41)	12 fewer per 1000 (from 134 fewer to 162 more)	⊕OOO VERY LOW	IMPORTANT
Extra-pancreatic infection (follow-up 1-6 weeks)												
6	randomised trials	no serious risk of bias	very serious[2]	no serious indirectness	very serious[3]	none	33/175 (18.9%)	40.5%	RR 0.47 (0.17 to 1.26)	215 fewer per 1000 (from 336 fewer to 105 more)	⊕OOO VERY LOW	IMPORTANT

Extra-pancreatic infection (Blood culture positive sepsis) (follow-up 14 days)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	4/30 (13.3%)	8/30 (26.7%)	RR 0.5 (0.17 to 1.48)	133 fewer per 1000 (from 221 fewer to 128 more)	⊕OOO VERY LOW	IMPORTANT
Extra-pancreatic infection (Pneumonia/ARDS) (follow-up 14 days)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	11/30 (36.7%)	17/30 (56.7%)	RR 0.65 (0.37 to 1.14)	198 fewer per 1000 (from 357 fewer to 79 more)	⊕⊕OO LOW	IMPORTANT
Extra-pancreatic infection (Urinary tract infection) (follow-up 14 days)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	6/30 (20%)	17/30 (56.7%)	RR 0.35 (0.16 to 0.77)	368 fewer per 1000 (from 130 fewer to 476 fewer)	⊕⊕OO LOW	IMPORTANT
Serious adverse events (Multiorgan failure) (follow-up 1-6 weeks)												
4	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	47/117 (40.2%)	39.4%	RR 0.93 (0.73 to 1.2)	28 fewer per 1000 (from 106 fewer to 79 more)	⊕⊕⊕O MODERATE	IMPORTANT
Serious adverse events (major organ complications) <6 months												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	5/25 (20%)	11/33 (33.3%)	RR 0.6 (0.24 to 1.51)	133 fewer per 1000 (from 253 fewer to 170 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 or 2 increments because of heterogeneity unexplained by subgroup analysis
[3] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.11.2 Clinical evidence profile: Antibiotic prophylaxis versus placebo

Quality assessment							No of patients		Effect		Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Antibiotic therapy	Placebo	Relative (95% CI)	Absolute		
Mortality (follow-up 10-42 days)												
3	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	17/130 (13.1%)	10.5%	RR 1.09 (0.58 to 2.08)	9 more per 1000 (from 44 fewer to 113 more)	⊕OOO VERY LOW	CRITICAL
Infected necrosis (follow-up 10-42 days)												
3	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	24/120 (20%)	15%	RR 1.18 (0.7 to 2)	27 more per 1000 (from 45 fewer to 150 more)	⊕OOO VERY LOW	CRITICAL
Extra-pancreatic infection (follow-up 10-42 days)												
3	randomised trials	no serious risk of bias[1]	no serious inconsistency	no serious indirectness	serious[2]	none	35/130 (26.9%)	36.4%	RR 0.77 (0.53 to 1.11)	84 fewer per 40 (from 171 fewer to 40 more)	⊕⊕⊕O MODERATE	IMPORTANT
Serious adverse events <6 months (follow-up 42 days)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	6/50 (12%)	9/50 (18%)	RR 0.67 (0.26 to 1.73)	59 fewer per 1000 (from 133 fewer to 131 more)	⊕OOO VERY LOW	IMPORTANT
Serious adverse events (Pulmonary insufficiency) (follow-up 21 days)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	26/58 (44.8%)	25/55 (45.5%)	RR 0.99 (0.66 to 1.48)	5 fewer per 1000 (from 155 fewer to 218 more)	⊕OOO VERY LOW	IMPORTANT
Serious adverse events (Renal insufficiency) (follow-up 21 days)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	7/58 (12.1%)	6/55 (10.9%)	RR 1.11 (0.4 to 3.09)	12 more per 1000 (from 65 fewer to 228 more)	⊕OOO VERY LOW	IMPORTANT
Serious adverse events (Shock) (follow-up 21 days)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	5/58 (8.6%)	7/55 (12.7%)	RR 0.68 (0.23 to 2.01)	41 fewer per 1000 (from 98 fewer to 129 more)	⊕OOO VERY LOW	IMPORTANT
Serious adverse events (SIRS) (follow-up 21 days)												
1	randomised	serious[1]	no serious	no serious	serious[2]	none	31/58	24/55	RR 1.22	96 more per 1000 (from	⊕⊕OO	IMPORTANT

	trials		inconsistency	indirectness			(53.4%)	(43.6%)	(0.83 to 1.8)	74 fewer to 349 more)	LOW	
Serious adverse event (multiorgan failure)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	13/22 (59.1%)	10/19 (52.6%)	RR 1.12 (0.65 to 1.95)	63 more per 1000 (from 184 fewer to 500 more)	⊕OOO VERY LOW	IMPORTANT
Colonisation by resistant organism <6 months (follow-up 42 days)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	5/40 (12.5%)	2/40 (5%)	RR 2.5 (0.51 to 12.14)	75 more per 1000 (from 25 fewer to 557 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.11.3 Clinical evidence profile: Prophylactic antimicrobial therapy versus other prophylactic antimicrobial therapy (Same class; Carbapenems)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Meropenem**	**Imipenem**	**Relative (95% CI)**	**Absolute**		
Mortality (follow-up 14 days)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	12/88 (13.6%)	10/88 (11.4%)	RR 1.2 (0.55 to 2.63)	23 more per 1000 (from 51 fewer to 185 more)	⊕OOO VERY LOW	CRITICAL
Infected necrosis (follow-up 14 days)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	10/88 (11.4%)	12/88 (13.6%)	RR 0.83 (0.38 to 1.83)	23 fewer per 1000 (from 85 fewer to 113 more)	⊕OOO VERY LOW	CRITICAL
Extra-pancreatic infection (follow-up 14 days)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	19/88 (21.6%)	21/88 (23.9%)	RR 0.9 (0.52 to 1.56)	24 fewer per 1000 (from 115 fewer to 134 more)	⊕OOO VERY	IMPORTANT

											LOW	
Serious adverse event (Multiorgan failure) (follow-up 14 days)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	6/88 (6.8%)	8/88 (9.1%)	RR 0.75 (0.27 to 2.07)	23 fewer per 1000 (from 66 fewer to 97 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.11.4 Prophylactic antimicrobial therapy versus other prophylactic antimicrobial therapy (Different class; Quinolones versus carbapenems)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Pefloxacin**	**Imipenem**	**Relative (95% CI)**	**Absolute**		
Mortality (follow-up 2 weeks)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	5/30 (16.7%)	3/30 (10%)	RR 1.67 (0.44 to 6.36)	67 more per 1000 (from 56 fewer to 536 more)	⊕OOO VERY LOW	CRITICAL
Infected necrosis (follow-up 2 weeks)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	10/30 (33.3%)	3/30 (10%)	RR 3.33 (1.02 to 10.92)	233 more per 1000 (from 2 more to 992 more)	⊕⊕OO LOW	CRITICAL
Extra-pancreatic infection (follow-up 2 weeks)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	13/30 (43.3%)	6/30 (20%)	RR 2.17 (0.95 to 4.94)	234 more per 1000 (from 10 fewer to 788 more)	⊕⊕OO LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.12 Methods of management of infected necrosis in people with acute pancreatitis

J.12.1 Clinical evidence profile: Minimally invasive surgery versus open surgery

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Minimally invasive surgery	Open surgery	Relative (95% CI)	Absolute		
Mortality (follow-up during admission)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	8/43 (18.6%)	7/45 (15.6%)	RR 1.2 (0.47 to 3.01)	31 more per 1000 (from 82 fewer to 313 more)	⊕⊕OO LOW	CRITICAL
Enterocutaneous fistula or perforation of a visceral organ requiring intervention (follow-up during admission)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	6/43 (14%)	10/45 (22.2%)	RR 0.63 (0.25 to 1.58)	82 fewer per 1000 (from 167 fewer to 129 more)	⊕⊕OO LOW	IMPORTANT
Intraabdominal bleeding (follow-up during admission)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	7/43 (16.3%)	10/45 (22.2%)	RR 0.73 (0.31 to 1.75)	60 fewer per 1000 (from 153 fewer to 167 more)	⊕⊕OO LOW	IMPORTANT
Multiple organ failure (follow-up during admission)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	5/43 (11.6%)	18/45 (40%)	RR 0.29 (0.12 to 0.71)	284 fewer per 1000 (from 116 fewer to 352 fewer)	⊕⊕⊕⊕ HIGH	IMPORTANT
Multiple systemic complications (follow-up during admission)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	0/43 (0%)	1/45 (2.2%)	RR 0.35 (0.01 to 8.33)	14 fewer per 1000 (from 22 fewer to 163 more)	⊕⊕⊕O MODERATE	IMPORTANT

New onset multiple organ failure (follow-up during admission)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	5/43 (11.6%)	19/45 (42.2%)	RR 0.28 (0.11 to 0.67)	304 fewer per 1000 (from 139 fewer to 376 fewer)	⊕⊕⊕⊕ HIGH	IMPORTANT
New onset diabetes (follow-up during admission)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	7/43 (16.3%)	17/45 (37.8%)	RR 0.43 (0.2 to 0.93)	215 fewer per 1000 (from 26 fewer to 302 fewer)	⊕⊕⊕O MODERATE	IMPORTANT
Use of pancreatic enzymes (follow-up during admission)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	3/43 (7%)	15/45 (33.3%)	RR 0.21 (0.07 to 0.67)	263 fewer per 1000 (from 110 fewer to 310 fewer)	⊕⊕⊕⊕ HIGH	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.12.2 Clinical evidence profile: Minimally invasive surgery (endoscopic) versus open surgery

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Endoscopic**	**Open**	**Relative (95% CI)**	**Absolute**		
Mortality (follow-up during admission)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	No serious imprecision	none	11/127 (8.7%)	34/127 (26.8%)	RR 0.32 (0.18 to 0.58)	182 fewer per 1000 (from 182 fewer to 220 fewer)[2]	⊕OOO VERY LOW	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Absolute risk not adjusted for paired data

J.12.3 Clinical evidence profile: Minimally invasive surgery (endoscopic) versus minimally invasive surgery (percutaneous)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Endoscopic	Percutaneous	Relative (95% CI)	Absolute		
Mortality (follow-up during admission)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	3/11 (27.3%)	3/13 (23.1%)	RR 1.18 (0.3 to 4.72)	42 more per 1000 (from 162 fewer to 858 more)	⊕OOO VERY LOW	CRITICAL
Length of stay (hospital) (Better indicated by lower values) (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	11	13	-	MD 26 lower (50.96 to 1.04 lower)	⊕OOO VERY LOW	CRITICAL
Length of stay (CCU) (Better indicated by lower values) (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	11	13	-	MD 8 lower (20.44 lower to 4.44 higher)	⊕OOO VERY LOW	CRITICAL
Complications (new-onset organ failure) (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/11 (18.2%)	2/13 (15.4%)	RR 1.18 (0.2 to 7.06)	28 more per 1000 (from 123 fewer to 932 more)	⊕OOO VERY LOW	CRITICAL
Complications (multiple organ failure) (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/11 (9.1%)	0/13 (0%)	Peto OR 8.86 (0.17 to 452.79)	91 more per 1000 (from 120 fewer to 302 more)[3]	⊕OOO VERY LOW	CRITICAL
Complications (upper gastrointestinal bleeding) (follow-up during admission)												

1	observational studies	very serious[2]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/11 (9.1%)	0/13 (0%)	Peto OR 8.86 (0.17 to 452.79)	91 more per 1000 (from 120 fewer to 302 more)[3]	⊕OOO VERY LOW	CRITICAL
Complications (intra-abdominal bleeding requiring intervention) (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/11 (9.1%)	2/13 (15.4%)	RR 0.59 (0.06 to 5.68)	63 fewer per 1000 (from 145 fewer to 720 more)	⊕OOO VERY LOW	CRITICAL
Complications (enterocutaneous fistula or perforation) (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/11 (9.1%)	5/13 (38.5%)	RR 0.24 (0.03 to 1.73)	292 fewer per 1000 (from 373 fewer to 281 more)	⊕OOO VERY LOW	CRITICAL
Complications (Pancreatic fistula) (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/11 (0%)	1/13 (7.7%)	OR 0.16 (0 to 8.06)	64 fewer per 1000 (from 77 fewer to 325 more)	⊕OOO VERY LOW	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.
[3] Risk difference calculated in Review Manager

J.12.4 Clinical evidence profile: Endoscopic step-up compared to minimally-invasive surgical step-up approach

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Endoscopic step-up**	**Surgical step-up**	**Relative (95% CI)**	**Absolute**		
Mortality (follow-up 6 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	9/51 (17.6%)	12.8%	RR 1.38 (0.53 to 3.59)	49 more per 1000 (from 60 fewer to 332 more)	⊕⊕OO LOW	CRITICAL
Length of hospital stay (follow-up 6 months; Better indicated by lower values)												

1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	51	47	-	MD 16 lower (32.86 lower to 0.86 higher)	⊕⊕⊕O MODERATE	CRITICAL
Complications - Bleeding requiring reintervention (follow-up 6 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	11/51 (21.6%)	21.3%	RR 1.01 (0.47 to 2.17)	2 more per 1000 (from 113 fewer to 249 more)	⊕⊕OO LOW	IMPORTANT
Complications - New onset multiple organ failure (follow-up 6 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	2/51 (3.9%)	12.8%	RR 0.31 (0.07 to 1.45)	88 fewer per 1000 (from 119 fewer to 58 more)	⊕⊕OO LOW	IMPORTANT
Complications - New onset single organ failure (follow-up 6 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	7/51 (13.7%)	27.7%	RR 0.5 (0.22 to 1.14)	139 fewer per 1000 (from 216 fewer to 39 more)	⊕⊕⊕O MODERATE	IMPORTANT
Complications - Pancreatic fistula (follow-up 6 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	2/42 (4.8%)	31.7%	RR 0.15 (0.04 to 0.62)	269 fewer per 1000 (from 120 fewer to 304 fewer)	⊕⊕⊕⊕ HIGH	IMPORTANT
Complications - Perforation of visceral organ or enterocutaneous fistula requiring intervention (follow-up 6 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	4/51 (7.8%)	17%	RR 0.46 (0.15 to 1.43)	92 fewer per 1000 (from 145 fewer to 73 more)	⊕⊕OO LOW	IMPORTANT
Pancreatic function - Endocrine insufficiency (follow-up 6 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	10/42 (23.8%)	22%	RR 1.08 (0.49 to 2.39)	18 more per 1000 (from 112 fewer to 306 more)	⊕⊕OO LOW	IMPORTANT
Pancreatic function - Exocrine insufficiency (follow-up 6 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	22/42 (52.4%)	46.3%	RR 1.13 (0.73 to 1.75)	60 more per 1000 (from 125 fewer to 347 more)	⊕⊕OO LOW	IMPORTANT

[1] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.12.5 Clinical evidence profile: Dual modality drainage versus percutaneous drainage

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Dual modality drainage	Percutaneous drainage	Relative (95% CI)	Absolute		
Mortality (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/49 (4.1%)	3/45 (6.7%)	RR 0.61 (0.11 to 3.5)	26 fewer per 1000 (from 59 fewer to 167 more)	⊕OOO VERY LOW	CRITICAL
Length of stay in hospital (Better indicated by lower values) (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	49	45	-	MD 30 lower (43.6 to 16.4 lower)	⊕OOO VERY LOW	CRITICAL
Psedoaneurysm (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/49 (0%)	5/45 (11.1%)	Peto OR 0.11 (0.02 to 0.68)	98 fewer per 1000 (from 33 fewer to 109 fewer)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.12.6 Clinical evidence profile: Minimally invasive surgery versus open surgery

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Minimally invasive surgery	Open surgery	Relative (95% CI)	Absolute		

Mortality (follow-up unclear)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	2/18 (11.1%)	34/88 (38.6%)	RR 0.29 (0.08 to 1.09)	274 fewer per 1000 (from 355 fewer to 35 more)	⊕OOO VERY LOW	CRITICAL
Mortality (follow-up during admission)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	64/334 (19.2%)	80/335 (23.9%)	RR 0.75 (0.57 to 0.98)	60 fewer per 1000 (from 5 fewer to 103 fewer)[3]	⊕OOO VERY LOW	CRITICAL
Complications (Bleeding) (follow-up unclear)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	3/18 (16.7%)	30/88 (34.1%)	RR 0.49 (0.17 to 1.43)	174 fewer per 1000 (from 283 fewer to 147 more)	⊕OOO VERY LOW	IMPORTANT
Complications (Bowel perforation) (follow-up unclear)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	3/18 (16.7%)	18/88 (20.5%)	RR 0.81 (0.27 to 2.48)	39 fewer per 1000 (from 149 fewer to 303 more)	⊕OOO VERY LOW	IMPORTANT
Number of procedures (Reintervention) (follow-up unclear)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	12/18 (66.7%)	64/88 (72.7%)	RR 0.92 (0.65 to 1.3)	58 fewer per 1000 (from 255 fewer to 218 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Absolute risk not adjusted for paired data
[3] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.12.7 Clinical evidence profile: Step-up approach versus open surgery

Quality assessment							No of patients		Effect		Quality	Importance
No of	Design	Risk of	Inconsistency	Indirectness	Imprecision	Other	Step-up	Open	Relative	Absolute		

studies		bias				considerations	approach	surgery	(95% CI)			
Mortality (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	20/190 (10.5%)	10/30 (33.3%)	RR 0.32 (0.16 to 0.61)	227 fewer per 1000 (from 130 fewer to 280 fewer)	⊕OOO VERY LOW	CRITICAL
Severe complication (Sepsis, persistent MODS or erosion bleeding) (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	85/190 (44.7%)	25/30 (83.3%)	RR 0.54 (0.43 to 0.67)	383 fewer per 1000 (from 275 fewer to 475 fewer)	⊕OOO VERY LOW	IMPORTANT
Emergence of type 3c diabetes (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	9/190 (4.7%)	10/30 (33.3%)	RR 0.14 (0.06 to 0.32)	287 fewer per 1000 (from 227 fewer to 313 fewer)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

J.12.8 Clinical evidence profile: Focused open necrosectomy versus conventional open necrosectomy

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Focused open necrosectomy	Conventional open necrosectomy	Relative (95% CI)	Absolute		
Mortality (follow-up during admission)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/31 (6.5%)	5/39 (12.8%)	RR 0.5 (0.1 to 2.42)	64 fewer per 1000 (from 115 fewer to 182 more)	⊕OOO VERY LOW	CRITICAL
Intestinal fistulae (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/31 (12.9%)	3/39 (7.7%)	RR 1.68 (0.41 to	52 more per 1000 (from 45 fewer to	⊕OOO VERY	IMPORTANT

									6.94)	457 more)	LOW	
Pancreatic fistulae (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/31 (12.9%)	5/39 (12.8%)	RR 1.01 (0.29 to 3.43)	1 more per 1000 (from 91 fewer to 312 more)	⊕OOO VERY LOW	IMPORTANT
Repeat necrosectomy (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	8/31 (25.8%)	18/39 (46.2%)	RR 0.56 (0.28 to 1.11)	203 fewer per 1000 (from 332 fewer to 51 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.12.9 Clinical evidence profile: Percutaneous drainage versus laparotomy plus necrosectomy plus active drainage

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**PCD**	**Lap + Nec + Active drainage**	**Relative (95% CI)**	**Absolute**		
Mortality (follow-up perioperative)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/10 (10%)	1/5 (20%)	RR 0.5 (0.04 to 6.44)	100 fewer per 1000 (from 192 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Complications (Wound infection, haemorrhage at surgical site, pancreatic fistula, intestinal fistula) (follow-up perioperative)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	2/10 (20%)	5/5 (100%)	RR 0.25 (0.08 to 0.76)	750 fewer per 1000 (from 240 fewer to 920 fewer)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.12.10 Clinical evidence profile: Percutaneous drainage versus laparotomy plus necrosectomy plus passive drainage

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	PCD	Lap + Nec + Passive drainage	Relative (95% CI)	Absolute		
Mortality (follow-up perioperative)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	1/10 (10%)	5/7 (71.4%)	RR 0.14 (0.02 to 0.95)	614 fewer per 1000 (from 36 fewer to 700 fewer)	⊕OOO VERY LOW	CRITICAL
Complications (Wound infection, haemorrhage at sugical site, pancreatic fistula, intestinal fistula) (follow-up perioperative)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	2/10 (20%)	7/7 (100%)	RR 0.24 (0.08 to 0.73)	760 fewer per 1000 (from 270 fewer to 920 fewer)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.12.11 Clinical evidence profile: Percutaneous drainage plus VARD versus laparotomy plus necrosectomy plus active drainage

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	PCD + VARD	Lap + Nec + AD	Relative (95% CI)	Absolute		
Mortality (follow-up perioperative)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	2/12 (16.7%)	1/5 (20%)	RR 0.83 (0.1 to 7.24)	34 fewer per 1000 (from 180 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Complications (Wound infection, haemorrhage at surgical site, pancreatic fistula, intestinal fistula) (follow-up perioperative)												

1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	6/12 (50%)	5/5 (100%)	RR 0.55 (0.3 to 0.99)	450 fewer per 1000 (from 10 fewer to 700 fewer)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.12.12 Clinical evidence profile: Percutaneous drainage plus VARD versus laparotomy plus necrosectomy plus passive drainage

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**PCD + VARD**	**Lap + Nec + PD**	**Relative (95% CI)**	**Absolute**		
Mortality (follow-up perioperative)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	2/12 (16.7%)	5/7 (71.4%)	RR 0.23 (0.06 to 0.9)	550 fewer per 1000 (from 71 fewer to 671 fewer)	⊕OOO VERY LOW	CRITICAL
Complications (Wound infection, haemorrhage at surgical site, pancreatic fistula, intestinal fistula) (follow-up perioperative)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	6/12 (50%)	7/7 (100%)	RR 0.53 (0.3 to 0.95)	470 fewer per 1000 (from 50 fewer to 700 fewer)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.12.13 Clinical evidence profile: Percutaneous drainage plus VARD versus percutaneous drainage

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**PCD + VARD**	**PCD**	**Relative (95% CI)**	**Absolute**		
Mortality (follow-up perioperative)												

1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/12 (16.7%)	1/10 (10%)	RR 1.67 (0.18 to 15.8)	67 more per 1000 (from 82 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Complications (Wound infection, haemorrhage at surgical site, pancreatic fistula, intestinal fistula) (follow-up perioperative)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	6/12 (50%)	2/10 (20%)	RR 2.5 (0.64 to 9.77)	300 more per 1000 (from 72 fewer to 1000 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.12.14 Clinical evidence profile: Percutaneous drainage versus laparotomy

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Percutaneous drainage**	**Laparotomy**	**Relative (95% CI)**	**Absolute**		
Mortality (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	1/15 (6.7%)	6/15 (40%)	RR 0.17 (0.02 to 1.22)	332 fewer per 1000 (from 392 fewer to 88 more)	⊕OOO VERY LOW	CRITICAL
Bleeding (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/15 (26.7%)	1/15 (6.7%)	RR 4 (0.5 to 31.74)	200 more per 1000 (from 33 fewer to 1000 more)	⊕OOO VERY LOW	IMPORTANT
Bowel perforation (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/15 (6.7%)	2/15 (13.3%)	RR 0.5 (0.05 to 4.94)	67 fewer per 1000 (from 127 fewer to 525 more)	⊕OOO VERY LOW	IMPORTANT
GI fistulas (follow-up during admission)												

1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/15 (6.7%)	3/15 (20%)	RR 0.33 (0.04 to 2.85)	134 fewer per 1000 (from 192 fewer to 370 more)	⊕OOO VERY LOW	IMPORTANT
Pancreatic fistulas (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/15 (13.3%)	0/15 (0%)	Peto OR 7.94 (0.47 to 133.26)	-	⊕OOO VERY LOW	IMPORTANT
Further necrosectomy (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	11/15 (73.3%)	13/15 (86.7%)	RR 0.85 (0.59 to 1.22)	130 fewer per 1000 (from 355 fewer to 191 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.12.15 Minimally invasive surgery (direct endoscopic necrosectomy) versus step-up approach

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Minimally invasive surgery**	**Step-up approach**	**Relative (95% CI)**	**Absolute**		
Mortality (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/12 (0%)	0/12 (0%)	Not estimable	No events	⊕OOO VERY LOW	CRITICAL
Floor length of stay (Better indicated by lower values) (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	12	12	-	MD 18.3 lower (22.07 to 14.53	⊕OOO VERY	IMPORTANT

										lower)	LOW	
Complications (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	1/12 (8.3%)	8/12 (66.7%)	RR 0.13 (0.02 to 0.85)	580 fewer per 1000 (from 100 fewer to 653 fewer)	⊕OOO VERY LOW	IMPORTANT
Number of procedures (Better indicated by lower values) (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	12	12	-	MD 1.3 lower (1.5 to 1.1 lower)	⊕OOO VERY LOW	IMPORTANT
Pancreatic function (new exocrine insufficiency) (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	3/12 (25%)	5/12 (41.7%)	RR 0.6 (0.18 to 1.97)	167 fewer per 1000 (from 342 fewer to 404 more)	⊕OOO VERY LOW	IMPORTANT
Pancreatic function (new endocrine insufficiency) (follow-up during admission)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/12 (0%)	7/12 (58.3%)	Peto OR 0.07 (0.01 to 0.37)	494 fewer per 1000 (from 242 fewer to 570 fewer)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.13 Timing of management of infected necrosis in people with acute pancreatitis

J.13.1 Clinical evidence profile: late intervention versus early intervention

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Late intervention**	**Early intervention**	**Relative (95% CI)**	**Absolute**		

OF: Mortality												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	3/21 (14.3%)	23/61 (37.7%)	RR 0.38 (0.13 to 1.13)	234 fewer per 1000 (from 328 fewer to 49 more)	⊕OOO VERY LOW	CRITICAL
OF: Number of procedures (Re-intervention)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/21 (9.5%)	17/61 (27.9%)	RR 0.34 (0.09 to 1.36)	184 fewer per 1000 (from 254 fewer to 100 more)	⊕OOO VERY LOW	IMPORTANT
OF: Complications (Intra-abdominal bleeding)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	5/21 (23.8%)	24/61 (39.3%)	RR 0.61 (0.26 to 1.38)	153 fewer per 1000 (from 291 fewer to 150 more)	⊕OOO VERY LOW	IMPORTANT
OF: Complications (Enterocutaneous fistula)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	3/21 (14.3%)	6/61 (9.8%)	RR 1.45 (0.40 to 5.30)	44 more per 1000 (from 59 fewer to 423 more)	⊕OOO VERY LOW	IMPORTANT
OF: Complications (New-onset organ failure)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	6/21 (28.6%)	16/61 (26.2%)	RR 1.09 (0.49 to 2.42)	24 more per 1000 (from 134 fewer to 372 more)	⊕OOO VERY LOW	IMPORTANT
NOF: Mortality												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	6/66 (9.1%)	5/75 (6.7%)	RR 1.36 (0.44 to 4.26)	24 more per 1000 (from 37 fewer to 217 more)	⊕OOO VERY LOW	CRITICAL
NOF: Number of procedures (Re-intervention)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	3/66 (4.5%)	7/75 (9.3%)	RR 0.49 (0.13 to 1.81)	48 fewer per 1000 (from 81 fewer to 76 more)	⊕OOO VERY LOW	IMPORTANT
NOF: Complications (Intra-abdominal bleeding)												

1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	3/66 (4.5%)	3/75 (4%)	RR 1.14 (0.24 to 5.44)	6 more per 1000 (from 30 fewer to 178 more)	⊕OOO VERY LOW	IMPORTANT
NOF: Complications (Enterocutaneous fistula)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	9/66 (13.6%)	6/75 (8%)	RR 1.7 (0.64 to 4.54)	56 more per 1000 (from 29 fewer to 283 more)	⊕OOO VERY LOW	IMPORTANT
NOF: Complications (New-onset organ failure)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/66 (1.5%)	4/75 (5.3%)	RR 0.28 (0.03 to 2.48)	38 fewer per 1000 (from 52 fewer to 79 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.14 Management of pain in people with chronic pancreatitis

J.14.1 Clinical evidence profile: Pharmacological therapy (antioxidants) versus placebo

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Antioxidant**	**Placebo**	**Relative (95% CI)**	**Absolute**		
Quality of life (activities of daily living) - crossover trial (follow-up 10 weeks; range of scores: 0-120; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	13	13	-	MD 3.3 lower (10.3 lower to 3.7 higher)	⊕⊕OO LOW	CRITICAL
Quality of life (EQ-5D) (follow-up 6 months; range of scores: 0-1; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	33	37	-	MD 0.04 higher (0.1 lower to 0.18 higher)	⊕OOO VERY LOW	CRITICAL

Quality of life (EQ-5D VAS) (follow-up 6 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	33	37	-	MD 2.3 higher (6.5 lower to 11.1 higher)	⊕⊕⊕O MODERATE	CRITICAL
Mortality (follow-up 6 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/76 (0%)	0/71 (0%)	-	0 fewer per 1000 (from 26 fewer to 26 more)	⊕⊕⊕O MODERATE	CRITICAL
Pain (visual analogue scale score) (follow-up 6 weeks - 6 months; range of scores: 0-10; Better indicated by lower values)												
3	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	54	57	-	MD 0.27 lower (0.69 lower to 0.15 higher)	⊕⊕⊕O MODERATE	CRITICAL
Pain (descriptive scale) (follow-up 10 weeks; range of scores: 0-5; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	13	13	-	MD 0.09 lower (0.29 lower to 0.11 higher)	⊕⊕OO LOW	CRITICAL
Pain (numerical rating scale) (follow-up 10 weeks; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	13	13	-	MD 0.25 lower (0.72 lower to 0.22 higher)	⊕⊕OO LOW	CRITICAL
Pain (reduction in pain medication) - Oral analgesic tablets per month (follow-up 6 months; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	71	56	-	MD 6.15 higher (3.02 to 9.28 higher)	⊕⊕⊕O MODERATE	CRITICAL
Pain (reduction in pain medication) - parallel trials - Parenteral analgesic injections per month (follow-up 6 months; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	71	56	-	MD 0.7 higher (0.5 lower to 1.9 higher)	⊕⊕OO LOW	CRITICAL
Pain (reduction in number of painful days per month) - parallel trials (follow-up 6 months; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	66	53	-	MD 4.16 higher (2.21 to 6.11 higher)	⊕⊕⊕O MODERATE	CRITICAL
Pain-free participants (follow-up 1 day - 6 months)												

3	randomised trials	serious[1]	serious[3]	no serious indirectness	serious[2]	none	64/136 (47.1%)	31.4%	RR 1.73 (0.95 to 3.15)	229 more per 1000 (from 16 fewer to 675 more)	⊕OOO VERY LOW	CRITICAL
Adverse effects (follow-up 10 weeks - 6 months)												
3	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	21/117 (17.9%)	5.4%	RR 3.44 (1.30 to 9.09)	132 more per 1000 (from 16 more to 437 more)	⊕⊕⊕O MODERATE	CRITICAL
Adverse effects (follow-up 6 - 20 weeks)												
3	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	3/47 (6.4%)	0/46 (0%)	Peto OR 8.28 (0.81 to 84.88)	64 more per 1000 (from 15 fewer to 143 more)	⊕OOO VERY LOW	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[3] Downgraded by 1 or 2 increments because heterogeneity, I2=71%, p= >0.1, unexplained by subgroup analysis

J.14.2 Clinical evidence profile: Enzyme replacement therapy versus placebo

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Enzyme replacement therapy**	**Placebo**	**Relative (95% CI)**	**Absolute**		
Pain (People experiencing long-lasting (>12 hour) pain attacks) (follow-up 4 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	14/22 (63.6%)	11/22 (50%)	RR 1.27 (0.75 to 2.15)	135 more per 1000 (from 125 fewer to 575 more)	⊕⊕OO LOW	CRITICAL
Pain (Use of analgesics) (follow-up 4 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	10/22 (45.5%)	5/22 (22.7%)	RR 2 (0.82 to 4.9)	227 more per 1000 (from 41 fewer to 886 more)	⊕⊕OO LOW	CRITICAL

Pain (Pain score) (follow-up 2 weeks; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	47	47	-	MD 0.18 lower (25.63 lower to 25.27 higher)	⊕⊕OO LOW	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.15 Management of pancreatic duct obstruction in people with chronic pancreatitis

J.15.1 Clinical evidence profile: ESWL and endotherapy versus surgery

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ESWL plus endotherapy	Surgery	Relative (95% CI)	Absolute		
QoL (SF-36; Mental health component at 2 years) (follow-up 2 years; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	19	20	-	MD 5 lower (10.65 lower to 0.65 higher)	⊕⊕OO LOW	CRITICAL
QoL (SF-36; Mental health component at 7 years) (follow-up 7 years; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	15	15	-	MD 2 lower (8.81 lower to 4.81 higher)	⊕OOO VERY LOW	CRITICAL
QoL (SF-36; Physical health component at 2 years) (follow-up 2 years; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	19	20	-	MD 9 lower (14.08 to 3.92 lower)	⊕⊕OO LOW	CRITICAL
QoL (SF-36; Physical health component at 7 years) (follow-up 7 years; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	16	15	-	MD 5 lower (12.06 lower to 2.06 higher)	⊕OOO VERY LOW	CRITICAL
Mortality (follow-up 2 years)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	1/19 (5.3%)	0/20 (0%)	Peto OR 7.79 (0.15 to 393.02)	-	⊕⊕OO LOW	CRITICAL
Pain (Pain relief at 2 years) (follow-up 2 years)												

1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	6/19 (31.6%)	15/20 (75%)	RR 0.42 (0.21 to 0.86)	435 fewer per 1000 (from 105 fewer to 593 fewer)	⊕⊕OO LOW	CRITICAL
Pain (Pain relief at 7 years) (follow-up 7 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	6/16 (37.5%)	12/15 (80%)	RR 0.47 (0.24 to 0.93)	424 fewer per 1000 (from 56 fewer to 608 fewer)	⊕OOO VERY LOW	CRITICAL
Pain (Izbicki pain score at 2 years) (follow-up 2 years; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	19	20	-	MD 26 higher (13.75 to 38.25 higher)	⊕OOO VERY LOW	CRITICAL
Pain (Izbicki pain score at 7 years) (follow-up 7 years; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	16	15	-	MD 17 higher (3.84 lower to 37.84 higher)	⊕OOO VERY LOW	CRITICAL
Pancreatic function (Endocrine insufficiency developed at 2 years) (follow-up 2 years)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	3/19 (15.8%)	1/20 (5%)	RR 3.16 (0.36 to 27.78)	108 more per 1000 (from 32 fewer to 1000 more)	⊕⊕OO LOW	IMPORTANT
Pancreatic function (Endocrine insufficiency developed at 7 years) (follow-up 7 years)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	7/16 (43.8%)	3/15 (20%)	RR 2.19 (0.69 to 6.94)	238 more per 1000 (from 62 fewer to 1000 more)	⊕OOO VERY LOW	IMPORTANT
Pancreatic function (Endocrine insufficiency persisted at 2 years) (follow-up 2 years)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	3/19 (15.8%)	4/20 (20%)	RR 0.79 (0.2 to 3.07)	42 fewer per 1000 (from 160 fewer to 414 more)	⊕⊕OO LOW	IMPORTANT
Pancreatic function (Endocrine insufficiency persisted at 7 years) (follow-up 7 years)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/16 (25%)	4/15 (26.7%)	RR 0.94 (0.28 to 3.09)	16 fewer per 1000 (from 192 fewer to 557 more)	⊕OOO VERY LOW	IMPORTANT

Pancreatic function (Exocrine insufficiency developed at 2 years) (follow-up 2 years)											
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	6/19 (31.6%)	1/20 (5%)	RR 6.32 (0.84 to 47.69)	266 more per 1000 (from 8 fewer to 1000 more)	⊕⊕⊕O MODERATE	IMPORTANT
Pancreatic function (Exocrine insufficiency developed at 7 years) (follow-up 7 years)											
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	6/16 (37.5%)	2/15 (13.3%)	RR 2.81 (0.67 to 11.83)	241 more per 1000 (from 44 fewer to 1000 more)	⊕OOO VERY LOW	IMPORTANT
Pancreatic function (Exocrine insufficiency persisted at 2 years) (follow-up 2 years)											
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	11/19 (57.9%)	13/20 (65%)	RR 0.89 (0.54 to 1.47)	72 fewer per 1000 (from 299 fewer to 306 more)	⊕⊕OO LOW	IMPORTANT
Pancreatic function (Exocrine insufficiency persisted at 7 years) (follow-up 7 years)											
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	10/16 (62.5%)	11/15 (73.3%)	RR 0.85 (0.52 to 1.39)	110 fewer per 1000 (from 352 fewer to 286 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.

[2]Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.15.2 Clinical evidence profile: Endotherapy versus surgery

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Endotherapy**	**Surgery**	**Relative (95% CI)**	**Absolute**		
Pain (Complete absence of abdominal pain) (follow-up 5 years)												

1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	5/36 (13.9%)	12/36 (33.3%)	RR 0.42 (0.16 to 1.06)	193 fewer per 1000 (from 280 fewer to 20 more)	⊕OOO VERY LOW	CRITICAL
Pain (Partial relief of abdominal pain) (follow-up 5 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	17/36 (47.2%)	19/36 (52.8%)	RR 0.89 (0.56 to 1.42)	58 fewer per 1000 (from 232 fewer to 222 more)	⊕OOO VERY LOW	CRITICAL
Pancreatic function (New onset diabetes) (follow-up 5 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	12/36 (33.3%)	14/36 (38.9%)	RR 0.86 (0.46 to 1.59)	54 fewer per 1000 (from 210 fewer to 229 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.

[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.15.3 Clinical evidence profile: ESWL versus ESWL and endotherapy

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**ESWL**	**ESWL plus endotherapy**	**Relative (95% CI)**	**Absolute**		
Pain (Pain relapse at 2 years) (follow-up 2 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	10/24 (41.7%)	13/24 (54.2%)	RR 0.77 (0.42 to 1.4)	125 fewer per 1000 (from 314 fewer to 217 more)	⊕OOO VERY LOW	CRITICAL
Pain (Pain intensity; VAS score) (follow-up mean 2 years; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	24	24	-	MD 0 higher (0.99 lower to 0.99 higher)	⊕OOO VERY	CRITICAL

											LOW	
Length of hospital stay (Better indicated by lower values) (follow-up 2 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	24	24	-	MD 5.5 lower (12.43 lower to 1.43 higher)	⊕OOO VERY LOW	IMPORTANT
Procedure related complications (follow-up 1 month)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	0/24 (0%)	1/24 (4.2%)	Peto OR 0.14 (0 to 6.82)	36 fewer per 1000 (from 42 fewer to 187 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.16 Management of small-duct disease in people with chronic pancreatitis

J.16.1 Clinical evidence profile: VSPL versus NCPB

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**VSPL**	**NCPB**	**Relative (95% CI)**	**Absolute**		
Pain (Use of opioids) (follow-up unclear)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	11/18 (61.1%)	17/30 (56.7%)	RR 1.08 (0.67 to 1.75)	45 more per 1000 (from 187 fewer to 425 more)	⊕OOO VERY LOW	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.17 Management of pseudocysts

J.17.1 Clinical evidence profile: Endoscopic drainage versus open surgical drainage or resection

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Endoscopic drainage	Surgical drainage or resection	Relative (95% CI)	Absolute		
Mortality (follow-up Median 4.7 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/41 (0%)	0/21 (0%)	-	- I	⊕OOO VERY LOW	CRITICAL
Complications - Grade 2 or greater (follow-up 16 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	7/45 (15.6%)	5/22 (22.7%)	RR 0.68 (0.24 to 1.91)	73 fewer per 1000 (from 173 fewer to 207 more)	⊕OOO VERY LOW	CRITICAL
Complications (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/10 (10%)	2/7 (28.6%)	RR 0.35 (0.04 to 3.15)	186 fewer per 1000 (from 274 fewer to 614 more)	⊕OOO VERY LOW	CRITICAL
Complications (follow-up Median 4.7 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	9/41 (22%)	6/21 (28.6%)	RR 0.77 (0.32 to 1.87)	66 fewer per 1000 (from 194 fewer to 249 more)	⊕OOO VERY LOW	CRITICAL
Resolution of presenting symptoms - Overall success rate (follow-up 16 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	38/45 (84.4%)	20/22 (90.9%)	RR 0.93 (0.77 to 1.11)	64 fewer per 1000 (from 209 fewer to 100 more)	⊕OOO VERY LOW	CRITICAL

Resolution of presenting symptoms - Primary success rate (follow-up 16 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	16/45 (35.6%)	18/22 (81.8%)	RR 0.43 (0.28 to 0.67)	466 fewer per 1000 (from 270 fewer to 589 fewer)	⊕OOO VERY LOW	CRITICAL
Recurrence of pseudocysts (follow-up 26 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/10 (40%)	1/7 (14.3%)	RR 2.8 (0.39 to 20.02)	257 more per 1000 (from 87 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Length of hospital stay (days) (follow-up unclear; Better indicated by lower values)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	10	7	-	MD 8.2 lower (12.87 to 3.53 lower)	⊕OOO VERY LOW	IMPORTANT
Repeated procedure (reintervention) (follow-up Median 4.7 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	9/41 (22%)	0/21 (0%)	Peto OR 5.7 (1.3 to 25.06)	220 more per 1000 (from 80 more to 360 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.17.2 Clinical evidence profile: Combined endoscopic drainage and pancreatic endoscopic stent versus open surgical drainage

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Combined endoscopic drainage and pancreatic endoscopic stent**	**Surgical drainage**	**Relative (95% CI)**	**Absolute**		
Mortality (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/24 (0%)	0/30	-	-	⊕OOO VERY	CRITICAL

								0%			LOW	
Complications (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	5/24 (20.8%)	6/30 (20%)	RR 1.04 (0.36 to 3)	8 more per 1000 (from 128 fewer to 400 more)	⊕OOO VERY LOW	CRITICAL
Complications (timing of exposure During admission)												
1	observational studies[3]	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0 cases 0 controls	0%	-	-	⊕OOO VERY LOW	CRITICAL
Complications - Overall complications (including wound infection, and haematemesis)) (follow-up 24 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	0/20 (0%)	2/20 (10%)	RR 0.2 (0.01 to 3.92)	80 fewer per 1000 (from 99 fewer to 292 more)	⊕⊕OO LOW	CRITICAL
Resolution of pseudocysts (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	21/24 (87.5%)	28/30 (93.3%)	RR 0.94 (0.78 to 1.12)	56 fewer per 1000 (from 205 fewer to 112 more)	⊕OOO VERY LOW	CRITICAL
Resolution of pseudocysts (timing of exposure 4-6 weeks)												
1	observational studies[3]	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	19 cases 10 controls	100%	RR 0.97 (0.82 to 1.16)	30 fewer per 1000 (from 180 fewer to 160 more)	⊕OOO VERY LOW	CRITICAL
Resolution of presenting symptoms - Treatment success (resolution of symptoms at 4 weeks for surgery group; resolution or a decrease in the size of the fluid collection to 2 cm or smaller on CT with resolution of symptoms at 8 weeks) (follow-up 4-8 weeks)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	19/20 (95%)	20/20 (100%)	RR 0.95 (0.83 to 1.09)	50 fewer per 1000 (from 170 fewer to 90 more)	⊕⊕⊕⊕ HIGH	CRITICAL

Recurrence (new onset abdominal pain in the presence of a pancreatic fluid collection on CT after resolution of the initial presentation) (follow-up 24 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	0/20 (0%)	1/20 (5%)	RR 0.33 (0.01 to 7.72)	34 fewer per 1000 (from 49 fewer to 336 more)	⊕⊕OO LOW	CRITICAL
Repeated procedures (reintervention) - Observational (timing of exposure during admission)												
1	observational studies[3]	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0 cases 1 controls	10%	RR 0.17 (0.01 to 3.94)	83 fewer per 1000 (from 99 fewer to 294 more)	⊕OOO VERY LOW	IMPORTANT
Repeated procedures (reintervention) - RCT (follow-up 24 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	1/20 (5%)	1/20 (5%)	RR 1 (0.07 to 14.9)	0 fewer per 1000 (from 47 fewer to 695 more)	⊕⊕OO LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.
[3] case-control

J.17.3 Clinical evidence profile: Endoscopic drainage versus combination of open and laparoscopic surgical techniques

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Endoscopic drainage**	**Combination of open and laparoscopic surgical techniques**	**Relative (95% CI)**	**Absolute**		
Mortality (follow-up ≤12 months)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/21 (0%)	1/43 (2.3%)	RR 0.67 (0.03 to 15.7)	8 fewer per 1000 (from 23 fewer to 342 more)	⊕OOO VERY LOW	CRITICAL
Overall complications (including bleeding, infection, stent migration) (follow-up Median (IQR) follow-up: endoscopic 270 (30-1915); combination 580 (0-4320) days)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	5/21 (23.8%)	11/43 (25.6%)	RR 0.93 (0.37 to	18 fewer per 1000 (from 161	⊕OOO VERY	CRITICAL

									2.33)	fewer to 340 more)	LOW	
Clinical success (complete resolution or decrease in the size of pseudocysts to 2cm or smaller on CT with associated resolution of symptoms). (follow-up 8 weeks)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	19/21 (90.5%)	39/43 (90.7%)	RR 1 (0.84 to 1.18)	0 fewer per 1000 (from 145 fewer to 163 more)	⊕OOO VERY LOW	CRITICAL
Recurrence (pancreatic pseudocyst found on CT in association with symptoms after initial resolution) (follow-up Median (IQR) follow-up: endoscopic 270 (30-1915); combination 580 (0-4320) days)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/21 (9.5%)	2/43 (4.7%)	RR 2.05 (0.31 to 13.54)	49 more per 1000 (from 32 fewer to 583 more)	⊕OOO VERY LOW	CRITICAL
Length of CCU stay (days) (follow-up Median (IQR) follow-up: endoscopic 270 (30-1915); combination 580 (0-4320) days; Better indicated by lower values)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	21	43	-	MD 1.21 lower (1.43 to 0.99 lower)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.17.4 Clinical evidence profile: Endoscopic drainage versus laparoscopic drainage

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Endoscopic**	**Laparoscopic drainage**	**Relative (95% CI)**	**Absolute**		
Complications (Grade 2 or greater) (follow-up 16 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	7/45 (15.6%)	4/16 (25%)	RR 0.62 (0.21 to 1.85)	95 fewer per 1000 (from 198 fewer to 213 more)	⊕OOO VERY LOW	CRITICAL
Resolution of presenting symptoms or pseudocysts - Overall success rate (follow-up 16 months)												
1	observational	serious[1]	no serious	no serious	serious[2]	none	38/45	15/16	RR 0.9 (0.75	94 fewer per 1000	⊕OOO	CRITICAL

	studies		inconsistency	indirectness			(84.4%)	(93.8%)	to 1.08)	(from 234 fewer to 75 more)	VERY LOW	
Resolution of presenting symptoms or pseudocysts - Primary success rate (follow-up 16 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	16/45 (35.6%)	14/16 (87.5%)	RR 0.41 (0.26 to 0.63)	516 fewer per 1000 (from 324 fewer to 648 fewer)	⊕OOO VERY LOW	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.17.5 Clinical evidence profile: Endoscopic drainage versus pancreatic endoscopic stent

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Endoscopic drainage**	**Pancreatic endoscopic stent**	**Relative (95% CI)**	**Absolute**		
Significant complications (follow-up 3-10 days after stent insertion)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/4 (0%)	4/6 (66.7%)	RR 0.16 (0.01 to 2.28)	560 fewer per 1000 (from 660 fewer to 853 more)	⊕OOO VERY LOW	CRITICAL
Resolution of pseudocysts (follow-up 4-8 weeks)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	4/4 (100%)	2/6 (33.3%)	RR 2.52 (0.89 to 7.1)	507 more per 1000 (from 37 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Recurrence of pseudocysts (follow-up 16.4+/- 11.4 months)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/4 (0%)	0/2 (0%)	-	-	⊕OOO VERY LOW	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.17.6 Clinical evidence profile: Endoscopic drainage versus standard treatment

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Endoscopic drainage	Standard treatment (observation)	Relative (95% CI)	Absolute		
Mortality (follow-up Median 4.7 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/41 (0%)	0/44 (0%)	-	-	⊕OOO VERY LOW	CRITICAL
Complications (follow-up Median 4.7 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	9/41 (22%)	0/44 (0%)	Peto OR 9.89 (2.5 to 39.09)	220 more per 1000 (from 90 more to 350 more)	⊕OOO VERY LOW	CRITICAL
Repeated procedure (reintervention) (follow-up Median 4.7 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	9/41 (22%)	0/44 (0%)	Peto OR 9.89 (2.5 to 39.09)	220 more per 1000 (from 90 more to 350 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

J.17.7 Clinical evidence profile: Percutaneous versus surgical drainage or resection

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Percutaneous	Surgical drainage or resection	Relative (95% CI)	Absolute		
Mortality (follow-up unclear)												

1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	6/66 (9.1%)	0/66 (0%)	RR 8 (1.56 to 40.9)	90 more per 1000 (from 20 more to 160 more)	⊕OOO VERY LOW	CRITICAL
Mortality (follow-up 4 years)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	479/8121 (5.9%)	179/6409 (2.8%)	RR 2.11 (1.78 to 2.5)	31 more per 1000 (from 22 more to 42 more)	⊕OOO VERY LOW	CRITICAL
Mortality (follow-up Median 4.7 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/8 (0%)	0/21 (0%)	-	-	⊕OOO VERY LOW	CRITICAL
Complications - Overall complications (follow-up unclear)												
1	observational studies	serious[1]	serious[3]	no serious indirectness	very serious[2]	none	2/4 (50%)	2/7 (28.6%)	RR 1.75 (0.38 to 8.06)	214 more per 1000 (from 177 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Complications - Intra-abdominal abscess and bleeding requiring transfusion (follow-up 4 years)												
1	observational studies	serious[1]	serious[3]	no serious indirectness	serious[2]	none	1335/8121 (16.4%)	864/6409 (13.5%)	RR 1.22 (1.13 to 1.32)	30 more per 1000 (from 18 more to 43 more)	⊕OOO VERY LOW	CRITICAL
Complications - Post-operative bleeding, infection or fistula (follow-up 10 years)												
1	observational studies	serious[1]	serious[3]	no serious indirectness	serious[2]	none	4/20 (20%)	2/3 (66.7%)	RR 0.3 (0.09 to 0.98)	467 fewer per 1000 (from 13 fewer to 607 fewer)	⊕OOO VERY LOW	CRITICAL
Complications (follow-up Median 4.7 months)												
1	observational studies	serious[1]	serious[3]	no serious indirectness	very serious[2]	none	1/8 (12.5%)	6/21 (28.6%)	RR 0.44 (0.06 to 3.09)	160 fewer per 1000 (from 269 fewer to 597 more)	⊕OOO VERY LOW	CRITICAL
Complications - Post-operative bleeding, infection or fistula (follow-up unclear)												
1	observational	serious[1]	serious[3]	no serious	no serious	none	41/66	17/66	RR 2.41 (1.54	363 more per 1000	⊕OOO	CRITICAL

	studies			indirectness	imprecision[2]		(62.1%)	(25.8%)	to 3.79)	(from 139 more to 719 more)	VERY LOW	
Resolution of pseudocyst or symptoms (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	33/66 (50%)	45/66 (68.2%)	RR 0.73 (0.55 to 0.98)	184 fewer per 1000 (from 14 fewer to 307 fewer)	⊕OOO VERY LOW	CRITICAL
Recurrence of pseudocyst - Failure: radiographic persistence of a symptomatic pseudocyst in the observed group and a persistent symptomatic pseudocyst requiring a further procedure in the intervention groups (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	38/66 (57.6%)	8/66 (12.1%)	RR 4.75 (2.4 to 9.39)	455 more per 1000 (from 170 more to 1000 more)	⊕OOO VERY LOW	CRITICAL
Recurrences (follow-up 10 years)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	15/20 (75%)	1/3 (33.3%)	RR 2.25 (0.45 to 11.37)	417 more per 1000 (from 183 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Recurrence of pseudocyst - Recurrence of pseudocysts (follow-up 26 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	3/4 (75%)	1/7 (14.3%)	RR 5.25 (0.78 to 35.13)	607 more per 1000 (from 31 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Length of hospital stay (follow-up unclear; Better indicated by lower values)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	66	66	-	MD 27 higher (25.7 to 28.3 higher)	⊕OOO VERY LOW	IMPORTANT
Length of hospital stay (follow-up 4 years; Better indicated by lower values)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	8121	6409	-	MD 6 higher (5.4 to 6.6 higher)	⊕OOO VERY LOW	IMPORTANT
Length of hospital stay (follow-up unclear; Better indicated by lower values)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4	7	-	MD 2.2 lower (6.95 lower to 2.55 higher)	⊕OOO VERY	IMPORTANT

											LOW	
Repeated procedure (reintervention) (follow-up Median 4.7 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	4/8 (50%)	0/21 (0%)	Peto OR 57.97 (5.69 to 590.19)	500 more per 1000 (from 170 more to 830 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.
[3] Downgraded by 1 or 2 increments because the point estimate varies widely across studies, unexplained by subgroup analysis.

J.17.8 Clinical evidence profile: Percutaneous drainage versus endoscopic drainage

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Percutaneous drainage**	**Endoscopic drainage**	**Relative (95% CI)**	**Absolute**		
Mortality (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/40 (0%)	0/41 (0%)	-	-	⊕OOO VERY LOW	CRITICAL
Mortality (follow-up Median 4.7 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/8 (0%)	0/41 (0%)	-	-	⊕OOO VERY LOW	CRITICAL
Complications (follow-up unclear)												
1	observational studies	serious[1]	serious[2]	no serious indirectness	very serious[3]	none	2/4 (50%)	1/10 (10%)	RR 5 (0.61 to 40.91)	400 more per 1000 (from 39 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Complications (follow-up Median 4.7 months)												

1	observational studies	serious[1]	serious[2]	no serious indirectness	very serious[3]	none	1/8 (12.5%)	9/41 (22%)	RR 0.57 (0.08 to 3.89)	94 fewer per 1000 (from 202 fewer to 634 more)	⊕OOO VERY LOW	CRITICAL
Procedural adverse events (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	6/40 (15%)	6/41 (14.6%)	RR 1.02 (0.36 to 2.91)	3 more per 1000 (from 94 fewer to 280 more)	⊕OOO VERY LOW	CRITICAL
Recurrence of pseudocysts (follow-up 16 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	3/4 (75%)	4/10 (40%)	RR 1.88 (0.73 to 4.83)	352 more per 1000 (from 108 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Length of hospital stay (follow-up unclear; Better indicated by lower values)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	40	41	-	MD 8.3 higher (3.39 to 13.21 higher)	⊕OOO VERY LOW	IMPORTANT
Length of hospital stay (follow-up unclear; Better indicated by lower values)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	4	10	-	MD 6 higher (1.43 to 10.57 higher)	⊕OOO VERY LOW	IMPORTANT
Repeated procedures (re-intervention) (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	17/40 (42.5%)	9.8%	RR 4.36 (1.61 to 11.82)	329 more per 1000 (from 60 more to 1000 more)	⊕OOO VERY LOW	IMPORTANT
Repeated procedures (re-intervention) (follow-up Median 4.7 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	4/8 (50%)	9/41 (22%)	RR 2.28 (0.92 to 5.61)	281 more per 1000 (from 18 fewer to 1000 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 or 2 increments because the point estimate varies widely across studies, unexplained by subgroup analysis.
[3] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.17.9 Clinical evidence profile: Percutaneous drainage versus standard treatment (observation)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Percutaneous drainage	Standard treatment (observation)	Relative (95% CI)	Absolute		
Mortality (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	6/66 (9.1%)	0/41 (0%)	Peto OR 5.48 (1.02 to 25.59)	90 more per 1000 (from 10 fewer to 170 more)	⊕OOO VERY LOW	CRITICAL
Mortality (follow-up Median 4.7 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/8 (0%)	0/44 (0%)	-	-	⊕OOO VERY LOW	CRITICAL
Complications - Post-operative bleeding, infection or fistula (follow-up 10 years)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/20 (20%)	0/21 (0%)	Peto OR 9.17 (1.19 to 70.44)	200 more per 1000 (from 10 more to 390 more)	⊕OOO VERY LOW	CRITICAL
Complications - Post-operative bleeding, infection or fistula (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision[2]	none	41/66 (62.1%)	5/41 (12.2%)	RR 5.09 (2.91 to 11.83)	499 more per 1000 (from 233 more to 1000 more)	⊕OOO VERY LOW	CRITICAL
Complications (follow-up Median 4.7 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	1/8 (12.5%)	0/44 (0%)	Peto OR 665.14 (2.91 to 152094.1)	130 more per 1000 (from 120 fewer to 370 more)	⊕OOO VERY LOW	CRITICAL
Resolution of pseudocyst or symptoms (follow-up after discharge)												

1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[1]	none	33/66 (50%)	28/41 (68.3%)	RR 0.73 (0.53 to 1.01)	184 fewer per 1000 (from 321 fewer to 7 more)	⊕OOO VERY LOW	CRITICAL
Failure (defined as radiographic persistence of a symptomatic pseudocyst in the observed group and a persistent symptomatic pseudocyst requiring a further procedure in the intervention groups) (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	38/66 (57.6%)	3/41 (7.3%)	RR 7.87 (2.6 to 23.85)	503 more per 1000 (from 117 more to 1000 more)	⊕OOO VERY LOW	CRITICAL
Recurrence (follow-up 10 years)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	14/20 (70%)	11/21 (52.4%)	RR 1.34 (0.81 to 2.2)	178 more per 1000 (from 100 fewer to 629 more)	⊕OOO VERY LOW	CRITICAL
Repeated procedure (re-intervention) (follow-up Median 4.7 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	4/8 (50%)	0/44 (0%)	Peto OR 998.5 (60.74 to 16415.31)	500 more per 1000 (from 170 more to 830 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.17.10 Laparoscopic drainage versus open surgical drainage or resection

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Laparoscopic drainage**	**Surgical drainage or resection**	**Relative (95% CI)**	**Absolute**		
Mortality (all-cause) (follow-up unclear)												
1	observational	serious[1]	no serious	no serious	very serious[2]	none	1/10	0/6	Peto OR 4.95	100 more per 1000	⊕OOO	CRITICAL

	studies		inconsistency	indirectness			(10%)	(0%)	(0.09 to 283.86)	(from 180 fewer to 380 more)	VERY LOW	
Complications - Overall (follow-up Median 22 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/10 (20%)	2/6 (33.3%)	RR 0.6 (0.11 to 3.21)	133 fewer per 1000 (from 297 fewer to 737 more)	⊕OOO VERY LOW	CRITICAL
Complications - Grade 2 or greater (follow-up 16 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/16 (25%)	5/22 (22.7%)	RR 1.1 (0.35 to 3.46)	23 more per 1000 (from 148 fewer to 559 more)	⊕OOO VERY LOW	CRITICAL
Resolution of presenting symptoms - Asymptomatic with no evidence of recurrent disease by CT scan (follow-up Median 22 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	10/10 (100%)	6/6 (100%)	RR 1 (0.78 to 1.27)	0 fewer per 1000 (from 220 fewer to 270 more)	⊕OOO VERY LOW	CRITICAL
Resolution of presenting symptoms - Overall success rate (follow-up 16 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	15/16 (93.8%)	20/22 (90.9%)	RR 1.03 (0.86 to 1.24)	27 more per 1000 (from 127 fewer to 218 more)	⊕OOO VERY LOW	CRITICAL
Resolution of presenting symptoms - Primary success rate (follow-up 16 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	14/16 (87.5%)	18/22 (81.8%)	RR 1.07 (0.82 to 1.4)	57 more per 1000 (from 147 fewer to 327 more)	⊕OOO VERY LOW	CRITICAL
Residual pseudocyst (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/10 (10%)	1/6 (16.7%)	RR 0.6 (0.05 to 7.92)	67 fewer per 1000 (from 158 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.17.11 Open surgical drainage/resection versus standard treatment (observation)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Surgical drainage/resection	Standard treatment (observation)	Relative (95% CI)	Absolute		
Mortality (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/66 (0%)	0/41 (0%)	-	-	⊕OOO VERY LOW	CRITICAL
Mortality (follow-up Median 4.7 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/21 (0%)	0/44 (0%)	-	-	⊕OOO VERY LOW	CRITICAL
Complications - Post-operative bleeding, infection or fistula (follow-up 10 years)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	2/3 (66.7%)	0/21 (0%)	Peto OR 4288.26 (59.08 to 311264.3)	670 more per 1000 (from 190 more to 1000 more)	⊕OOO VERY LOW	CRITICAL
Complications - Post-operative bleeding, infection or fistula (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	17/66 (25.8%)	5/41 (12.2%)	RR 2.11 (0.84 to 5.29)	135 more per 1000 (from 20 fewer to 523 more)	⊕OOO VERY LOW	CRITICAL
Complications (follow-up Median 4.7 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	6/21 (28.6%)	0/44 (0%)	Peto OR 28.72 (4.83 to 170.64)	290 more per 1000 (from 90 more to 480 more)	⊕OOO VERY LOW	CRITICAL
Resolution of pseudocyst and symptoms (after hospital discharge; defined as recurrent cyst, recurrent pancreatitis, fistula, infection) (follow-up unclear)												

1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	45/66 (68.2%)	28/41 (68.3%)	RR 1 (0.77 to 1.3)	0 fewer per 1000 (from 157 fewer to 205 more)	⊕OOO VERY LOW	CRITICAL
Failure (radiographic persistence of a symptomatic pseudocyst) (follow-up unclear)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	8/66 (12.1%)	3/41 (7.3%)	RR 1.66 (0.47 to 5.89)	48 more per 1000 (from 39 fewer to 358 more)	⊕OOO VERY LOW	CRITICAL
Recurrence (follow-up 10 years)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/3 (33.3%)	11/21 (52.4%)	RR 0.64 (0.12 to 3.32)	189 fewer per 1000 (from 461 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Repeated procedure (reintervention) (follow-up Median 4.7 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/21 (0%)	0/44 (0%)	Not estimable	-	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.18 Management of pancreatic ascites and pleural effusion secondary to pancreatitis

None

J.19 Management of biliary obstruction in people with chronic pancreatitis

J.19.1 Clinical evidence profile: Metal stents versus plastic stents

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Covered metal stents	Multiple plastic stents	Relative (95% CI)	Absolute		
Mortality (follow-up mean 2 years)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	3/28 (10.7%)	4/30 (13.3%)	RR 0.8 (0.2 to 3.28)	27 fewer per 1000 (from 107 fewer to 304 more)	⊕OOO VERY LOW	CRITICAL
Recurrent strictures (follow-up mean 2 years)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/28 (7.1%)	3/30 (10%)	RR 0.71 (0.13 to 3.96)	29 fewer per 1000 (from 87 fewer to 296 more)	⊕OOO VERY LOW	CRITICAL
Adverse events (follow-up mean 2 years)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	8/28 (28.6%)	7/30 (23.3%)	RR 1.22 (0.51 to 2.93)	51 more per 1000 (from 114 fewer to 450 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.19.2 Clinical evidence profile: Stenting versus surgery

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Stenting	Surgery	Relative (95% CI)	Absolute		
Mortality												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/16 (0%)	0/23 (0%)	Not estimable	No events	⊕OOO VERY LOW	CRITICAL

Successful treatment											
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	10/16 (62.5%)	20/23 (87%)	RR 0.72 (0.48 to 1.08)	243 fewer per 1000 (from 452 fewer to 70 more)	⊕OOO VERY LOW	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

J.20 Management of type 3c diabetes secondary to pancreatitis

None.

J.21 Receiving specialist input in people with acute pancreatitis

None.

J.22 Follow-up of pancreatic exocrine function in people with chronic pancreatitis

None.

J.23 Follow-up to identify diabetes in people with chronic pancreatitis

None.

J.24 Follow-up to identify pancreatic cancer in people with chronic pancreatitis

None.

Appendix K: Forest plots

K.1 Patient information

None

K.2 Lifestyle interventions: stopping or reducing alcohol consumption

K.2.1 Structured programme to support people with acute pancreatitis in stopping or reducing alcohol consumption versus usual care

Figure 26: Recurrent episodes of pancreatitis (number of recurrent episodes of acute pancreatitis) at 36 months

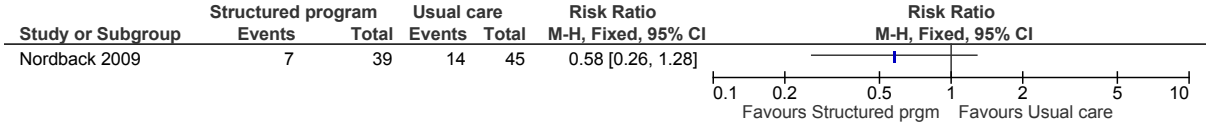
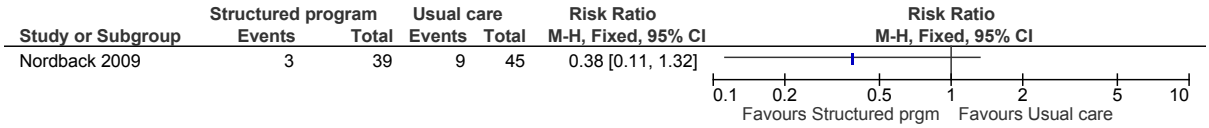


Figure 27: Admissions to hospital (n of patients admitted for abdominal complaints fulfilling criteria of recurrent acute pancreatitis) at 2 years



K.3 Aetiology of acute pancreatitis

None

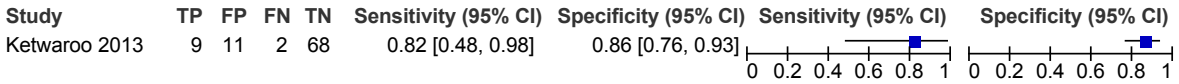
K.4 Aetiology of chronic pancreatitis

None

K.5 Diagnosing chronic pancreatitis

K.5.1 Coupled sensitivity and specificity forest plots

Figure 28: Sensitivity and specificity of index test Secretin Pancreatic Function test (SPFT) for chronic pancreatitis in people with suspected chronic pancreatitis whose diagnosis has not been confirmed by any of CT scan, ultrasound scan or upper GI endoscopy



K.6 Type of intravenous fluid for resuscitation in people with acute pancreatitis

K.6.1 Balanced crystalloid (Ringer-lactate) vs normal saline (RCT)

Figure 29: Mortality <1 year

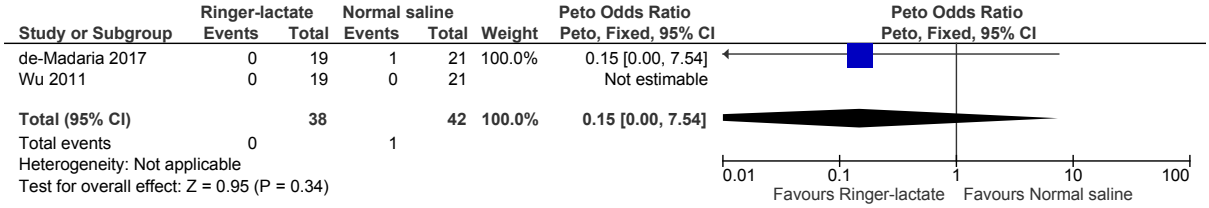


Figure 30: Serious adverse events (transfer to CCU) <1 year

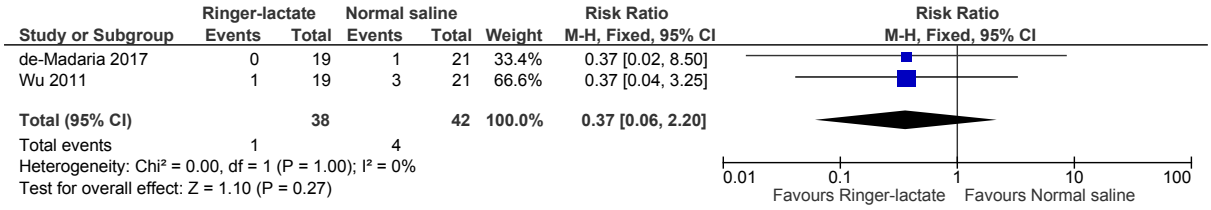


Figure 31: Local complications (infection) <6 months

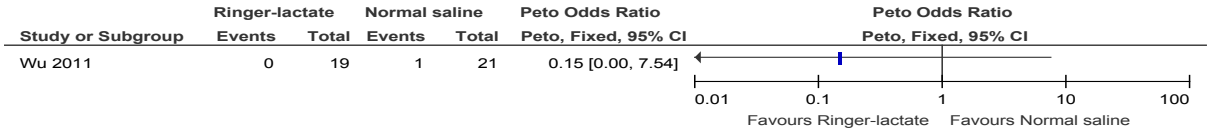


Figure 32: Local complications (necrosis) <6 months

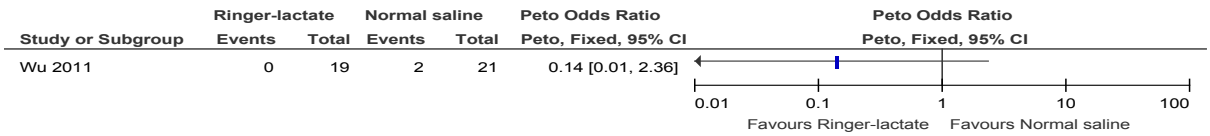


Figure 33: Local complications (peri-pancreatic necrosis) <6 months

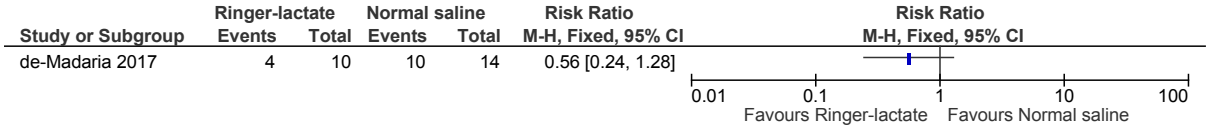


Figure 34: Systemic complications (renal failure) <6 months

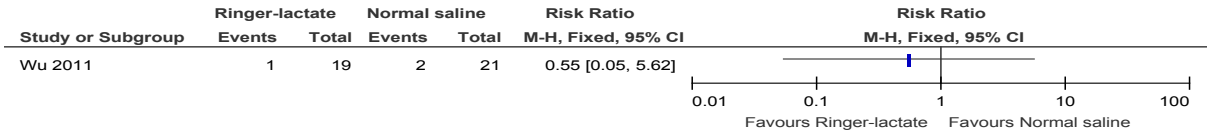


Figure 35: Systemic complications (respiratory organ failure) <6 months

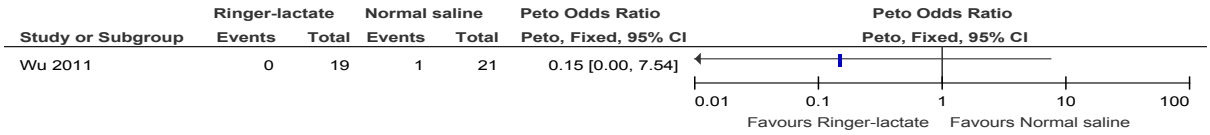


Figure 36: Systemic complications (shock) <6 months

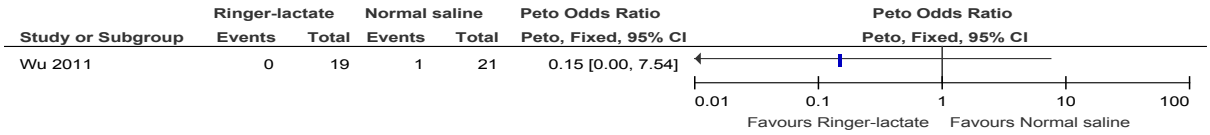
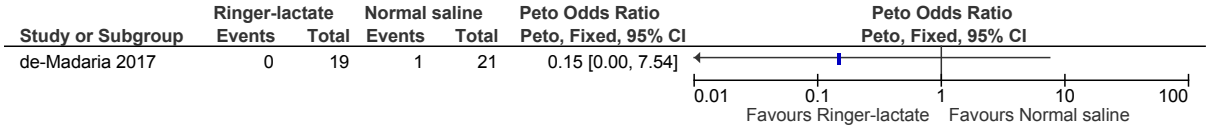


Figure 37: Systemic complications (persistent organ failure) <6 months



K.6.2 Balanced crystalloid (Ringer-lactate) vs normal saline (non-randomised comparative studies)

Figure 38: Mortality <1 year

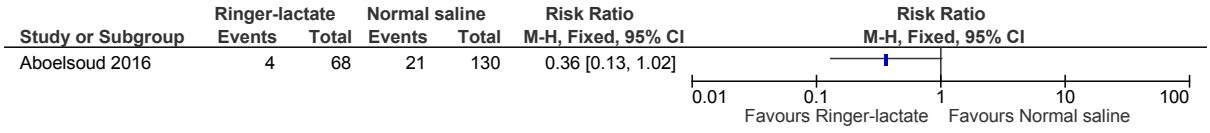
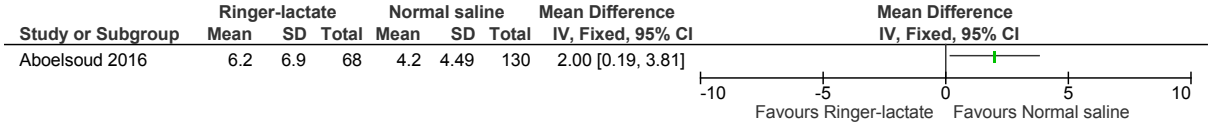


Figure 39: Length of stay (in CCU) <1 year



K.7 Speed of intravenous fluid for resuscitation in people with acute pancreatitis

K.7.1 Aggressive fluid resuscitation versus conservative fluid resuscitation (Randomised controlled trials)

K.7.1.1 Adults (>16 years)

Figure 40: Mortality at <1 year

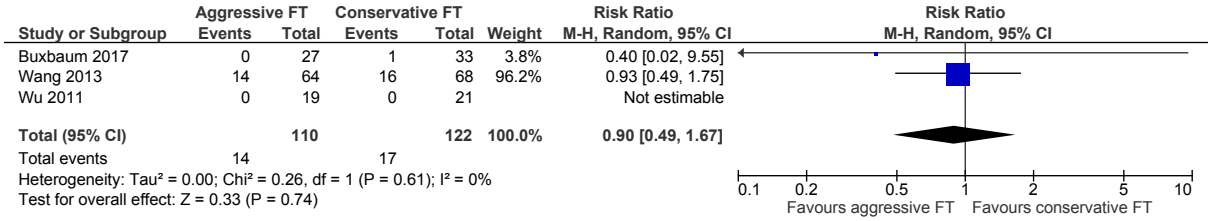


Figure 41: Length of stay (CCU) <1 year

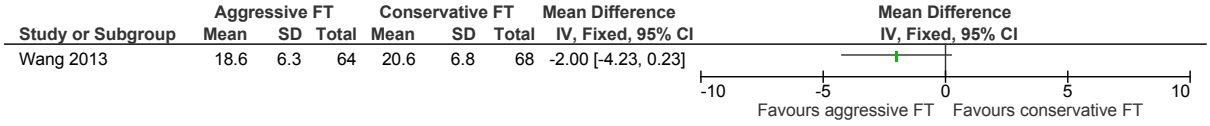


Figure 42: Local complications (infection) <6 months

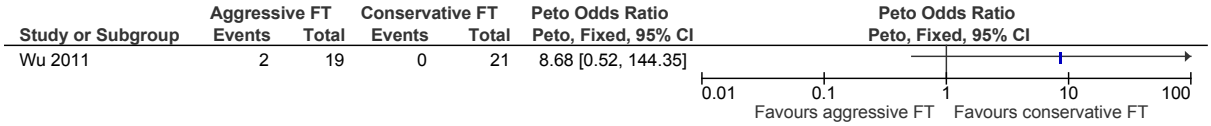


Figure 43: Local complications (necrosis) <6 months

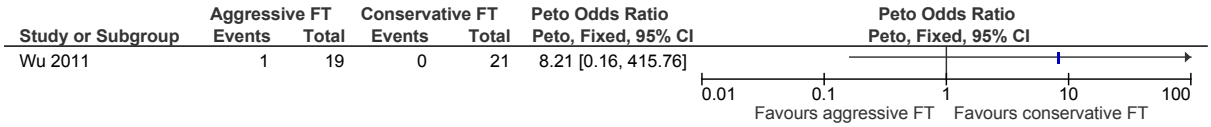


Figure 44: Systemic complications (multiple organ dysfunction syndrome) during admission

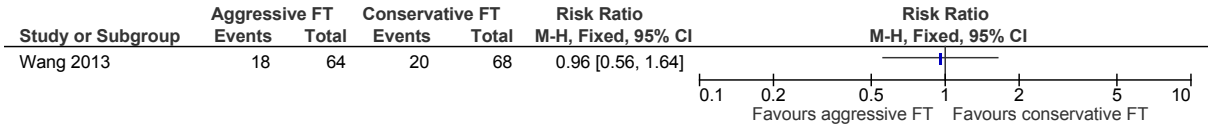


Figure 45: Systemic complications (sepsis) during admission

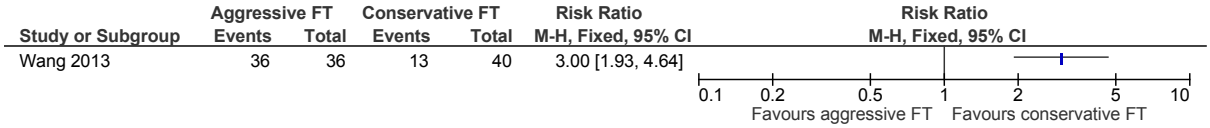


Figure 46: Systemic complications (abdominal compartment syndrome) during admission

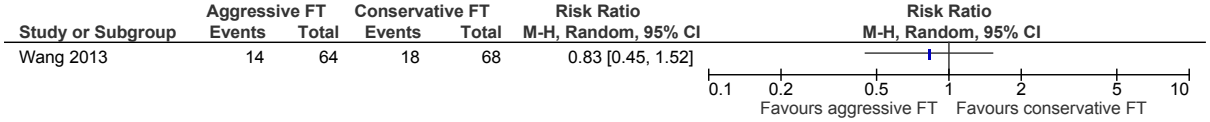


Figure 47: Systemic complications (Development of SIRS) during admission

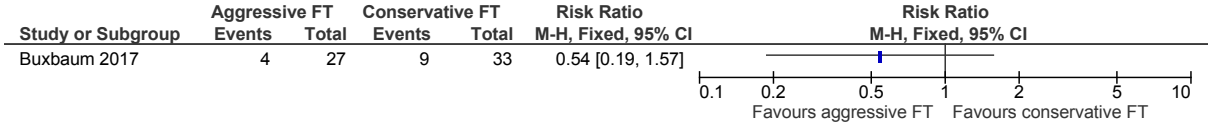


Figure 48: Systemic complications (persistent SIRS) during admission

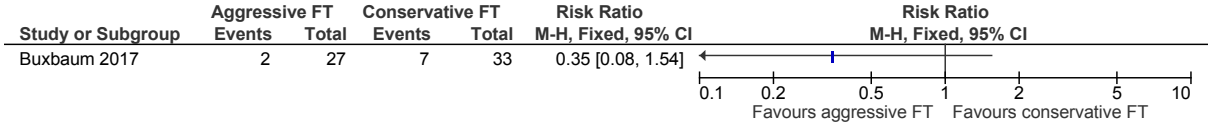


Figure 49: Systemic complications (renal failure) during admission

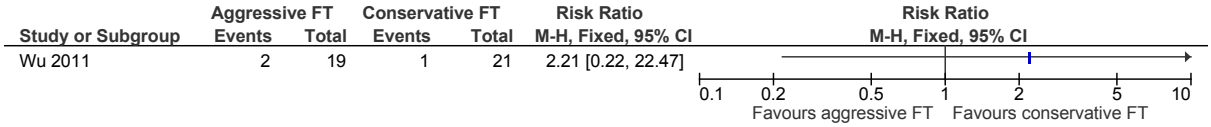


Figure 50: Systemic complications (respiratory failure) during admission

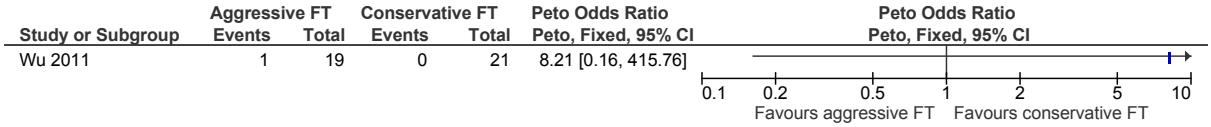


Figure 51: Systemic complications (shock) during admission

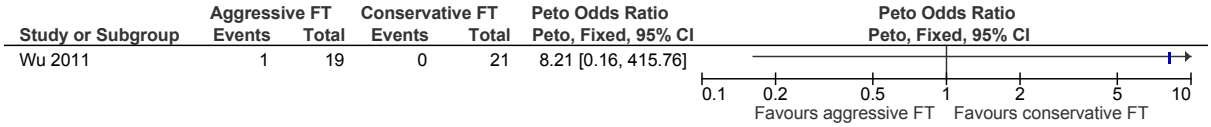


Figure 52: Serious adverse events (days using ventilation) during admission

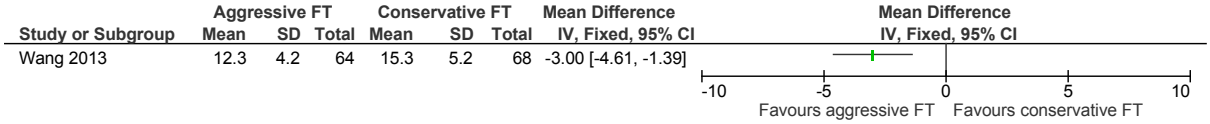


Figure 53: Serious adverse events (transfer to CCU) during admission

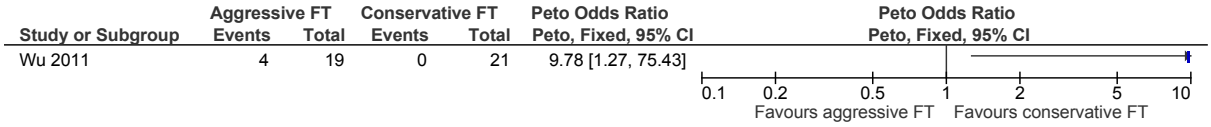
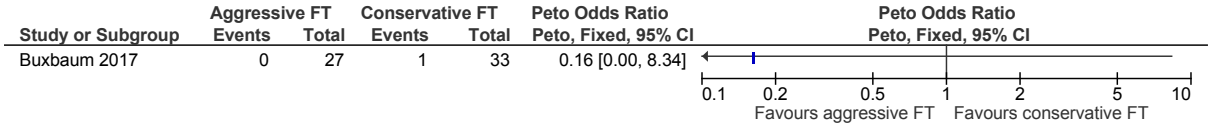


Figure 54: Serious adverse events (development of severe acute pancreatitis) during admission



K.7.2 Aggressive fluid resuscitation versus conservative fluid resuscitation (Non-randomised comparative studies)

K.7.2.1 Adults and young people (>16 years)

Figure 55: Mortality at <1 year

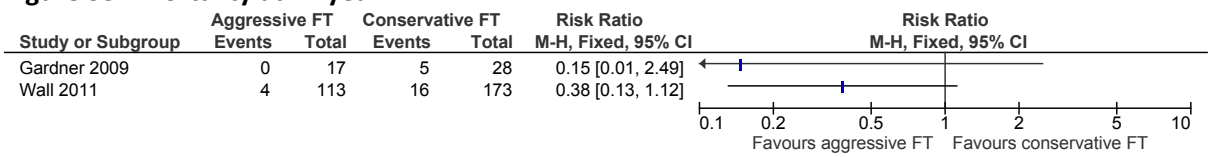
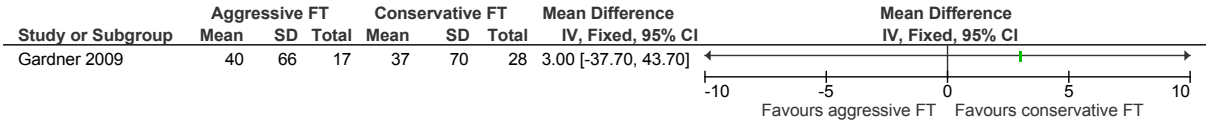


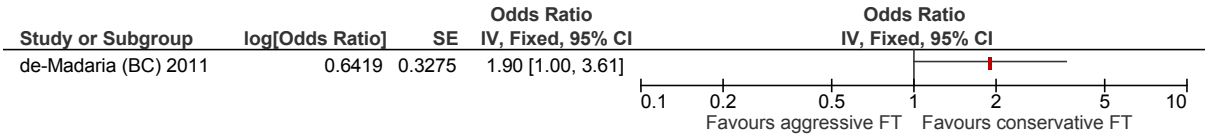
Figure 56: Mortality at <1 year

Figure 57: Length of stay (in hospital) <1 year



1

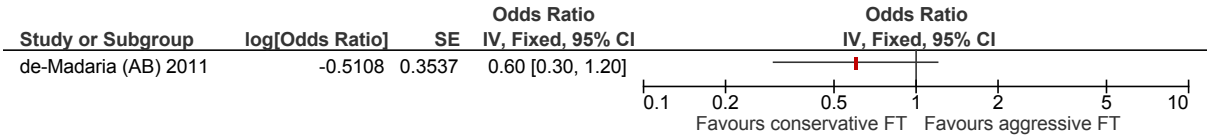
Figure 58: Local complications (acute collection) at <6 months



Note: Group B: 3100-4100ml; Group C: >4100ml

2

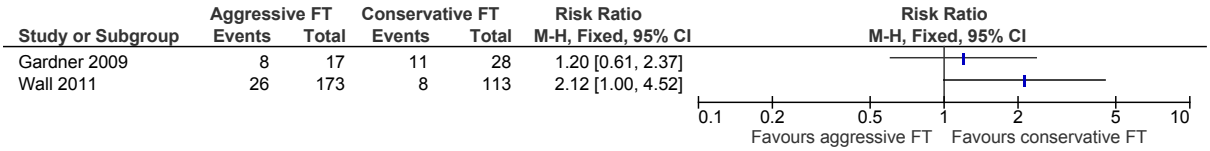
Figure 59: Local complications (acute collection) at <1 year



Note: Group A: <3100ml; Group B: 3100-4100ml

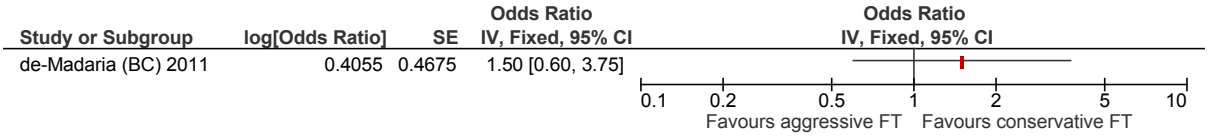
3

Figure 60: Local complications (pancreatic necrosis) at <6 months



4

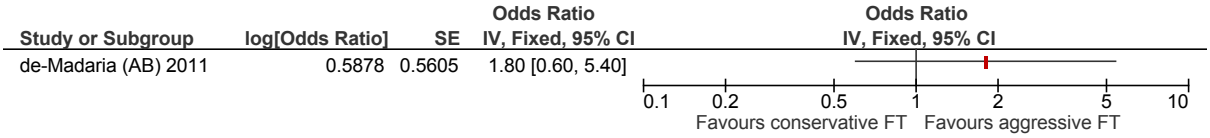
Figure 61: Local complications (pancreatic necrosis) at <6 months



Note: Group B: 3100-4100ml; Group C: >4100ml

5

Figure 62: Local complications (pancreatic necrosis) at <6 months



Note: Group A: <3100ml; Group B: 3100-4100ml

Figure 63: Local complications (Development of a pseudocyst) at <6 months

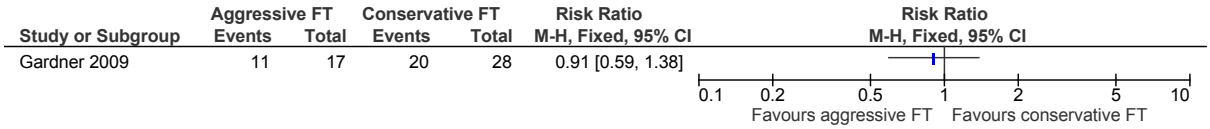


Figure 64: Local complications (acute peripancreatic fluid collections and/or pancreatic necrosis and/or peripancreatic necrosis) during admission

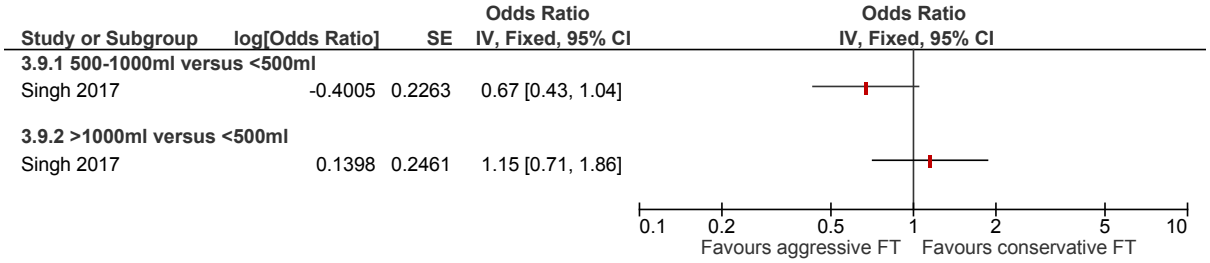


Figure 65: Systemic complications (cardiovascular failure) during admission

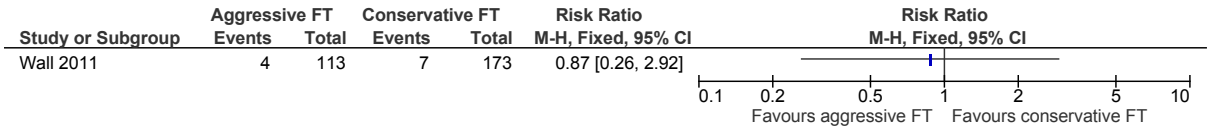


Figure 66: Systemic complications (pulmonary failure) during admission

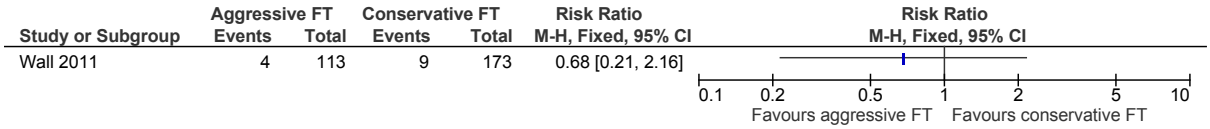


Figure 67: Systemic complications (multi-system organ failure) during admission

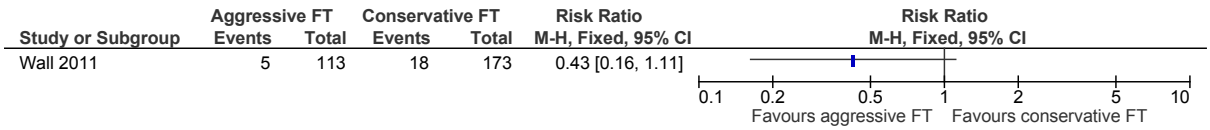
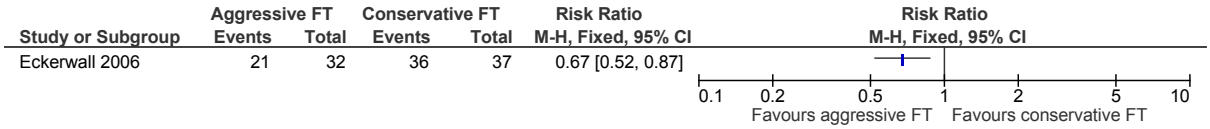


Figure 68: Systemic complications (respiratory complications) during admission



Note: Respiratory complications included pleural effusions, atelectases and pneumonia.

Figure 69: Systemic complications (persistent organ failure) during admission

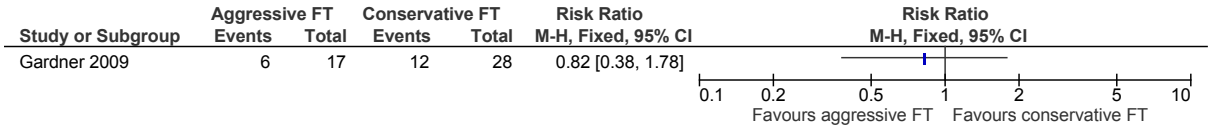
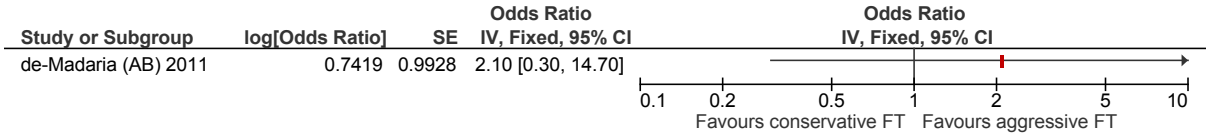
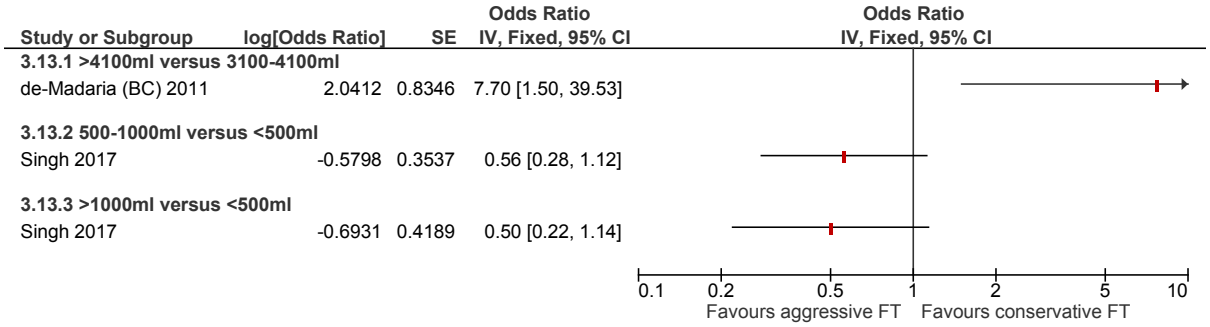


Figure 70: Systemic complications (persistent organ failure) during admission



Note: Group A: <3100ml; Group B: 3100-4100ml

Figure 71: Systemic complications (persistent organ failure) during admission



Note: De-Madaria 2011 Group B: 3100-4100ml; Group C: >4100ml

Figure 72: Systemic complications (renal failure) during admission

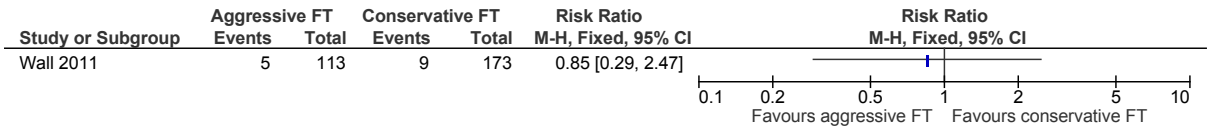
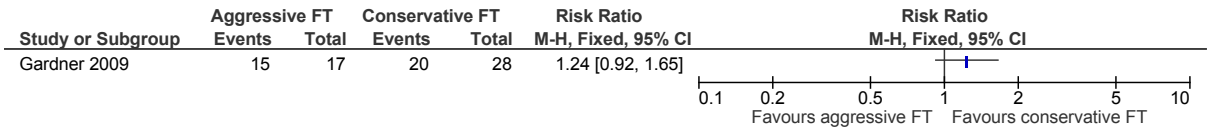


Figure 73: Systemic complications (SIRS) during admission



K.7.2.2 Children (<16 years)

Figure 74: Serious adverse events (CCU transfer rate) during admission

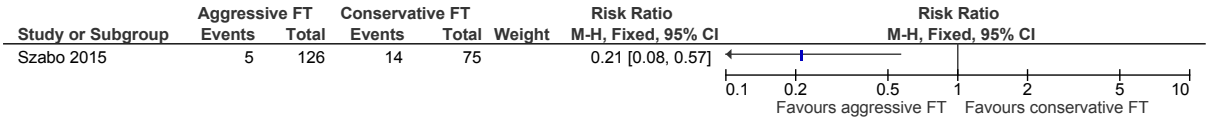


Figure 75: Serious adverse events (readmission rate) during admission

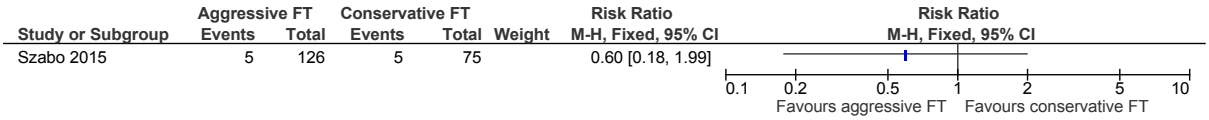
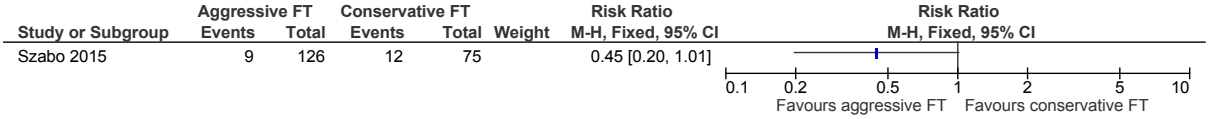


Figure 76: Serious adverse events (severe acute pancreatitis rate) during admission



K.8 Route of feeding in people with severe acute pancreatitis

K.8.1 Enteral (jejunal or duodenal) versus parenteral nutrition for acute pancreatitis

Figure 77: Mortality at ≤1 year

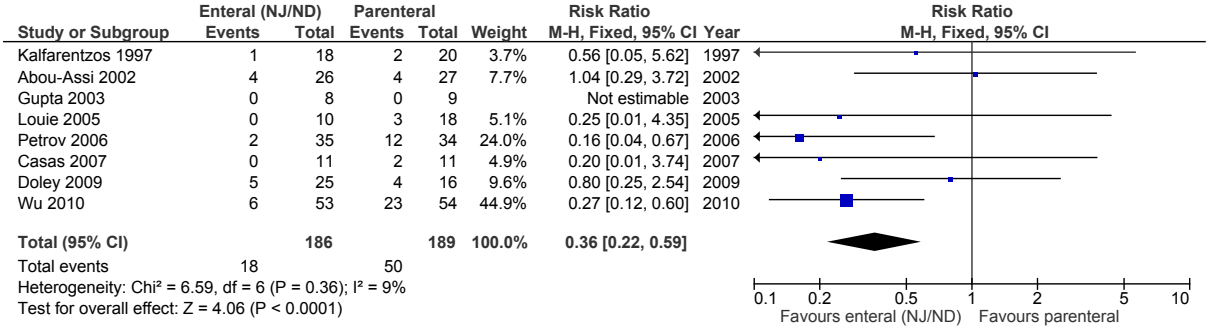


Figure 78: Length of hospital stay (days) at ≤1 year

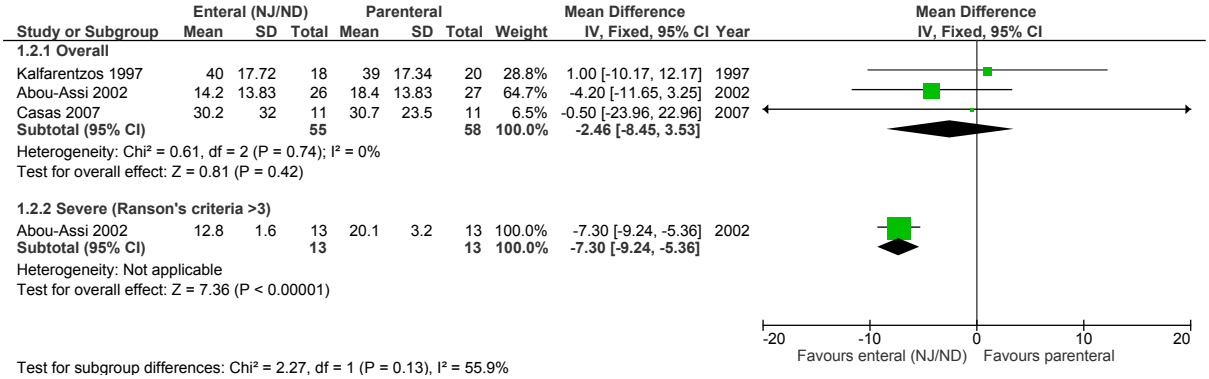
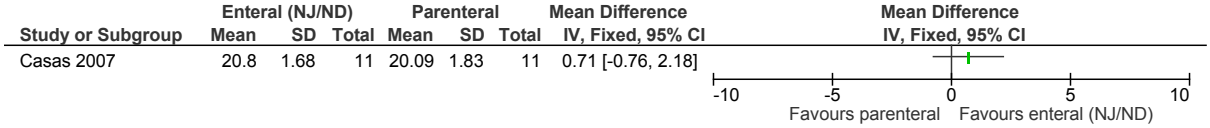
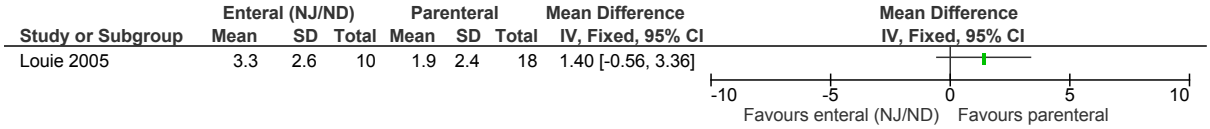


Figure 79: Achieving nutrition (kcal/kg/day) at ≤1 year



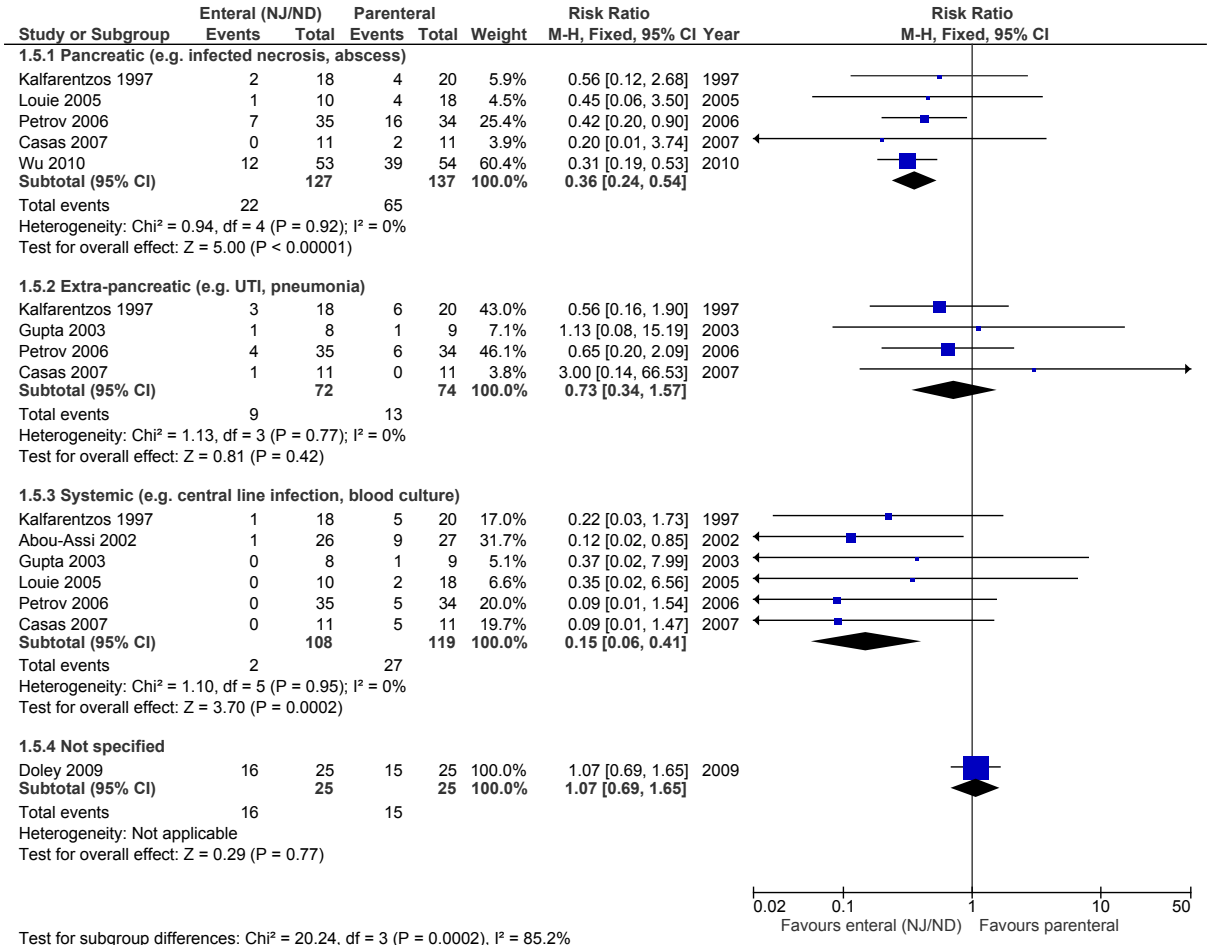
1

Figure 80: Achieving nutrition (days to goal) at ≤1 year



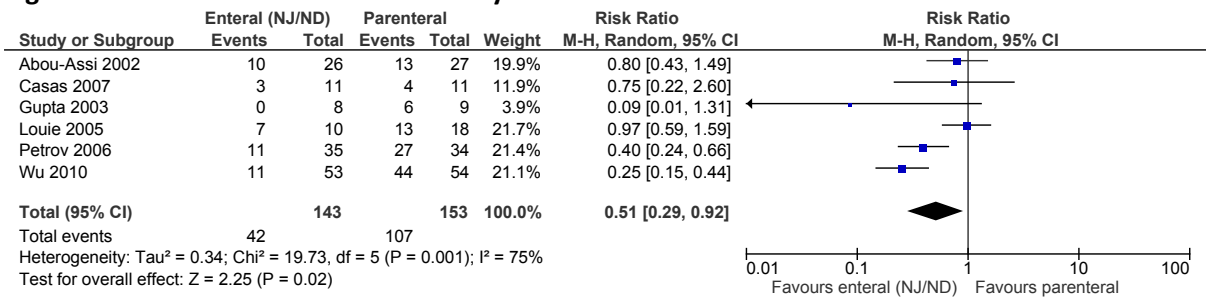
2

Figure 81: Infections at ≤1 year



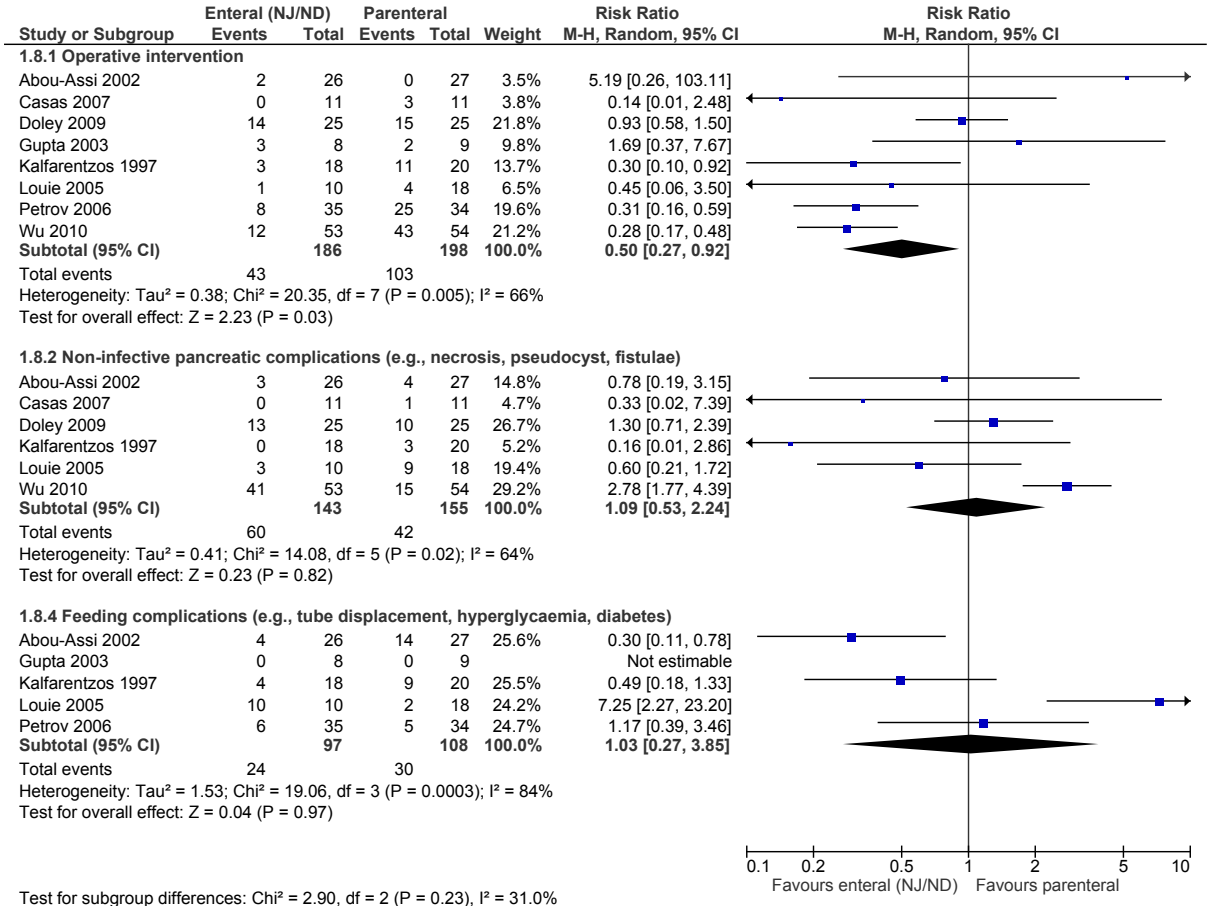
3

Figure 82: Serious adverse events at ≤1 year



1

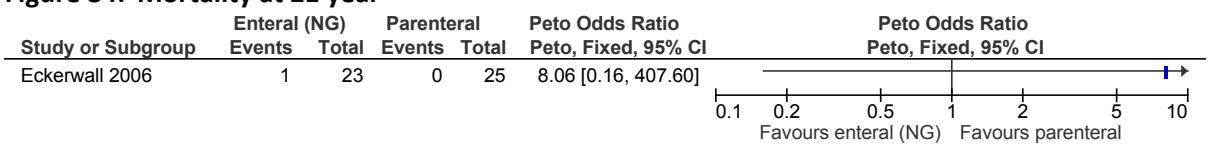
Figure 83: Adverse events at ≤1 year



2

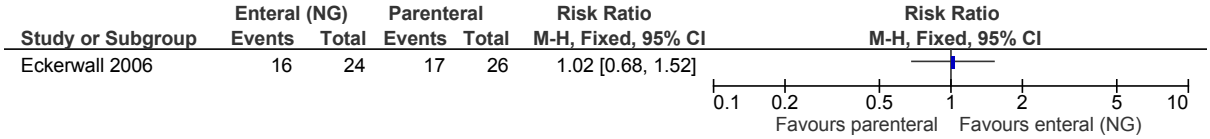
3 K.8.2 Enteral (gastric) versus parenteral nutrition for acute pancreatitis

Figure 84: Mortality at ≤1 year



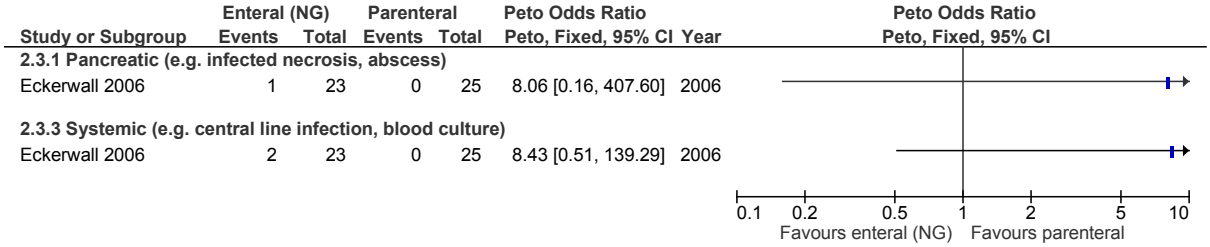
4

Figure 85: Achieving nutrition (25 kcal/kg/day) at ≤1 year



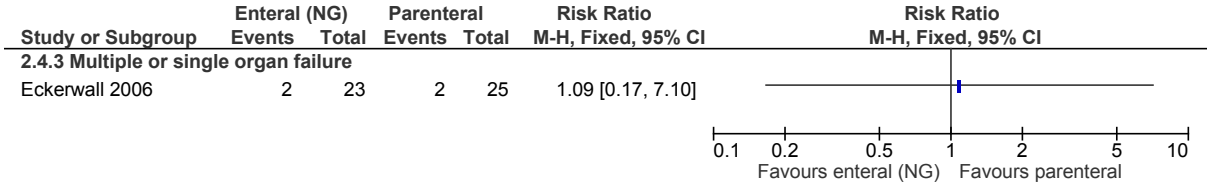
1

Figure 86: Infections at ≤1 year



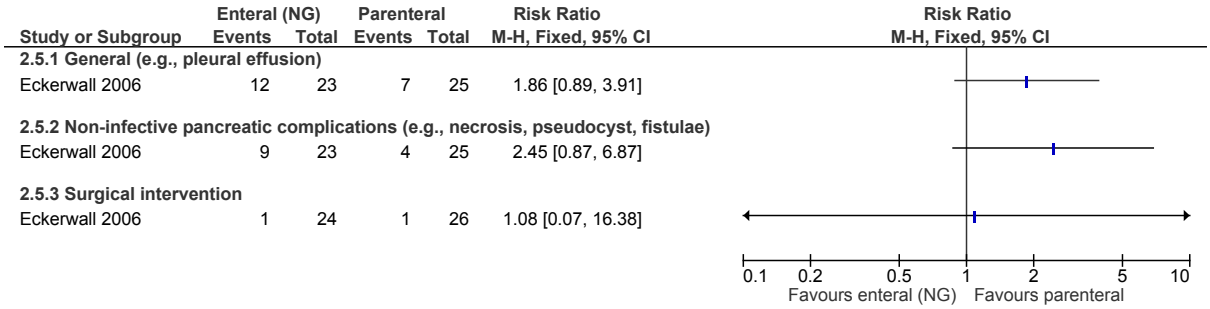
2

Figure 87: Serious adverse events at ≤1 year



3

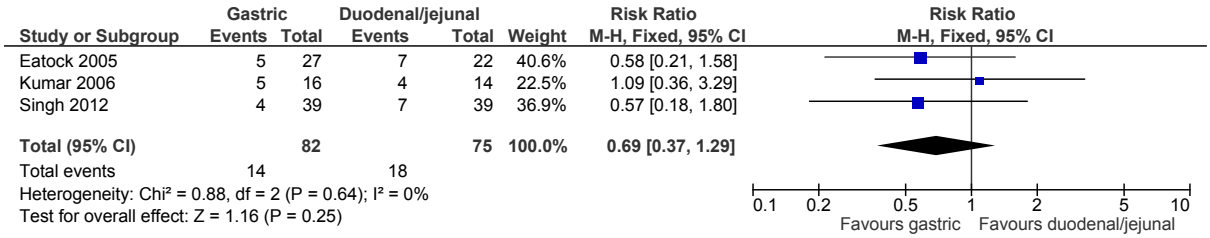
Figure 88: Adverse events at ≤1 year



4

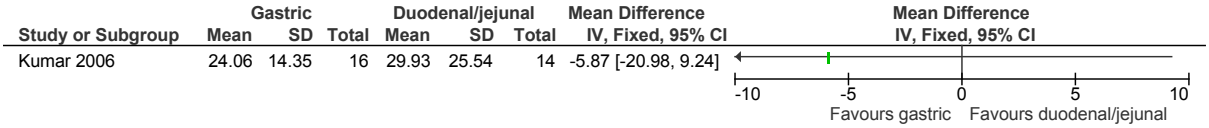
5 K.8.3 Enteral (gastric) versus enteral (jejunal or duodenal nutrition for acute pancreatitis

Figure 89: Mortality at ≤1 year



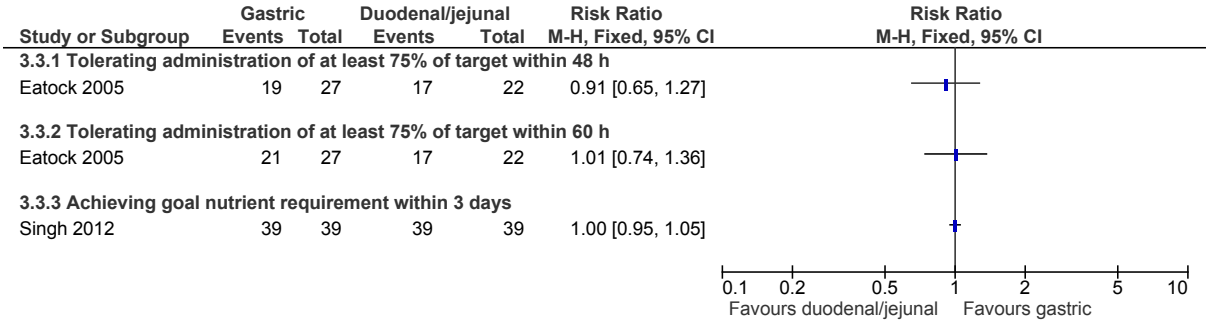
1

Figure 90: Length of hospital stay (days) at ≤1 year



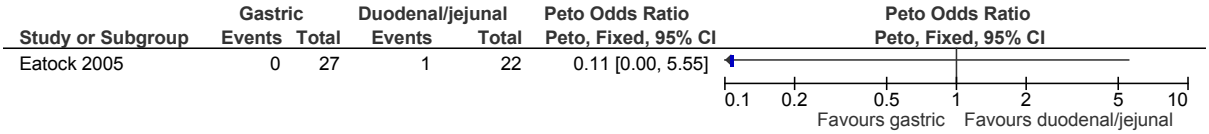
2

Figure 91: Achieving nutrition at ≤1 year



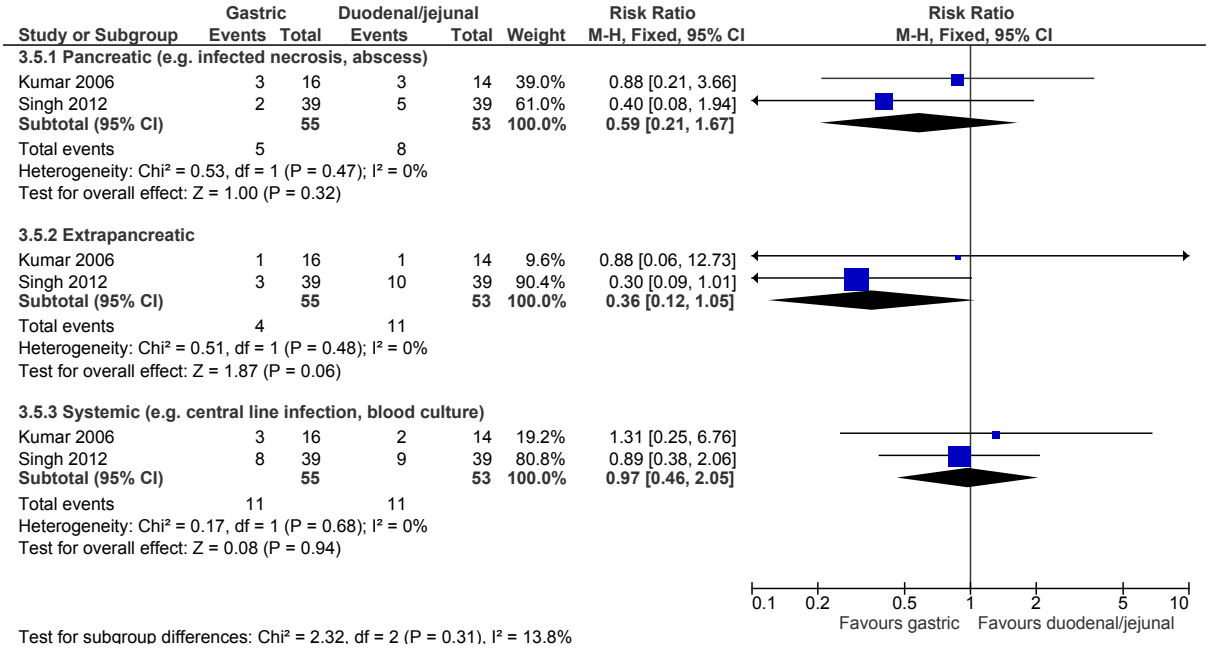
3

Figure 92: Requiring total parenteral nutrition at ≤1 year



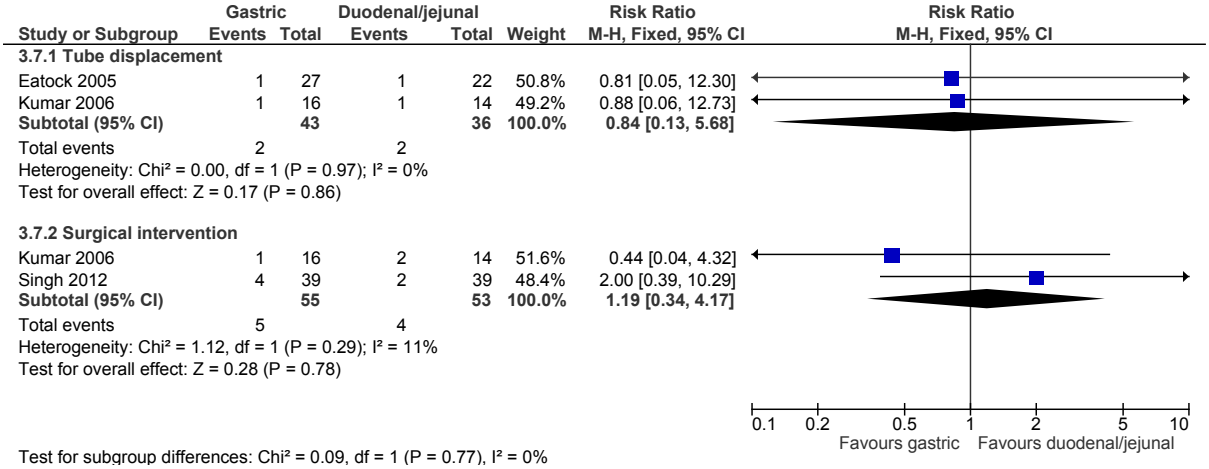
4

Figure 93: Infections at ≤1 year



5

Figure 94: Adverse events at ≤1 year



K.8.4 Early versus conventional (delayed) oral 're-feeding' for acute pancreatitis

Figure 95: Length of hospital stay (days) at ≤1 year

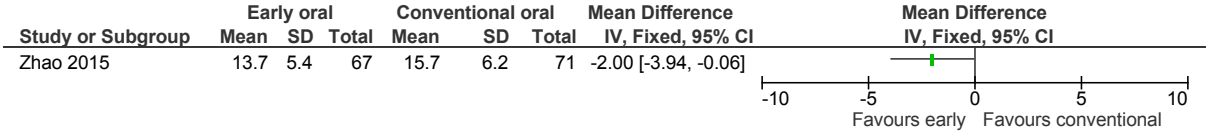


Figure 96: Requiring parenteral nutrition at ≤1 year

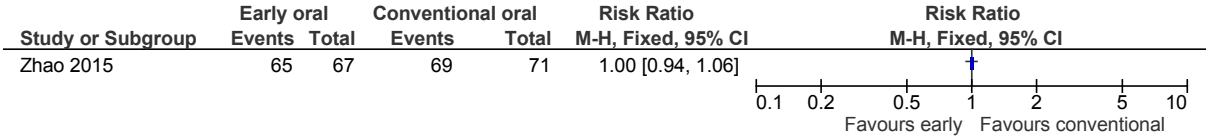
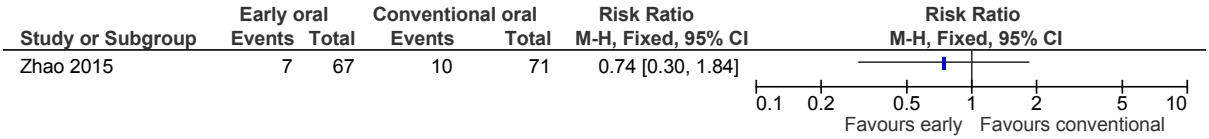


Figure 97: Abdominal pain relapse at ≤1 year



K.8.5 Early versus on-demand enteral nutrition for acute pancreatitis

Figure 98: Mortality at ≤1 year

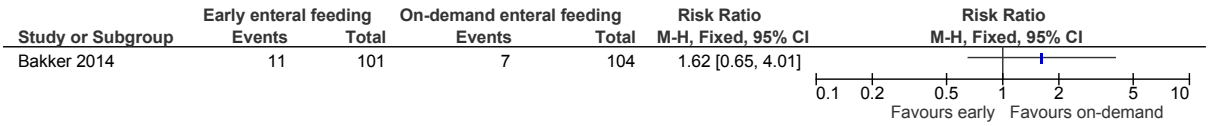
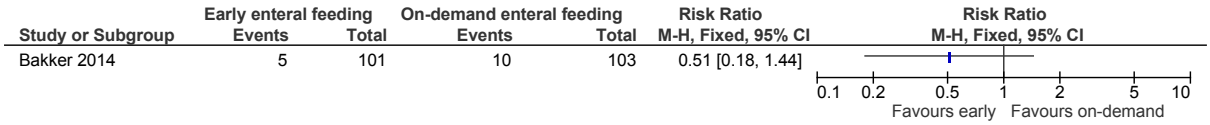
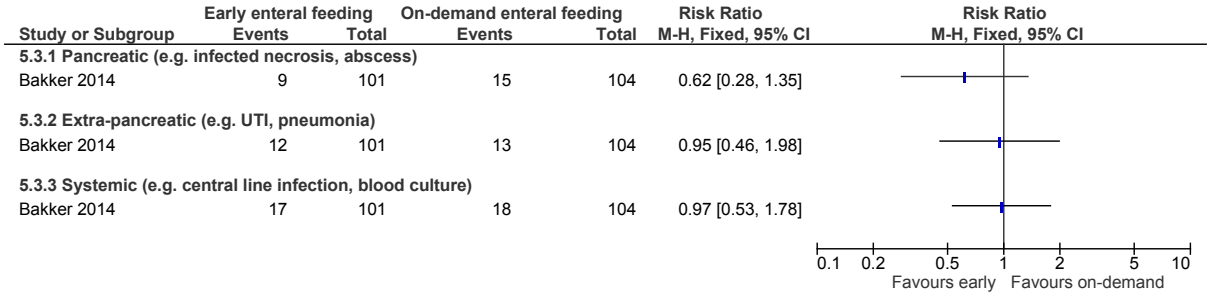


Figure 99: Requiring parenteral nutrition at ≤1 year



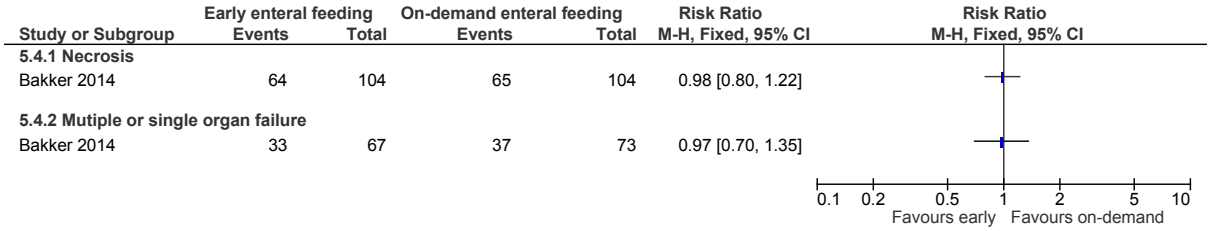
1

Figure 100: Infection at ≤1 year



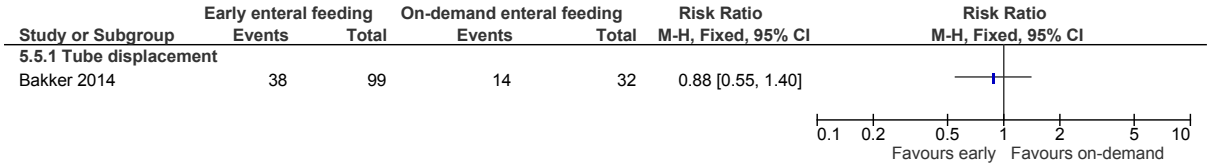
2

Figure 101: Serious adverse events at ≤1 year



3

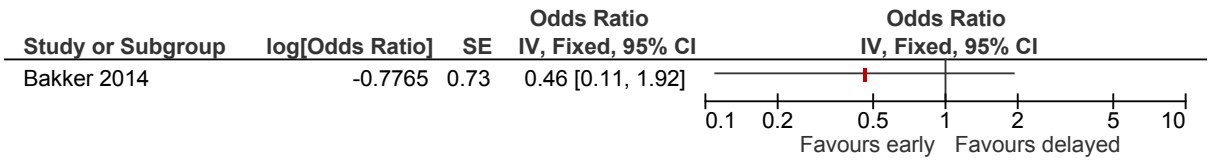
Figure 102: Adverse events at ≤1 year



4 ## K.8.6 Early versus late enteral nutrition for acute pancreatitis

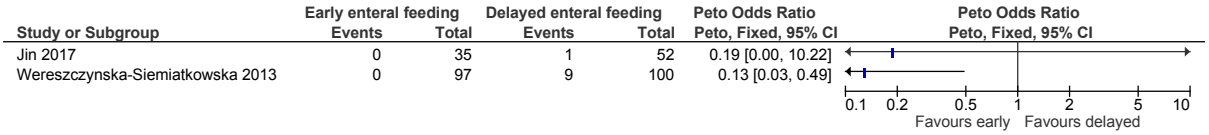
5

Figure 103: Mortality at ≤1 year



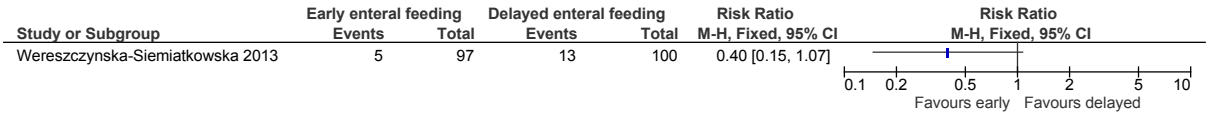
6

Figure 104: Mortality at ≤1 year



1

Figure 105: Additional parenteral nutrition at ≤1 year



2

Figure 106: Pancreatic infections at ≤1 year

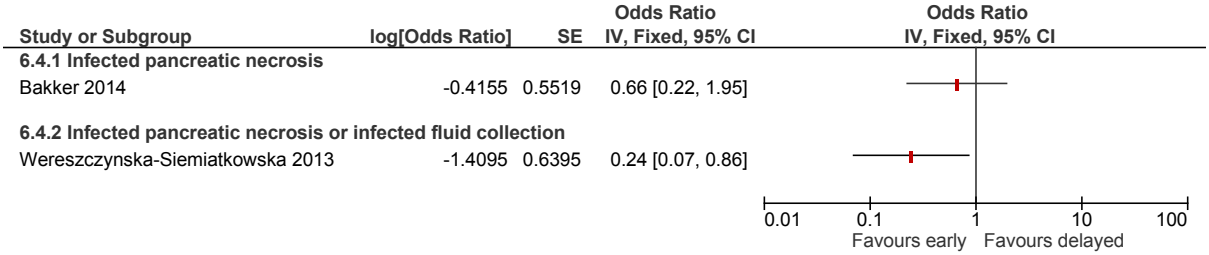


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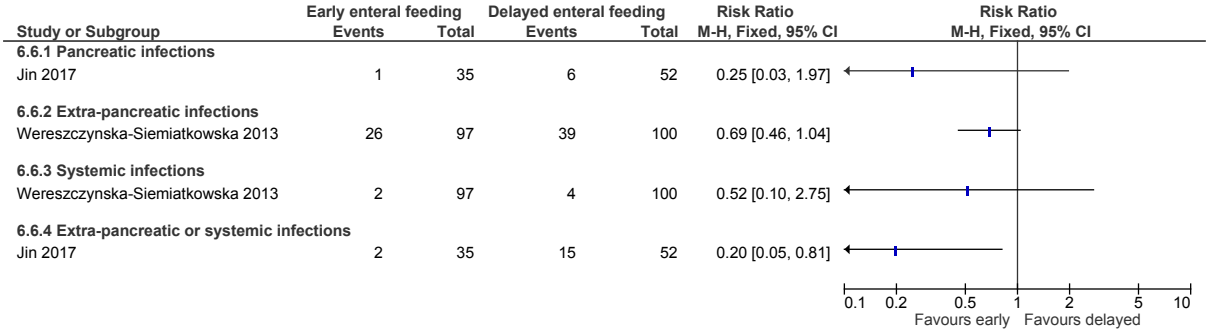
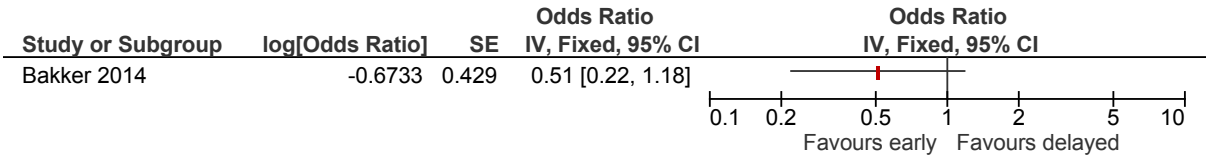
Figure 107: Infections at ≤1 year



4

Figure 108: Serious adverse events – organ failure at ≤1 year



5

Figure 109: Serious adverse events – multi-organ failure at ≤1 year

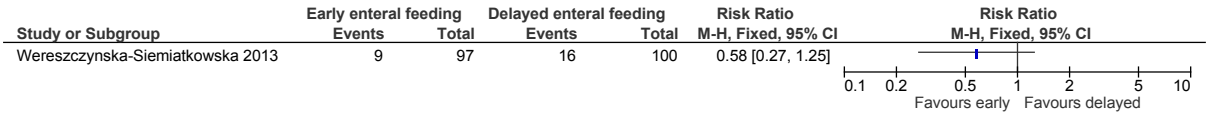
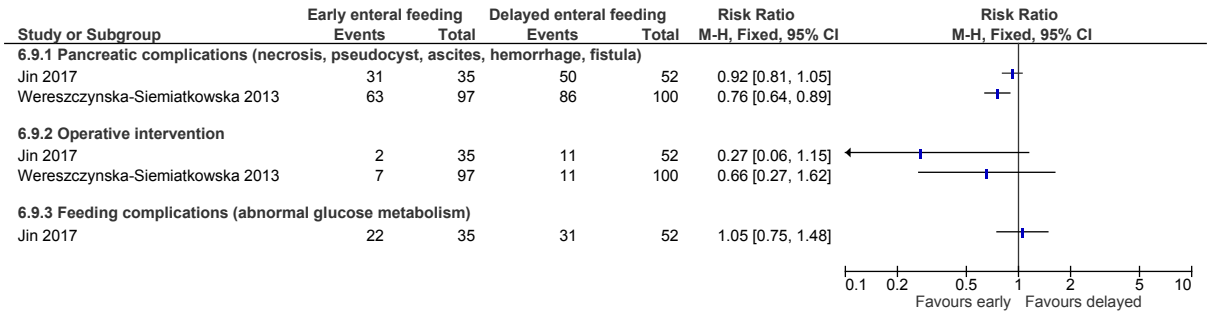


Figure 110: Adverse events at ≤1 year



K.9 Early versus late nutritional intervention in people with chronic pancreatitis

None.

K.10 Specialist versus non-specialist nutritional assessment in people with chronic pancreatitis

None.

K.11 Prophylactic antimicrobial agents to prevent infection in people with acute pancreatitis

K.11.1 Prophylactic antimicrobial therapy versus no prophylactic antimicrobial therapy

Figure 111: Mortality <1 year

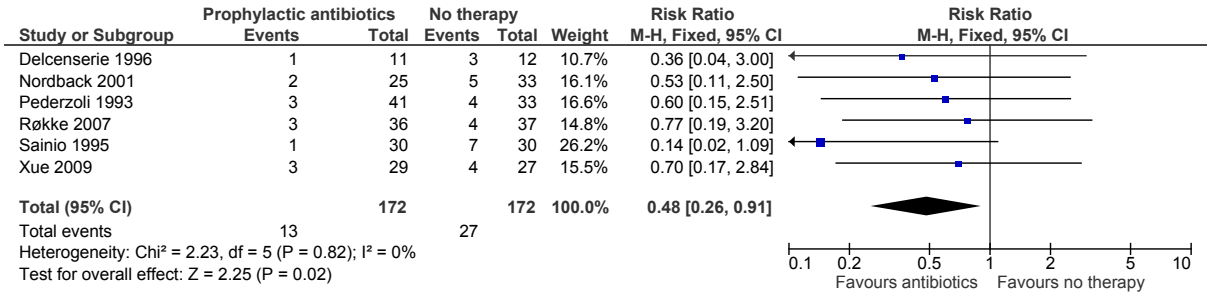


Figure 112: Mortality (Selective decontamination) <1 year

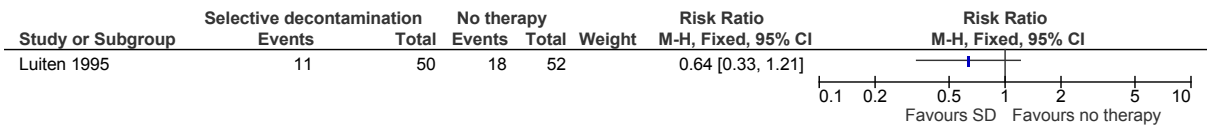
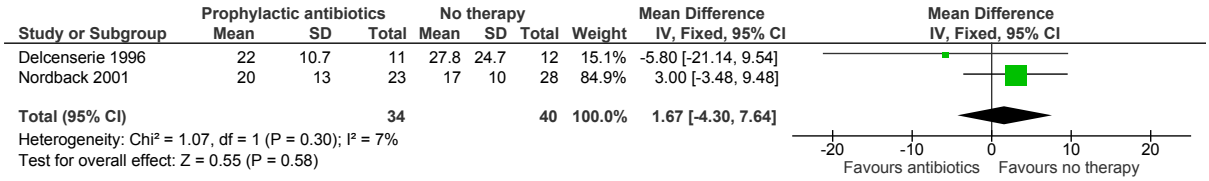
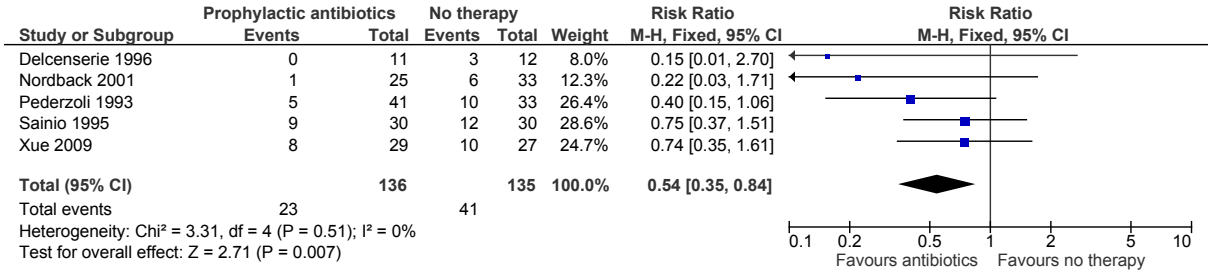


Figure 113: Length of hospital stay <1 year



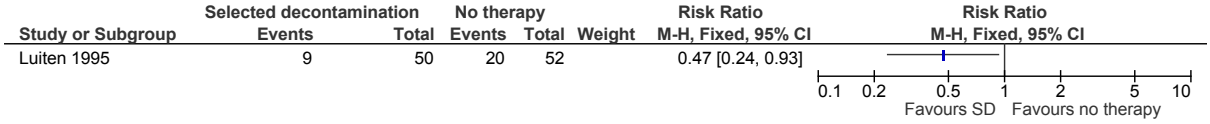
1

Figure 114: Infected necrosis <1 year



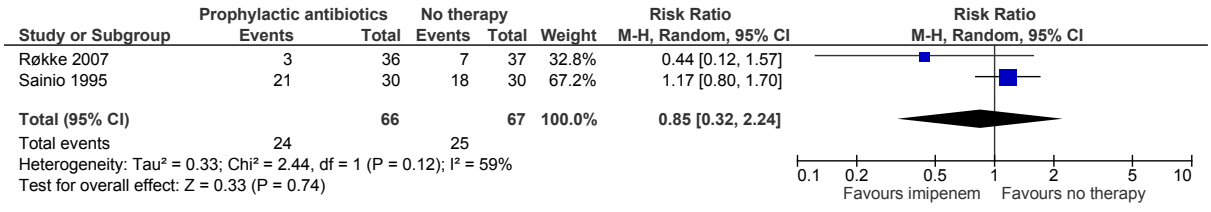
2

Figure 115: Infected necrosis (Selective decontamination) <1 year



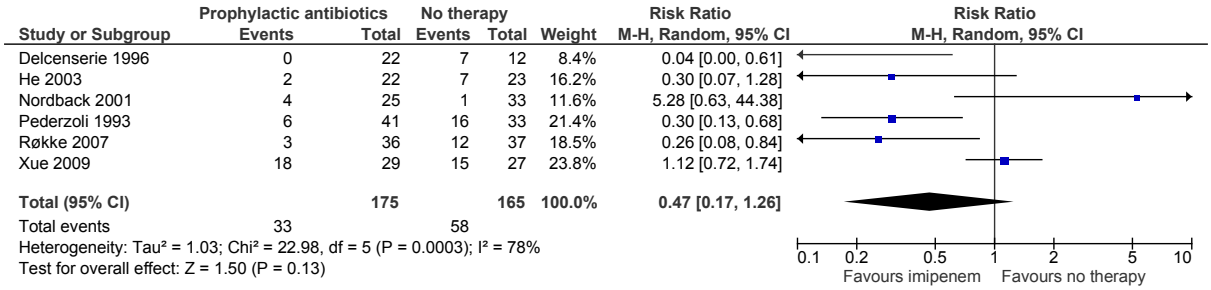
3

Figure 116: Infected necrosis (Peri-pancreatic infection) <1 year



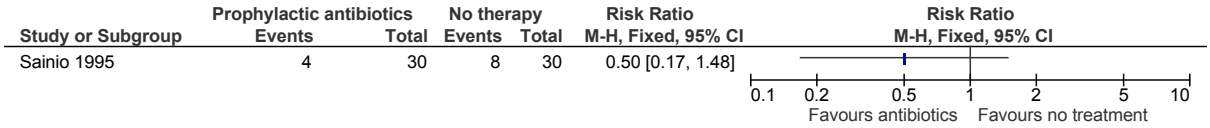
4

Figure 117: Extra-pancreatic infection <1 year



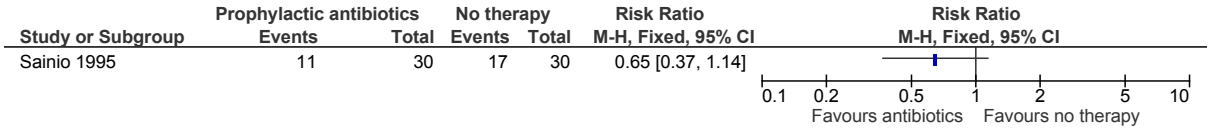
1

Figure 118: Extra-pancreatic infection (Blood culture positive sepsis) <1 year



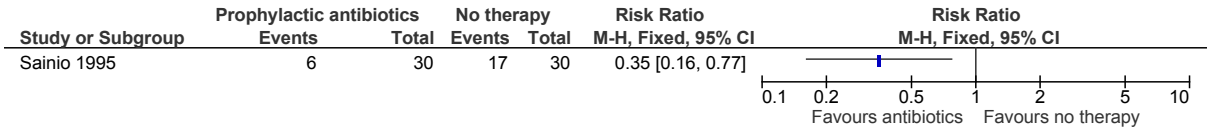
2

Figure 119: Extra-pancreatic infection (Pneumonia/ARDS) <1 year



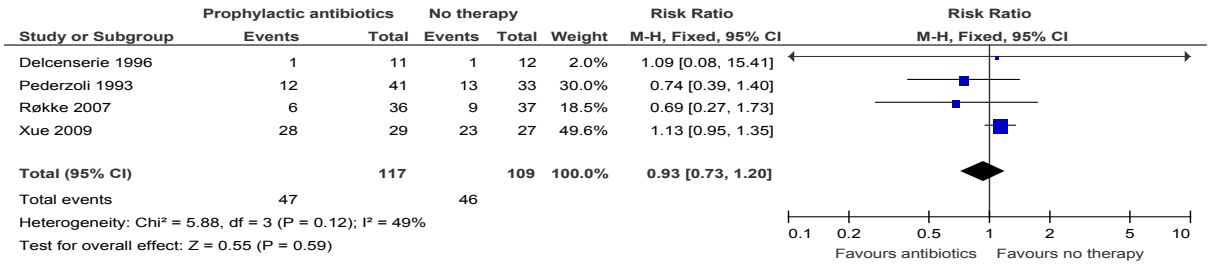
3

Figure 120: Extra-pancreatic infection (Urinary tract infection) <1 year



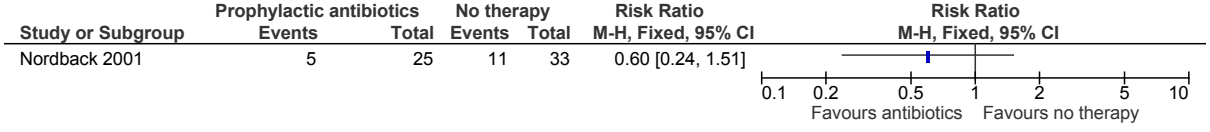
4

Figure 121: Serious adverse events (multi-organ failure) <6 months



5

Figure 122: Serious adverse events (major organ complication) <6 months



K.11.2 Prophylactic antimicrobial therapy versus placebo

Figure 123: Mortality <1 year

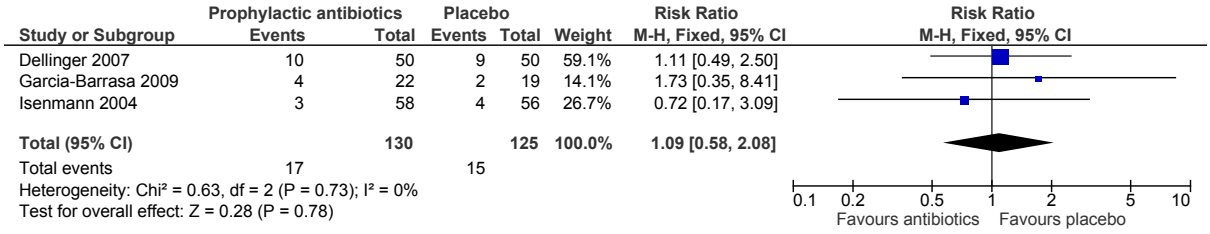


Figure 124: Infected necrosis <1 year

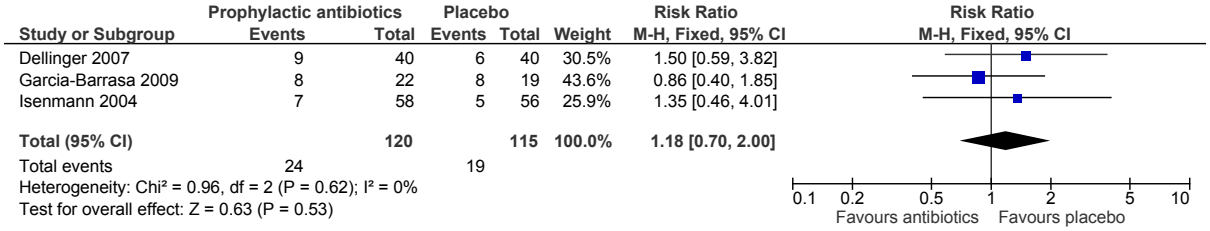


Figure 125: Extra-pancreatic infection <1 year

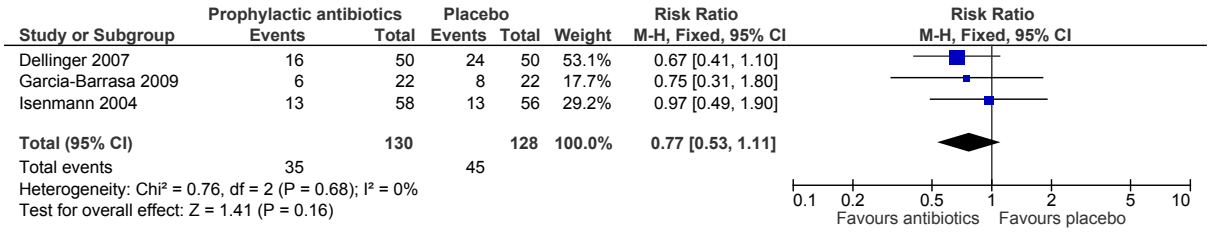


Figure 126: Serious adverse events <6 months

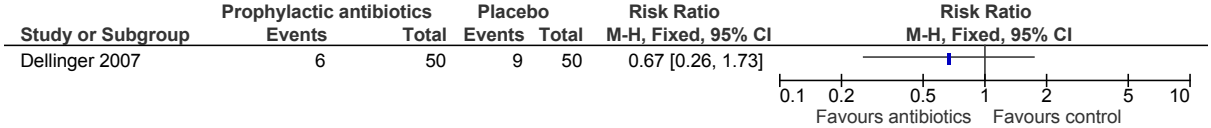


Figure 127: Serious adverse events (Pulmonary insufficiency) <6 months

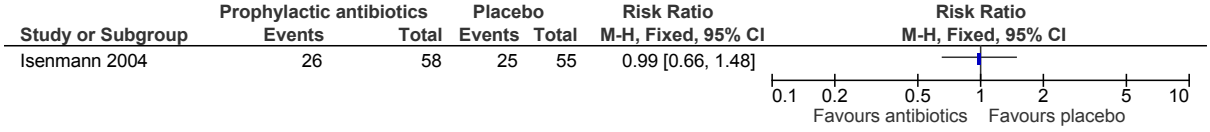


Figure 128: Serious adverse events (Renal insufficiency) <6 months

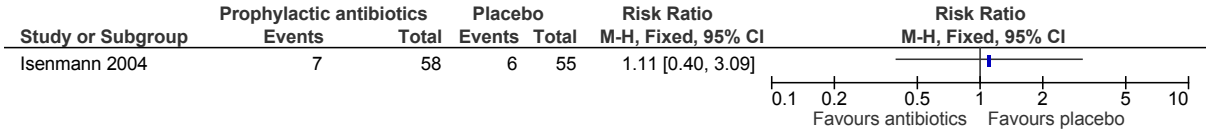


Figure 129: Serious adverse events (Shock) <6 months

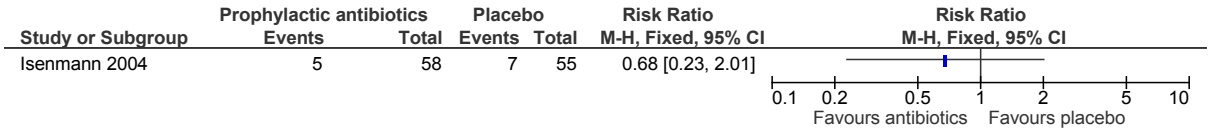
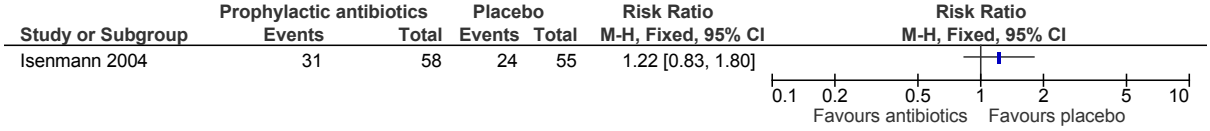
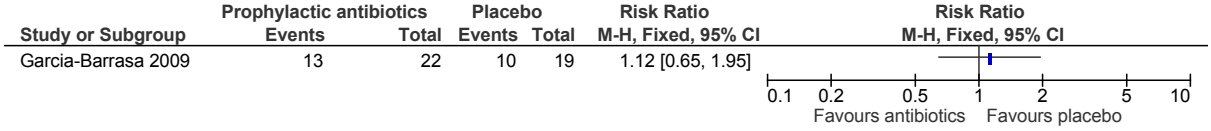


Figure 130: Serious adverse events (SIRS) <6 months



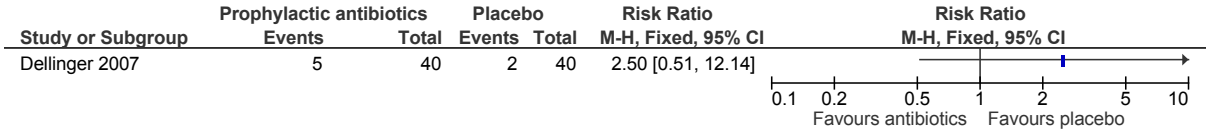
1

Figure 131: Serious adverse events (multi-organ failure) <6 months



2

Figure 132: Colonisation by resistant organisms <6 months



3

K.11.3 Prophylactic antimicrobial therapy versus other prophylactic antimicrobial therapy (same class)

K.11.3.1 Carbapenems

Figure 133: Mortality <1 year

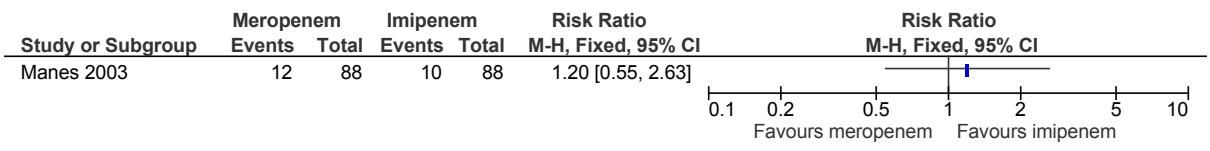


Figure 134: Infected necrosis <1 year

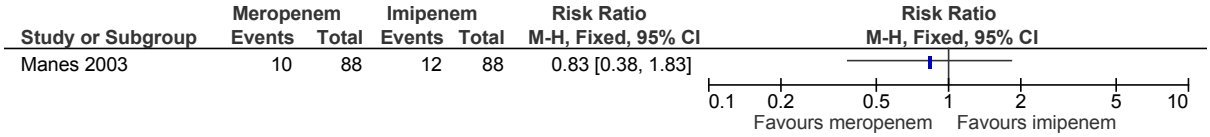


Figure 135: Extra-pancreatic infection <1 year

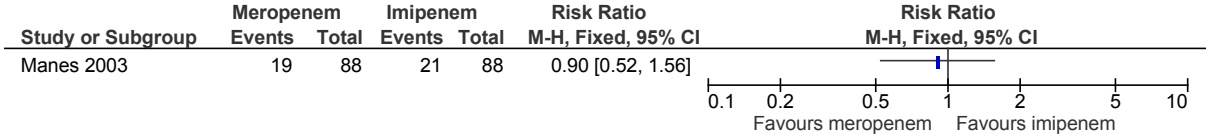
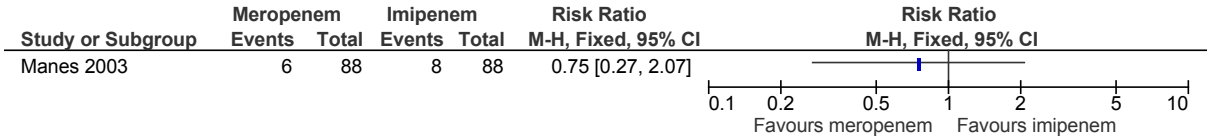


Figure 136: Serious adverse events (multi-organ failure) <6 months



K.11.4 Prophylactic antimicrobial therapy versus other prophylactic antimicrobial therapy (different class)

K.11.4.1 Quinolones versus carbapenems

Figure 137: Mortality <1 year

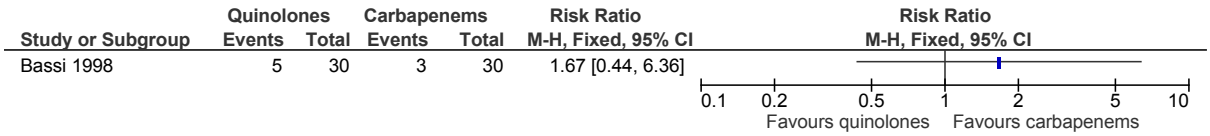


Figure 138: Infected necrosis <1 year

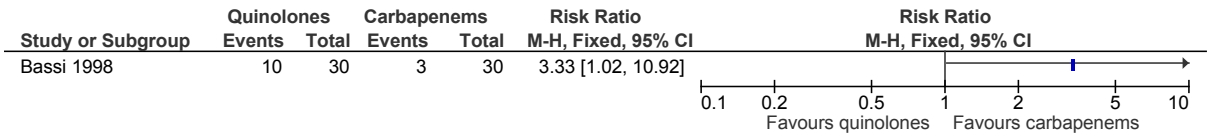
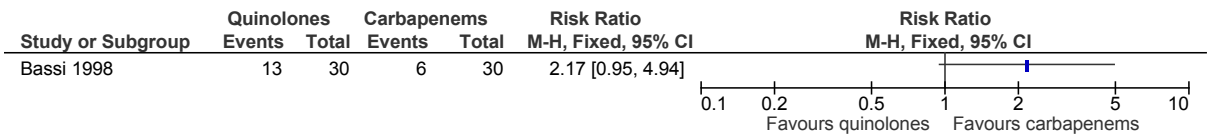


Figure 139: Extra-pancreatic infection <1 year



K.12 Methods of management of infected necrosis in people with acute pancreatitis

K.12.1 Minimally invasive surgery versus open surgery (randomised controlled trial)

Figure 140: Mortality at ≤1 year

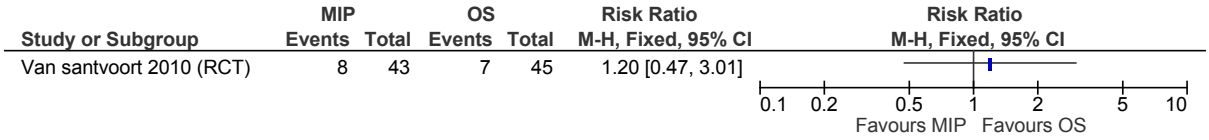


Figure 141: Complications (enterocutaneous fistula or perforation of a visceral organ requiring intervention) at ≤1 year

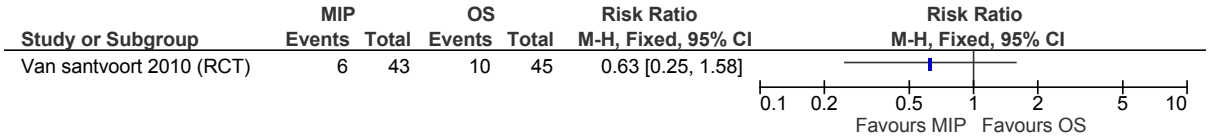


Figure 142: Complications (intra-abdominal bleeding) at ≤1 year

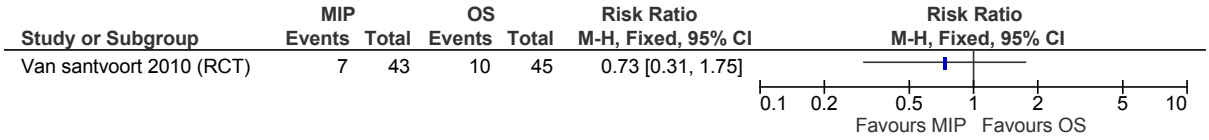


Figure 143: Complications (multiple organ failure) at ≤1 year

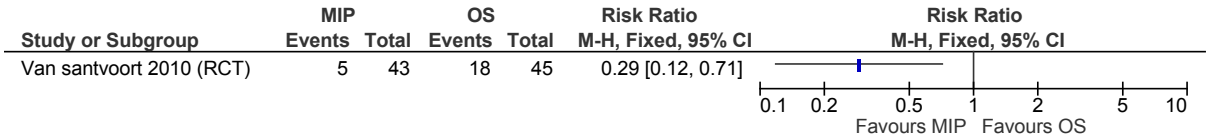


Figure 144: Complications (multiple systemic complications) at ≤1 year

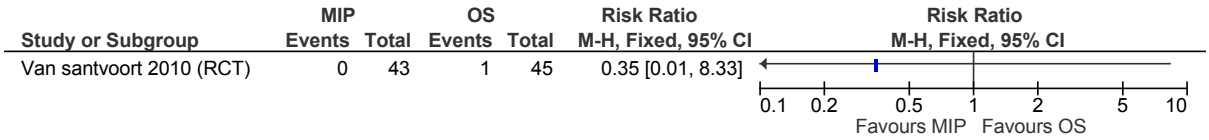
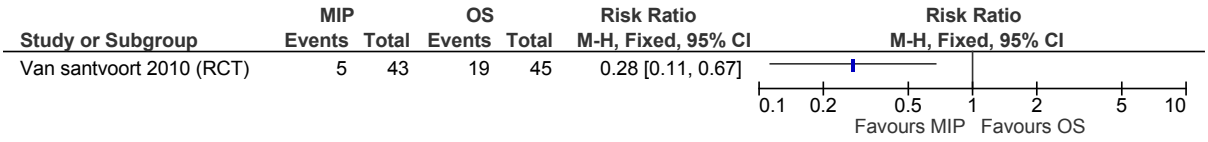
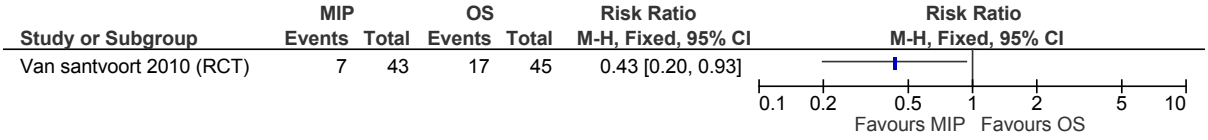


Figure 145: Complications (new-onset multiple organ failure) at ≤1 year



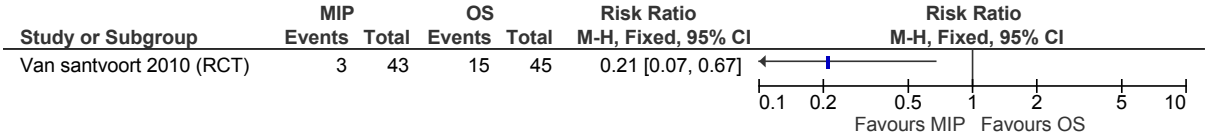
1

Figure 146: Pancreatic functions (new-onset diabetes) at ≤1 year



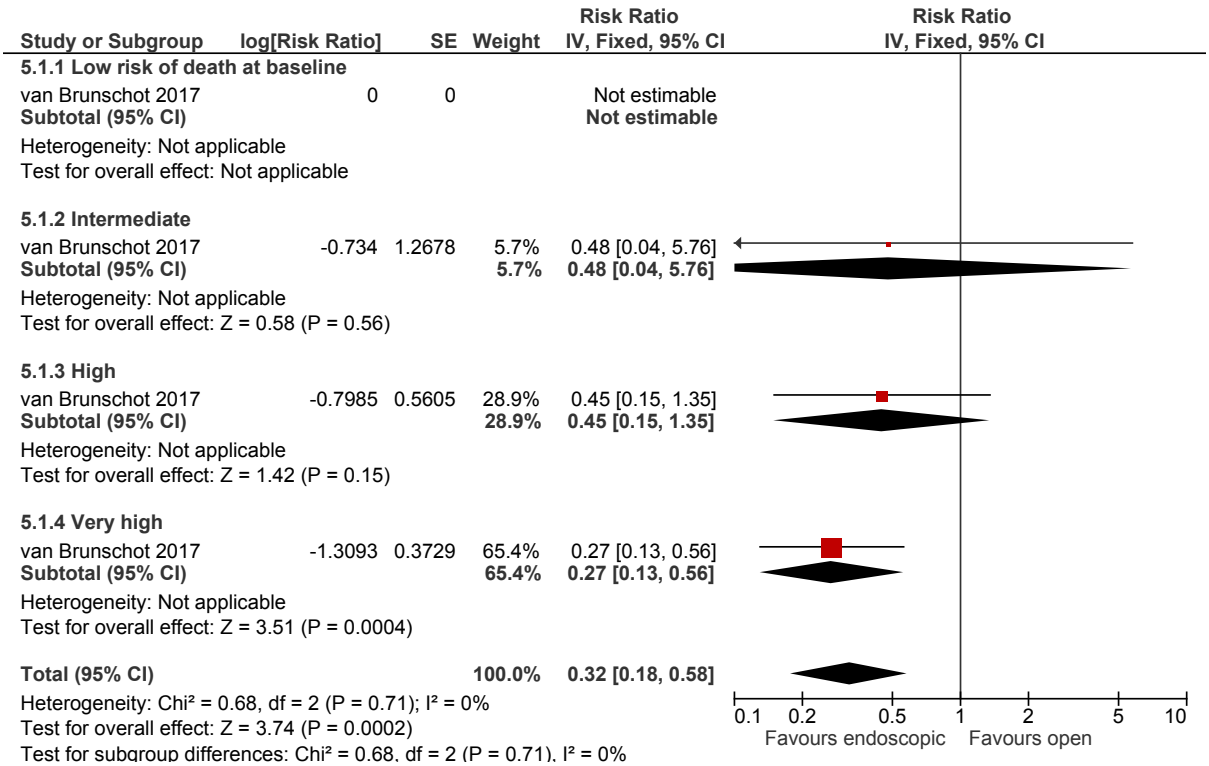
2

Figure 147: Pancreatic functions (use of pancreatic enzymes) at ≤1 year



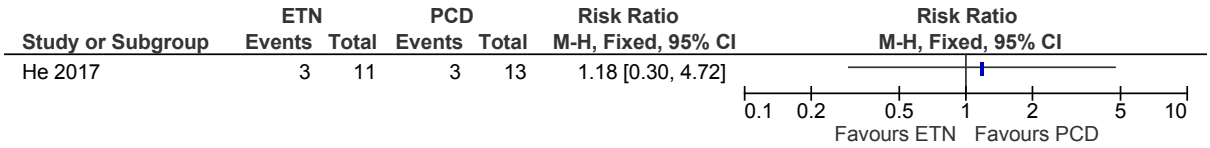
3 ## K.12.2 Minimally invasive surgery (endoscopic) versus open surgery

Figure 148: Mortality at ≤1 year



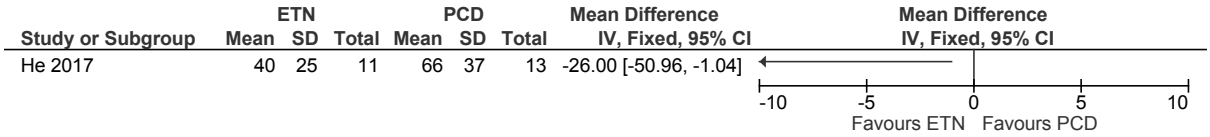
4 ## K.12.3 Endoscopic step-up versus percutaneous drainage with step-up to open surgery

Figure 149: Mortality at ≤1 year



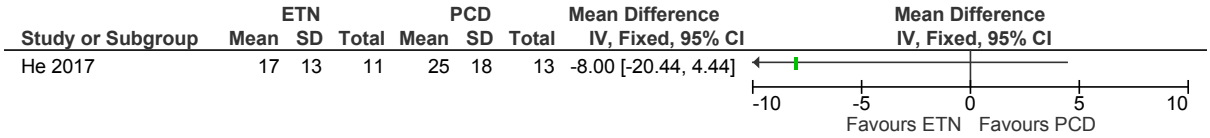
1

Figure 150: Length of stay (hospital) at ≤1 year



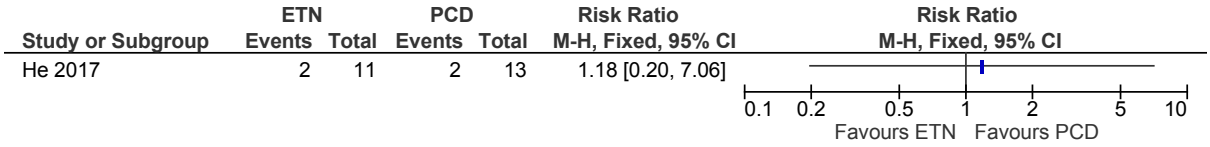
2

Figure 151: Length of stay (CCU) at ≤1 year



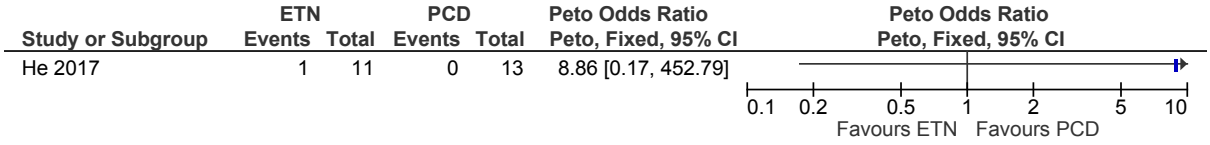
3

Figure 152: Complications (new-onset organ failure) at ≤1 year



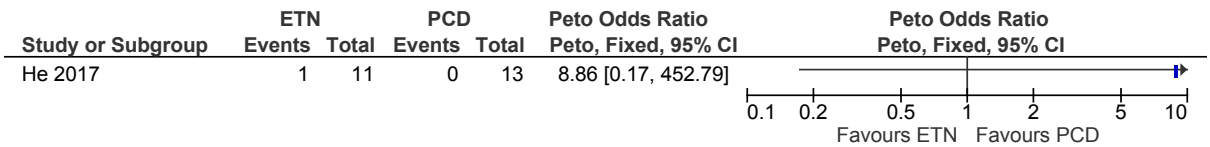
4

Figure 153: Complications (multiple organ failure) at ≤1 year



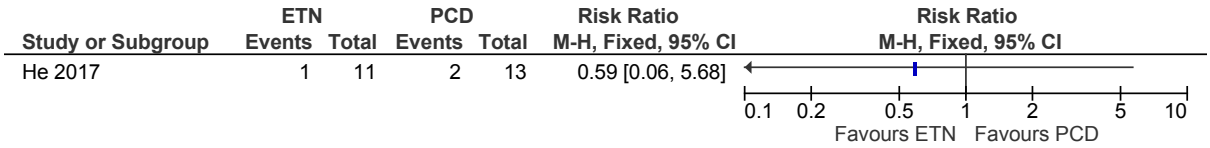
5

Figure 154: Complications (upper gastrointestingal bleeding) at ≤1 year



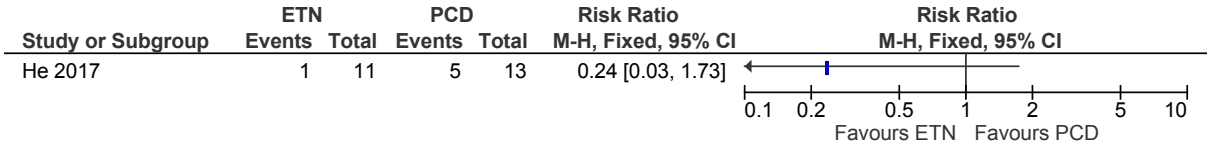
6

Figure 155: Complications (intra-abdominal bleeding requiring intervention) at ≤1 year



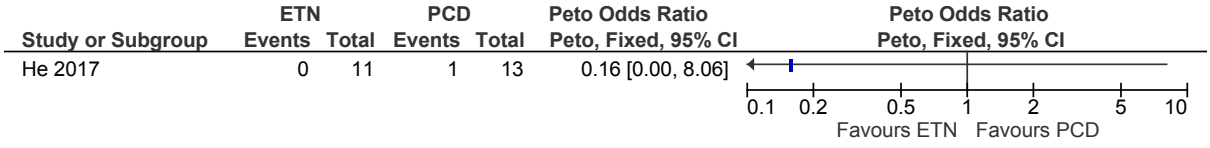
1

Figure 156: Complications (enterocutaneous fistula or perforation) at ≤1 year



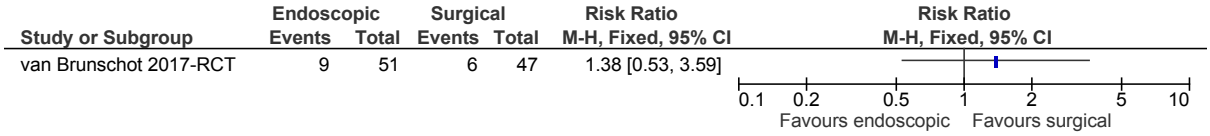
2

Figure 157: Complications (pancreatic fistula) at ≤1 year



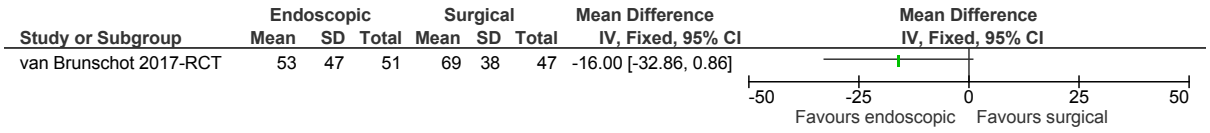
3 **K.12.4 Endoscopic step-up compared to minimally-invasive surgical step-up approach**

Figure 158: Mortality at ≤1 year



4

Figure 159: Length of hospital stay at ≤1 year



5

Figure 160: Complications at ≤1 year

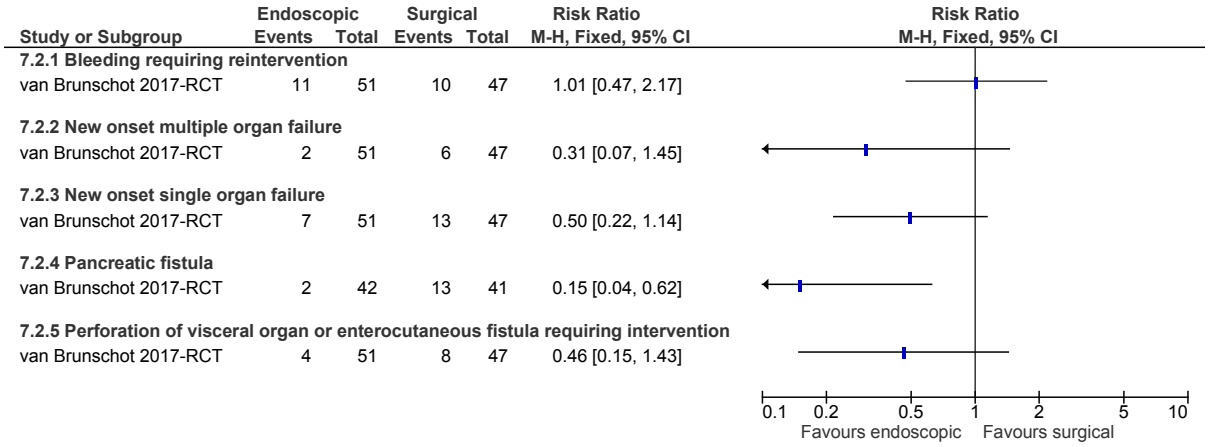
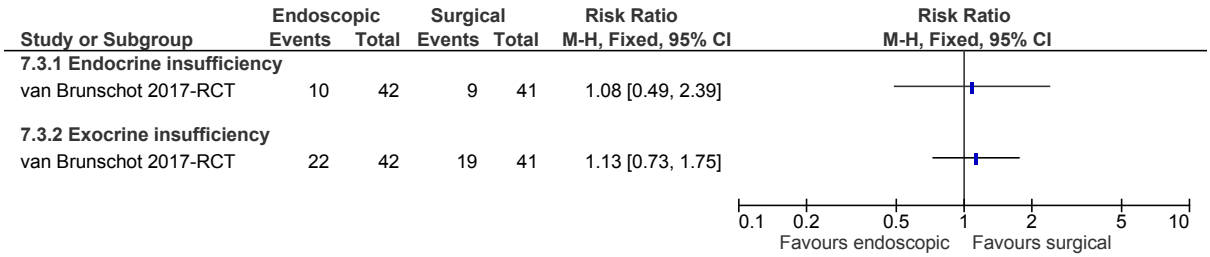


Figure 161: Pancreatic function at ≤1 year



K.12.5 Minimally invasive procedure (endoscopic – dual modality drainage) versus percutaneous drainage

Figure 162: Mortality at ≤1 year

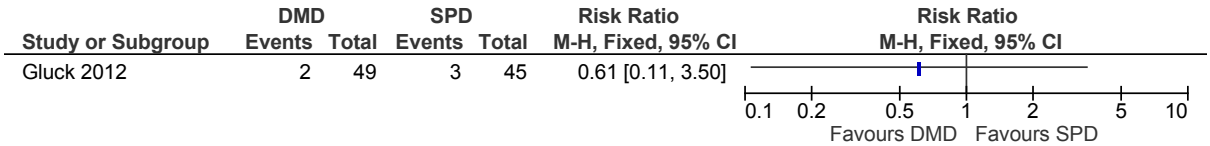


Figure 163: Length of stay in hospital at ≤1 year

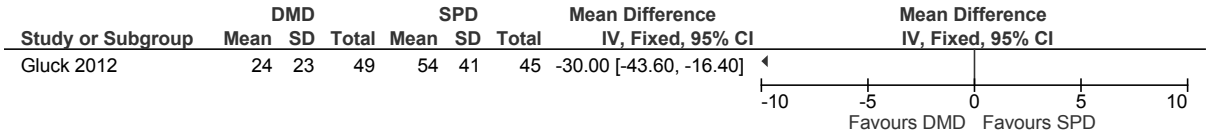
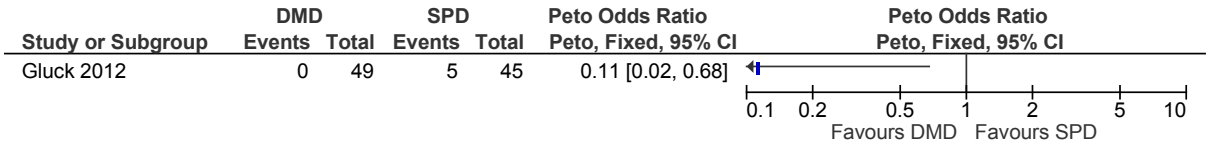


Figure 164: Complications (pseudoaneurysm) at ≤1 year



K.12.6 Minimally invasive surgery (open or videoscopically assisted retroperitoneal debridement) versus open surgery (open abdomen strategy; continuous postoperative lavage; laparotomy with primary abdomen closure)

Figure 165: Mortality at ≤1 year

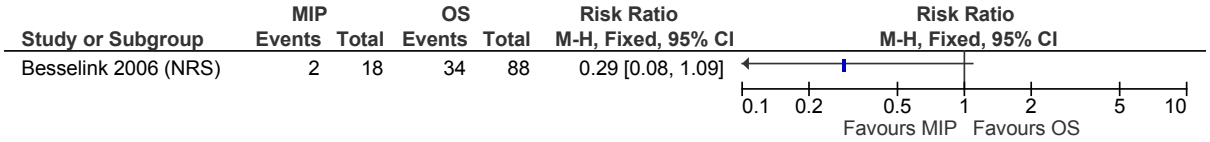


Figure 166: Mortality at ≤1 year

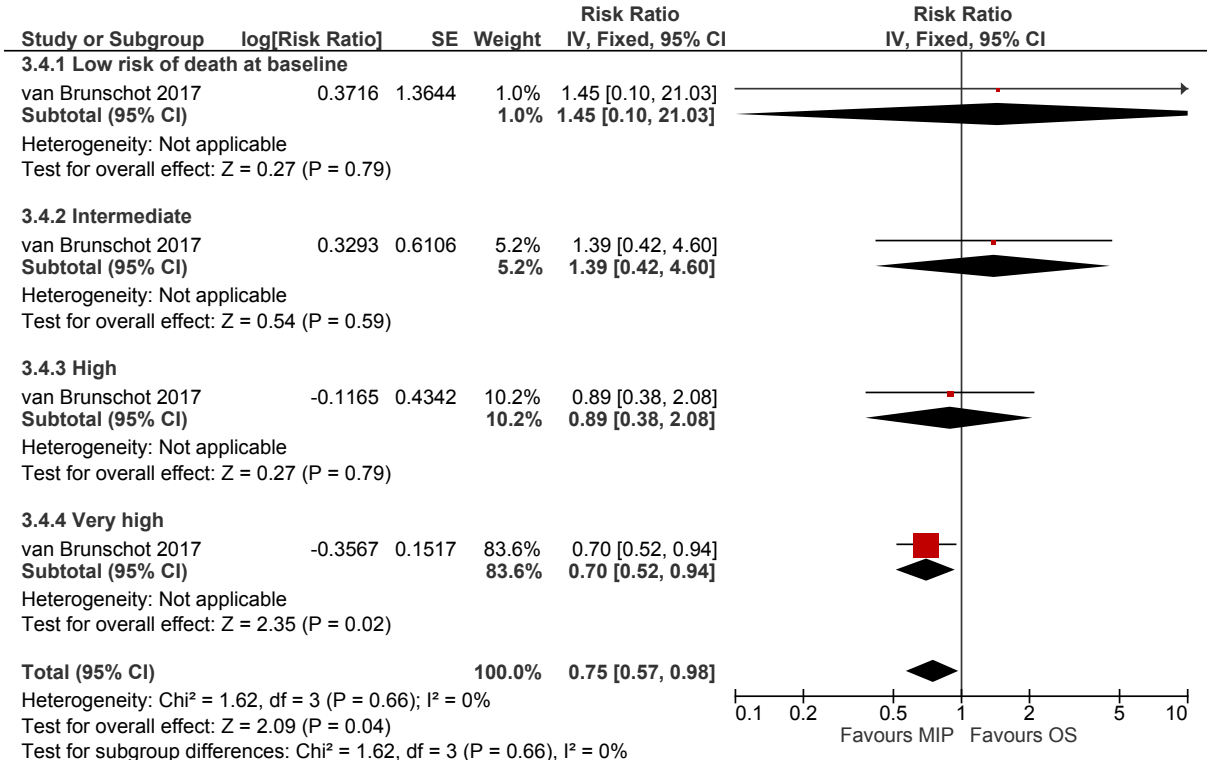


Figure 167: Complications (bleeding) at ≤1 year

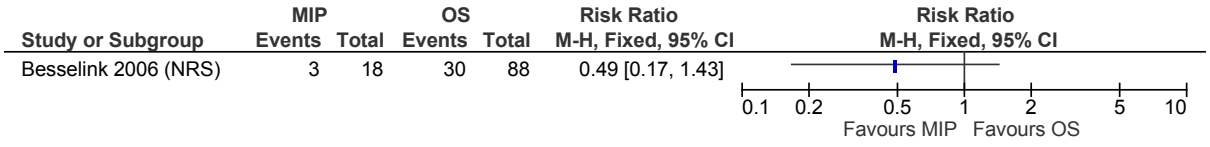


Figure 168: Complications (bowel perforation) at ≤1 year

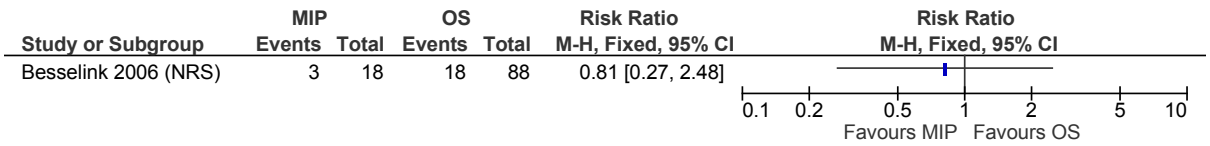
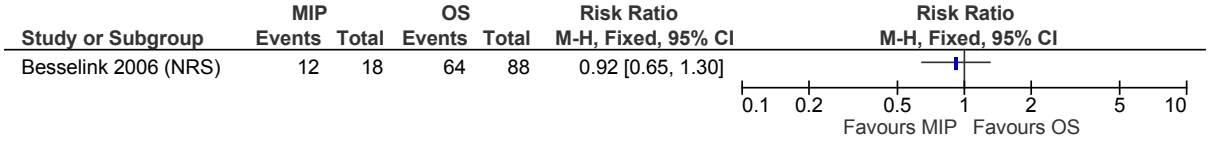


Figure 169: Number of procedures (re-intervention) at ≤1 year



K.12.7 Combination of interventions (step-up approach) versus open surgery

Figure 170: Mortality at ≤1 year

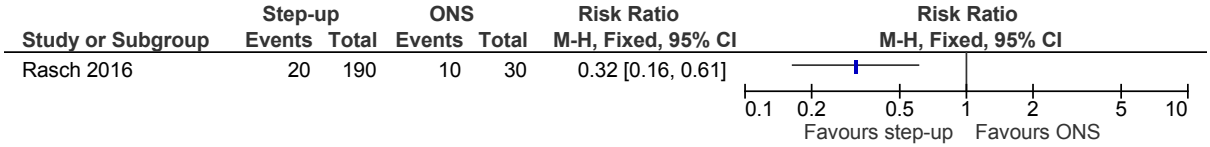


Figure 171: Severe complication (sepsis, persistent MODS or erosion bleeding) at ≤1 year

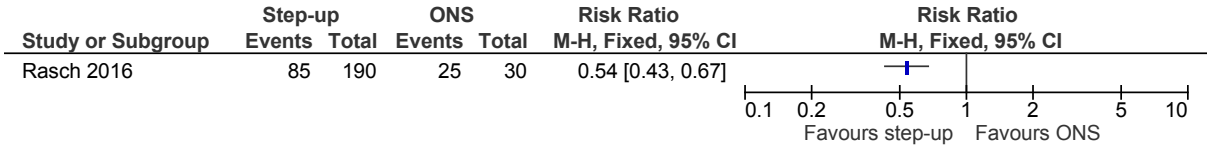
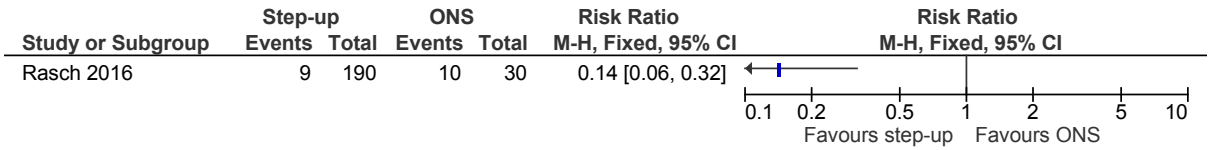


Figure 172: Pancreatic function (emergence of type 3c diabetes) at ≤1 year



K.12.8 Minimally invasive surgery (focused open necrosectomy) versus open surgery (conventional open necrosectomy)

Figure 173: Mortality at ≤1 year

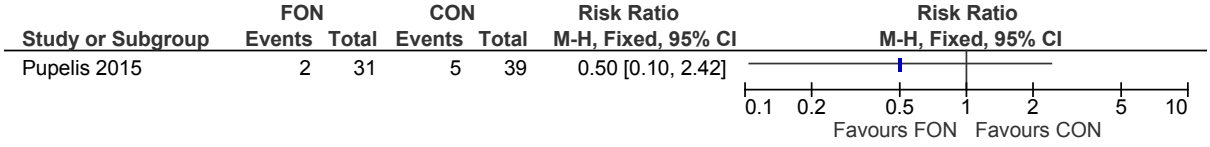


Figure 174: Complications (intestinal fistulae) at ≤1 year

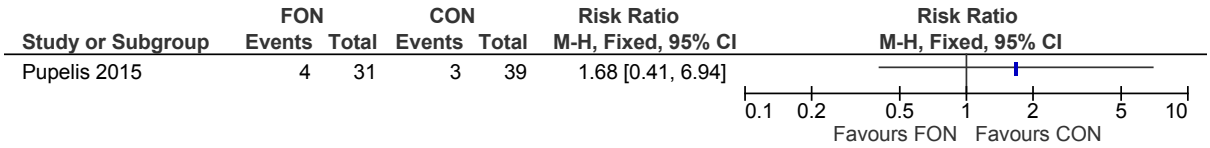


Figure 175: Complications (pancreatic fistulae) at ≤1 year

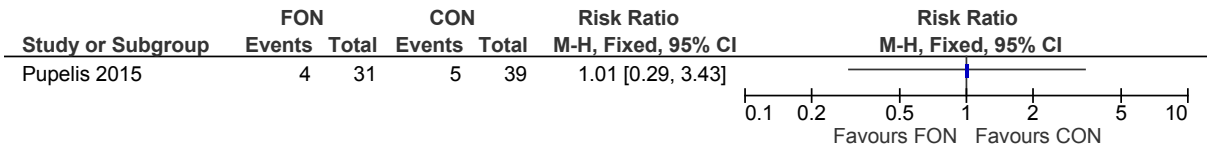
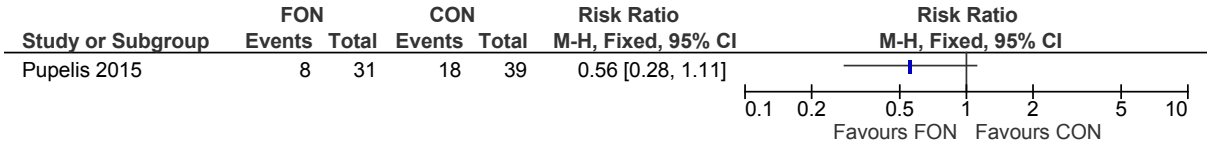


Figure 176: Number of procedures (repeat necrosectomy) at ≤1 year



K.12.9 Percutaneous drainage versus combination of interventions (laparotomy, necrosectomy and active drainage)

Figure 177: Mortality at ≤1 year

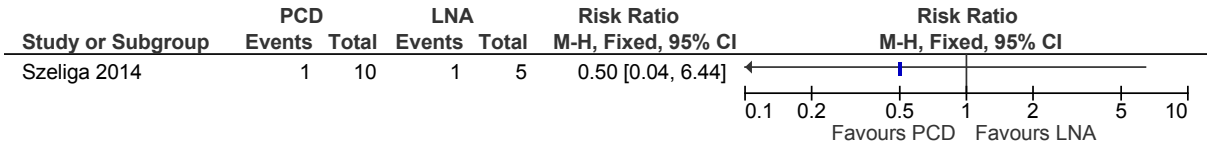
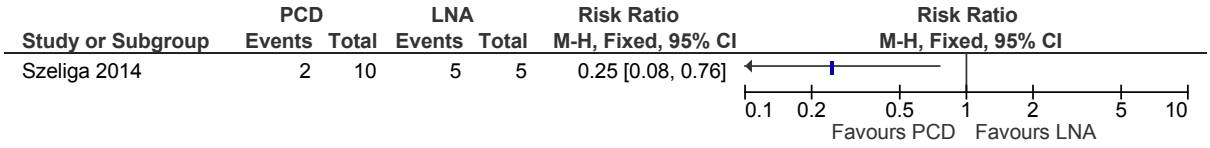


Figure 178: Complications (Wound infection, haemorrhage at surgical site, pancreatic fistula, intestinal fistula) at ≤1 year



K.12.10 Percutaneous drainage versus combination of interventions (laparotomy, necrosectomy and passive drainage)

Figure 179: Mortality at ≤1 year

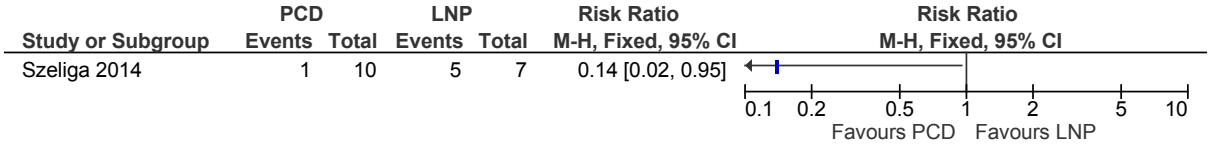
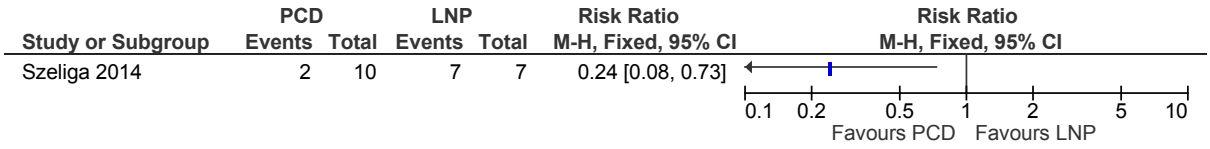


Figure 180: Complications (wound infection, haemorrhage at surgical site, pancreatic fistula, intestinal fistula) at ≤1 year



K.12.11 Combination of interventions (percutaneous drainage and VARD) versus combination of interventions (laparotomy, necrosectomy and active drainage)

Figure 181: Mortality at ≤1 year

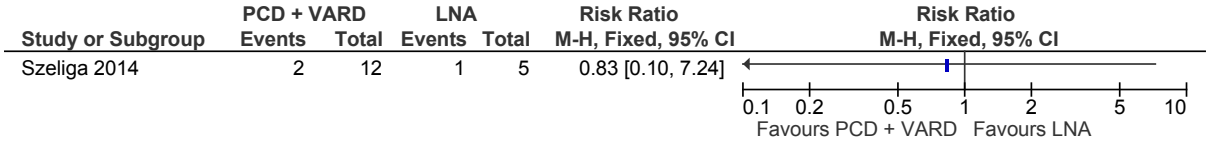
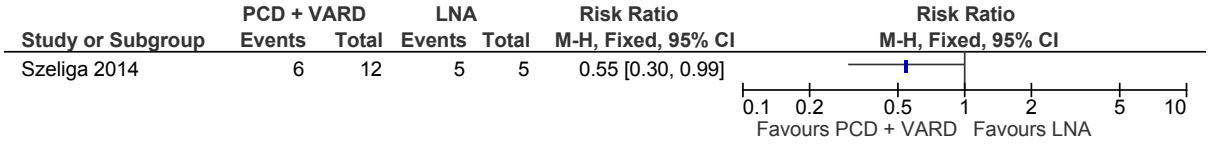


Figure 182: Complications (wound infection, haemorrhage at surgical site, pancreatic fistula, intestinal fistula) at ≤1 year



K.12.12 Combination of interventions (percutaneous drainage and VARD) versus combination of interventions (laparotomy, necrosectomy and passive drainage)

Figure 183: Mortality at ≤1 year

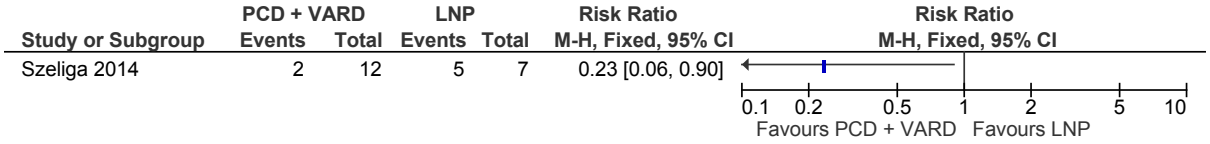
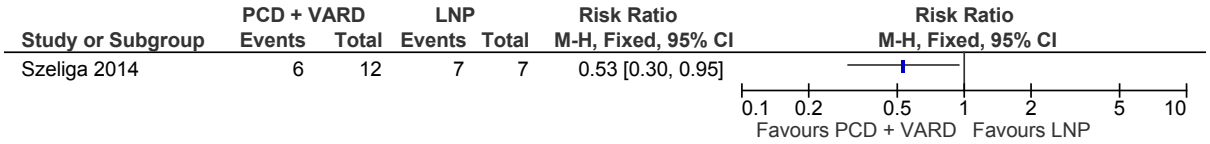
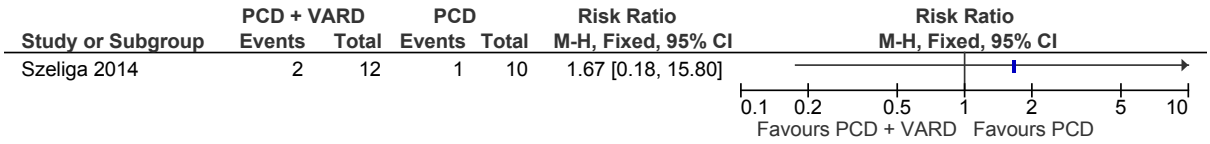


Figure 184: Complications (wound infection, haemorrhage at surgical site, pancreatic fistula, intestinal fistula) at ≤1 year



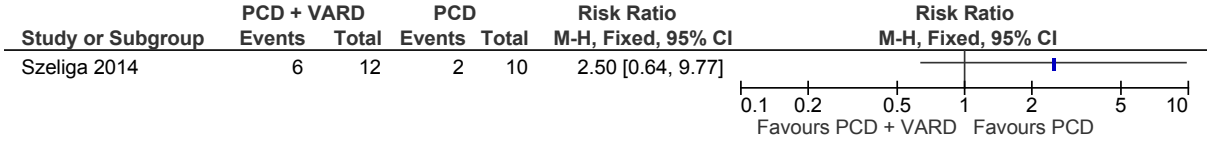
K.12.13 Combination of interventions (percutaneous drainage and VARD) versus percutaneous drainage

Figure 185: Mortality at ≤1 year



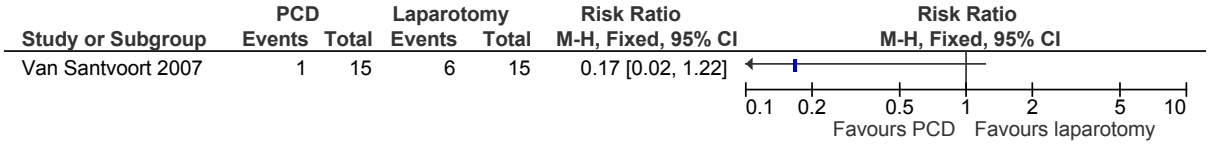
1

Figure 186: Complications (wound infection, haemorrhage at surgical site, pancreatic fistula, intestinal fistula) at ≤1 year



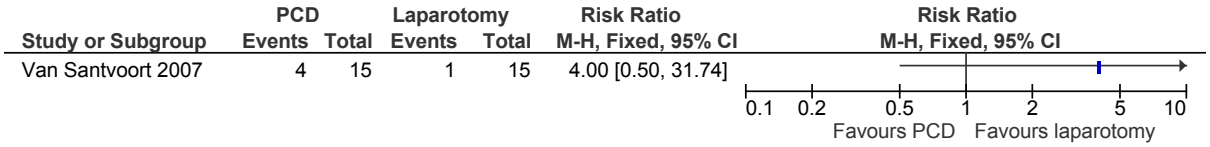
2 **K.12.14 Percutaneous drainage versus open surgery (laparotomy)**

Figure 187: Mortality at ≤1 year



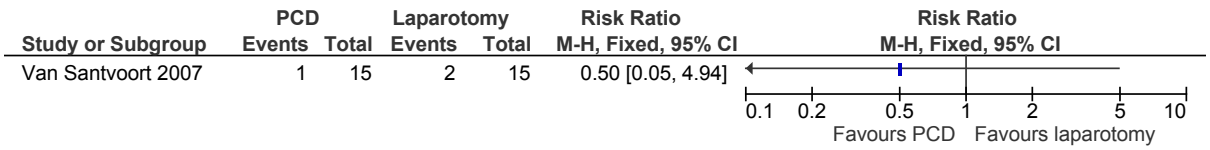
3

Figure 188: Complications (bleeding) at ≤1 year



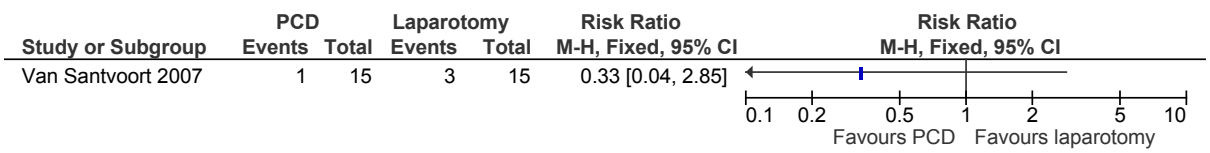
4

Figure 189: Complications (bowel perforation) at ≤1 year



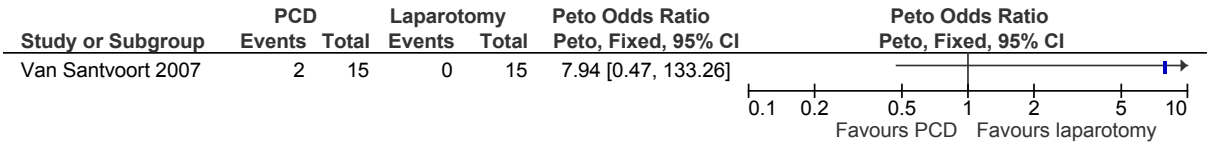
5

Figure 190: Complications (GI fistulas) at ≤1 year



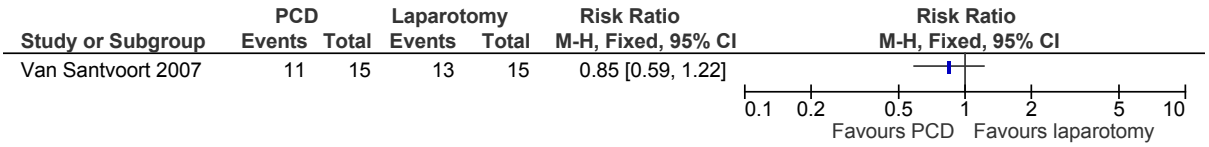
6

Figure 191: Complications (pancreatic fistulas) at ≤1 year



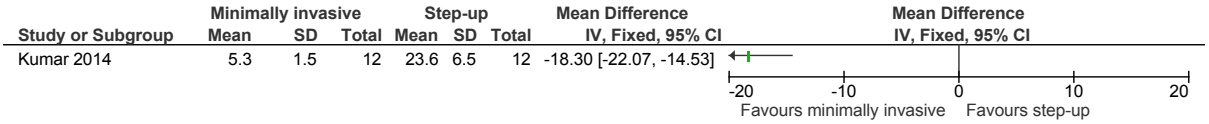
1

Figure 192: Number of procedures (further necrosectomy) at ≤1 year



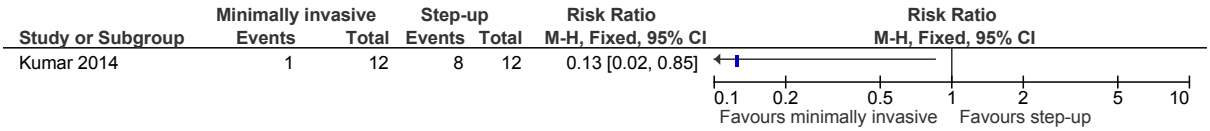
2 **K.12.15 Minimally invasive surgery versus step-up approach**

Figure 193: Floor length of stay at ≤1 year



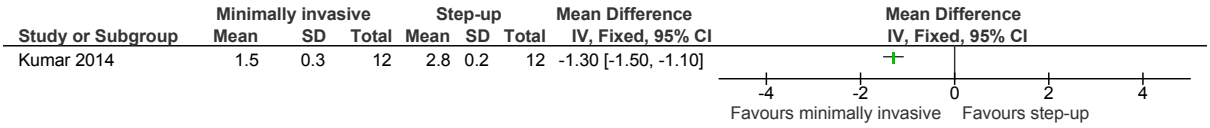
3

Figure 194: Complications at ≤1 year



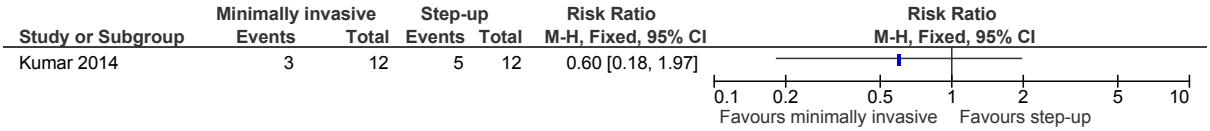
4

Figure 195: Number of procedures at ≤1 year



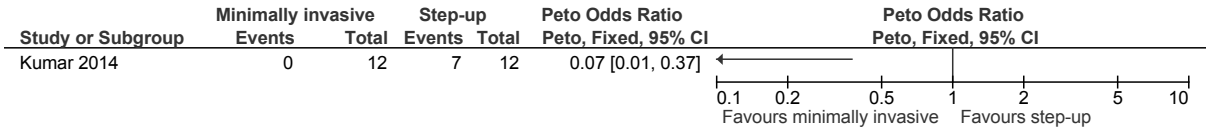
5

Figure 196: Pancreatic function (new exocrine insufficiency) at ≤1 year



6

Figure 197: Pancreatic function (new endocrine insufficiency) at ≤1 year



K.13 Timing of management of infected necrosis in people with acute pancreatitis

K.13.1 Minimally invasive surgery versus step-up approach

Figure 198: Mortality at ≤1 year

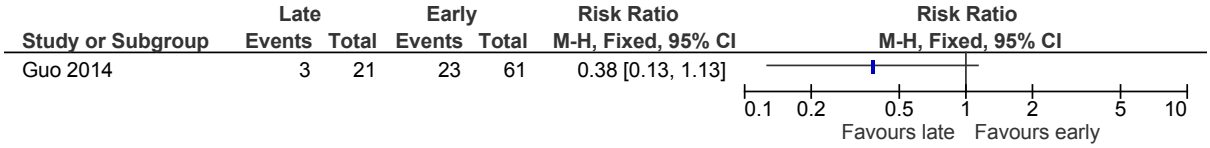


Figure 199: Number of procedures (Re-intervention) at ≤1 year

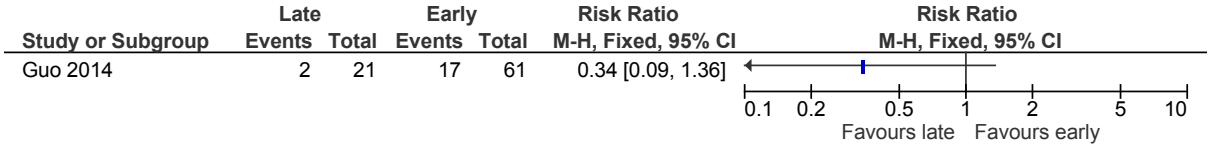


Figure 200: Complications (Intra-abdominal bleeding) at ≤1 year

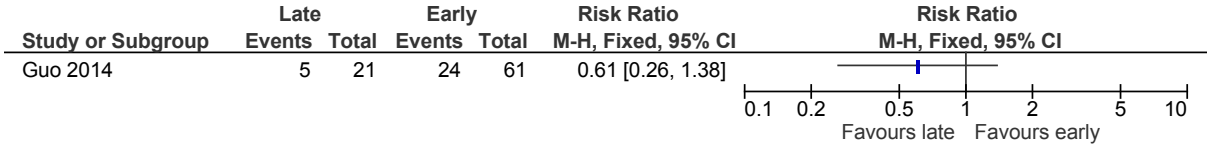


Figure 201: Complications (Enterocutaneous fistula) at ≤1 year

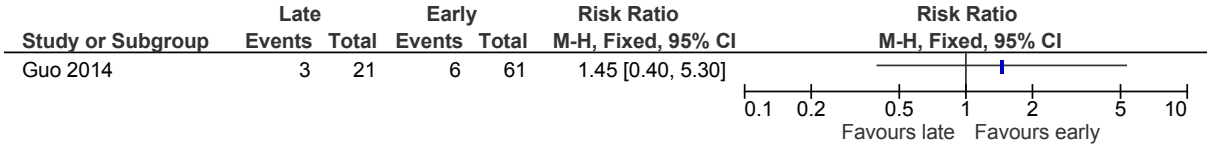
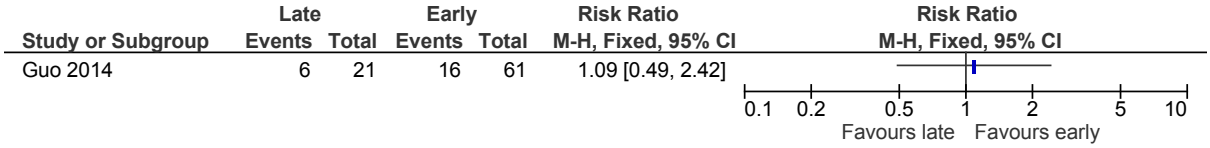


Figure 202: Complications (New-onset organ failure) at ≤1 year



K.13.2 Late intervention versus early intervention in people with no organ failure

Figure 203: Mortality at ≤1 year

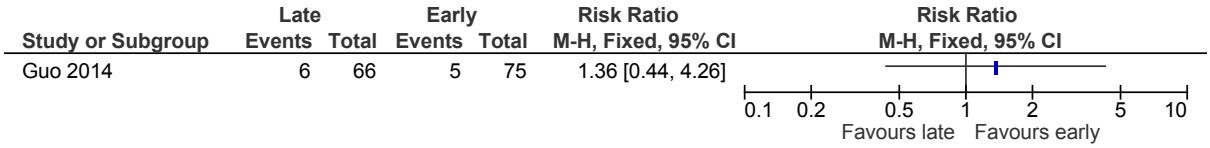


Figure 204: Number of procedures (Re-intervention) at ≤1 year

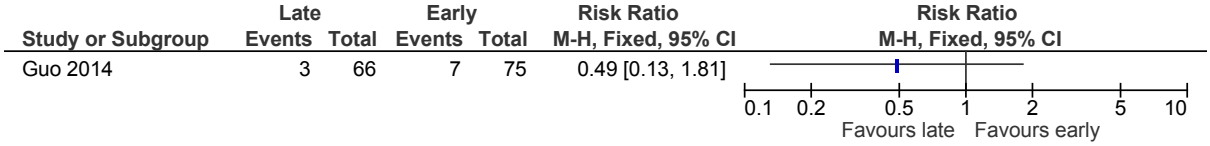


Figure 205: Complications (Intra-abdominal bleeding) at ≤1 year

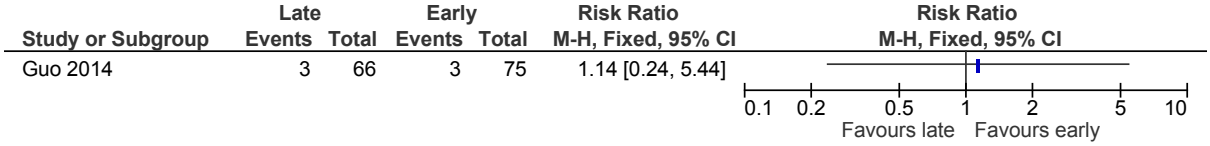


Figure 206: Complications (Enterocutaneous fistula) at ≤1 year

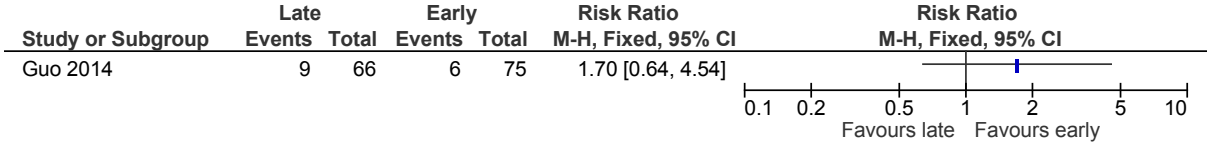
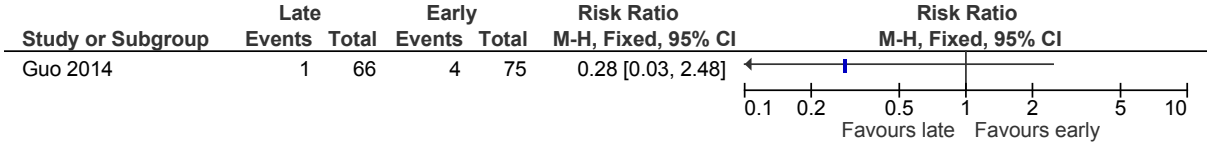


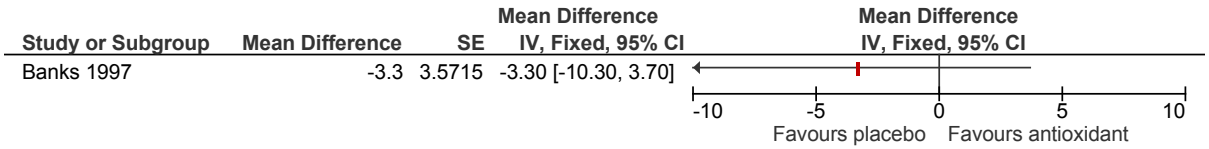
Figure 207: Complications (New-onset organ failure) at ≤1 year



K.14 Management of pain in people with chronic pancreatitis

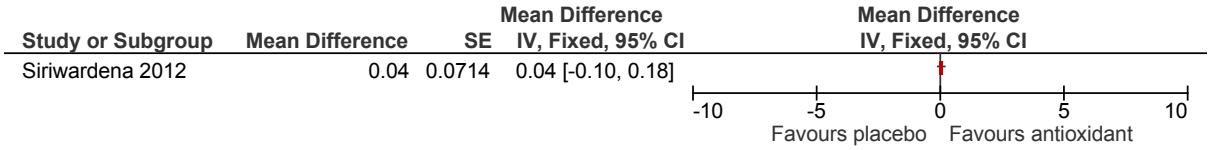
K.14.1 Pharmacological therapy versus placebo

Figure 208: Quality of life (Activities of Daily Living) at 10 weeks



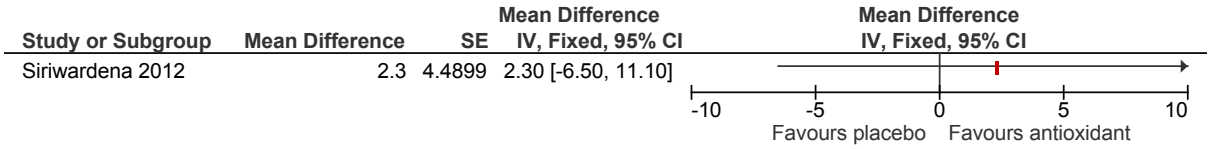
1

Figure 209: Quality of life (EQ5D) at 6 months



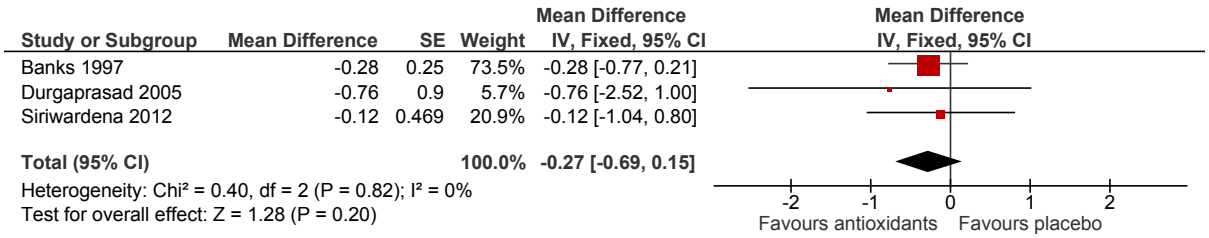
2

Figure 210: Quality of life (EQ-VAS) at 6 months



3

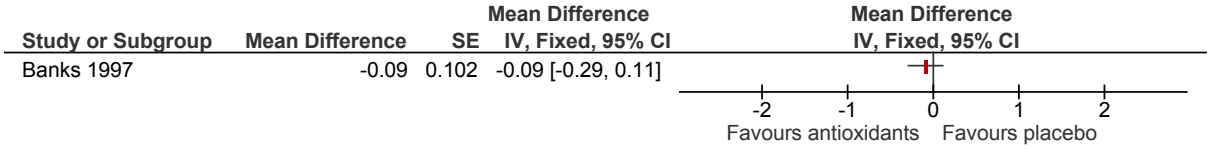
Figure 211: Pain (VAS) at ≤6 months



Note: Banks 1997 is a crossover trial, the variance has been adjusted to account for paired data

4

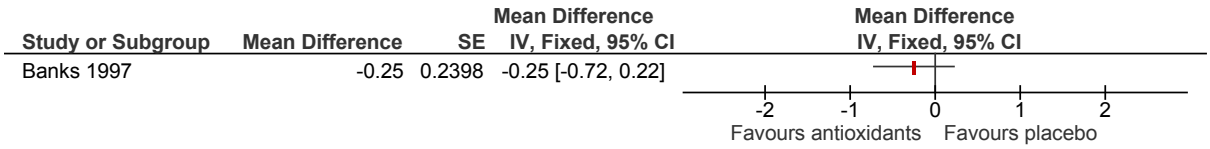
Figure 212: Pain (descriptive scale) at 10 weeks



Note: Banks 1997 is a crossover trial

5

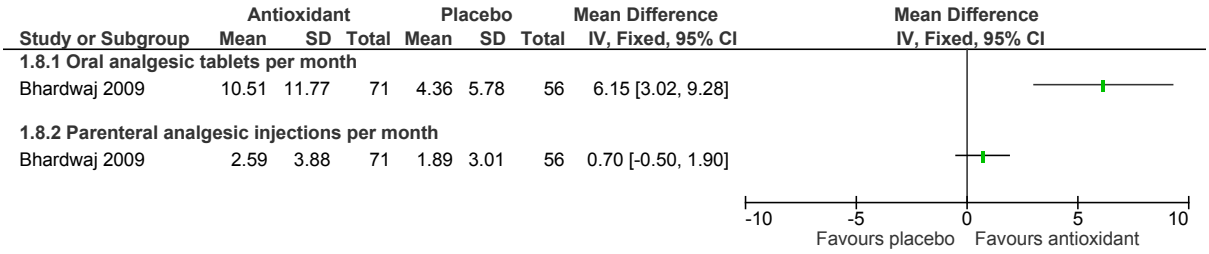
Figure 213: Pain (numerical rating scale) at 10 weeks



Note: Banks 1997 is a crossover trial

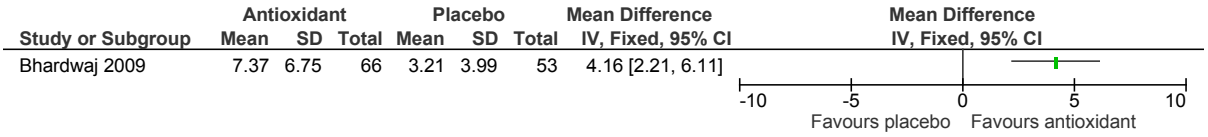
1

Figure 214: Pain (reduction in pain medication) at 6 months



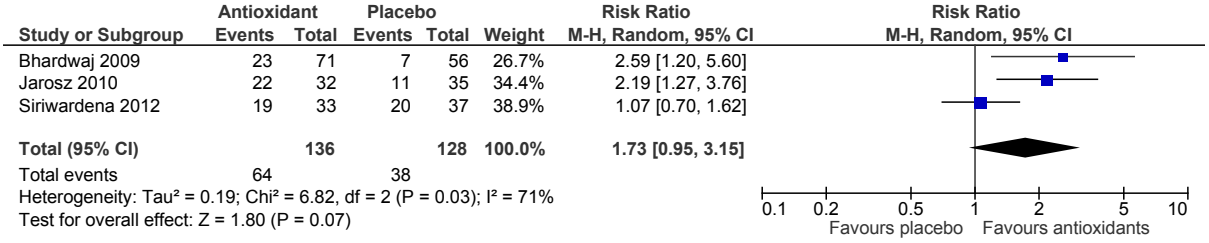
2

Figure 215: Pain (reduction in number of painful days) at 6 months



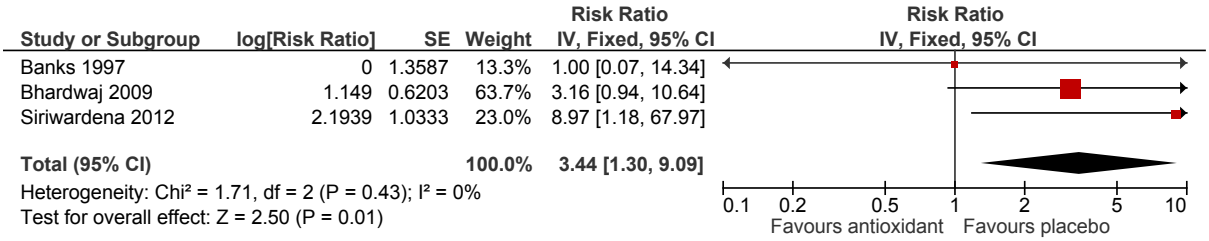
3

Figure 216: Pain (pain free participants) at 6 months



4

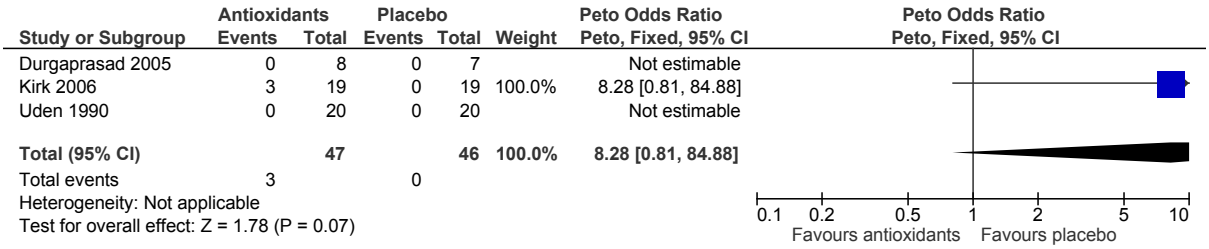
Figure 217: Adverse events at ≤6 months



Note: Banks 1997 is a crossover trial, the variance has been adjusted to account for paired data

5

Figure 218: Adverse events at ≤ 20 weeks

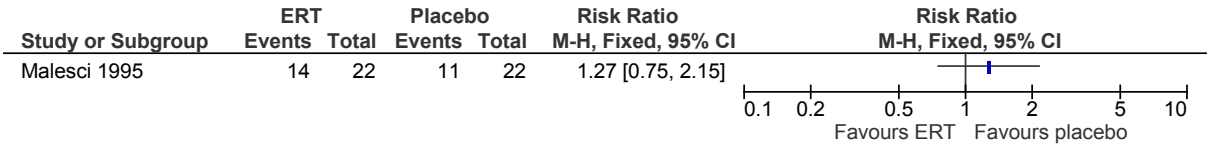


Uden 1990 and Kirk 2006 are crossover trials, adjustment was not possible due to there being zero events in one or both arms

1

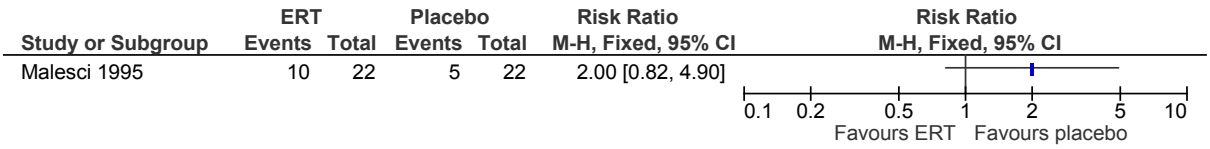
2 K.14.2 Enzyme replacement therapy versus placebo

Figure 219: Pain (People experiencing long-lasting (>12 hour) pain attacks) at 4 months



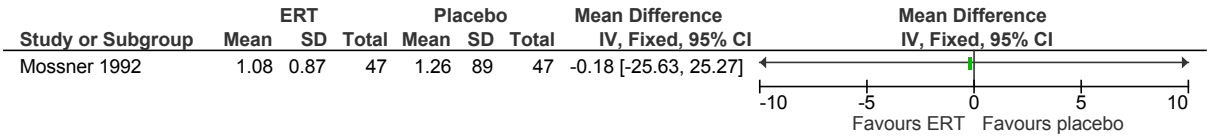
3

Figure 220: Pain (Use of analgesics) at 4 months



4

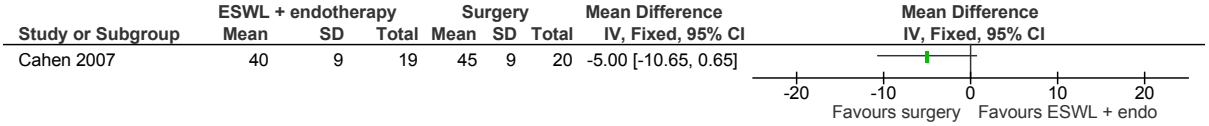
Figure 221: Pain (Pain score) at 2 weeks



5 # K.15 Management of pancreatic duct obstruction in people with chronic
6 pancreatitis

7 K.15.1 ESWL and endotherapy versus surgery

Figure 222: Quality of life (SF-36, Mental health component) at 2 years



8

Figure 223: Quality of life (SF-36, Mental health component) at 7 years

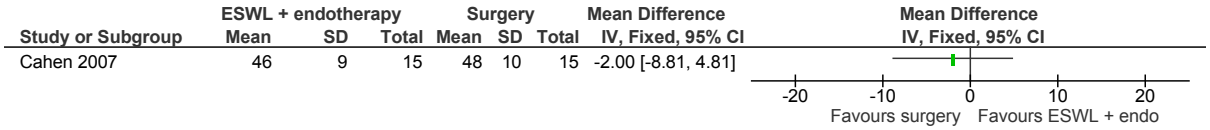


Figure 224: Quality of life (SF-36, Physical health component) at 2 years

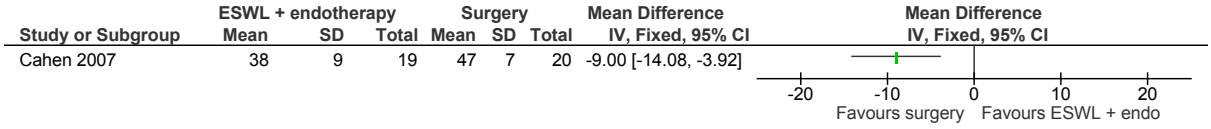


Figure 225: Quality of life (SF-36, Physical health component) at 7 years

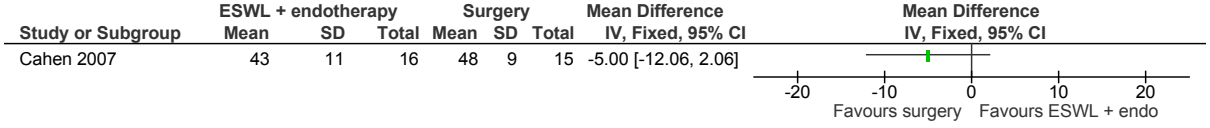


Figure 226: Mortality at 2 years

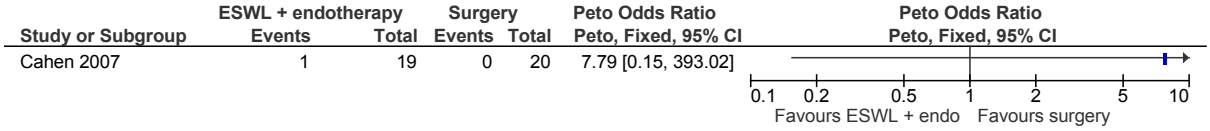


Figure 227: Pain (Pain relief) at 2 years

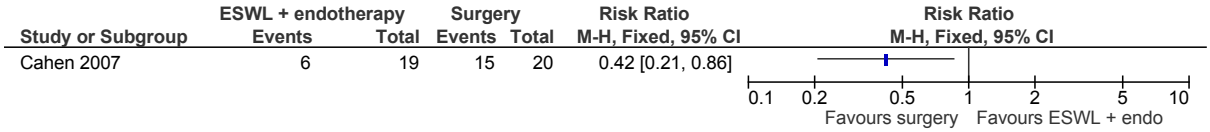


Figure 228: Pain (Pain relief) at 7 years

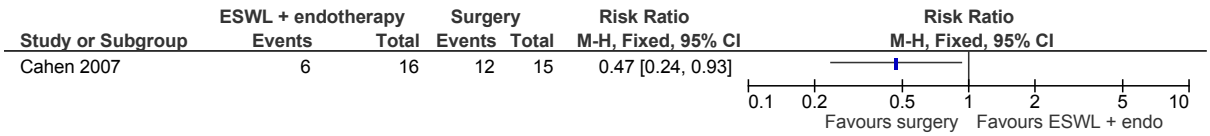


Figure 229: Pain (Izbicki pain score at 2 years)

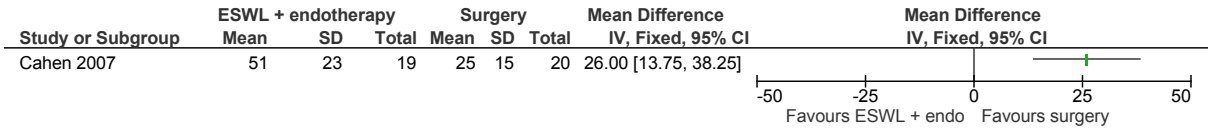
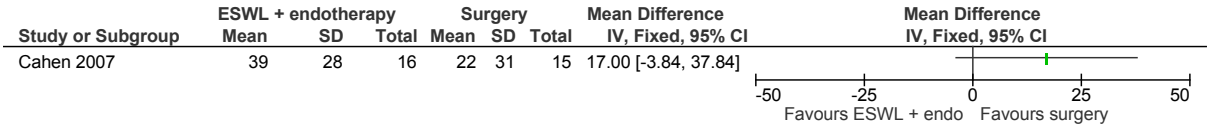
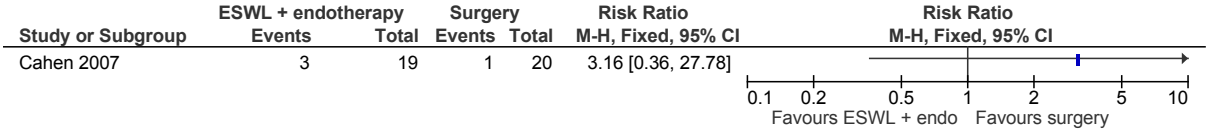


Figure 230: Pain (Izbicki pain score at 7 years)



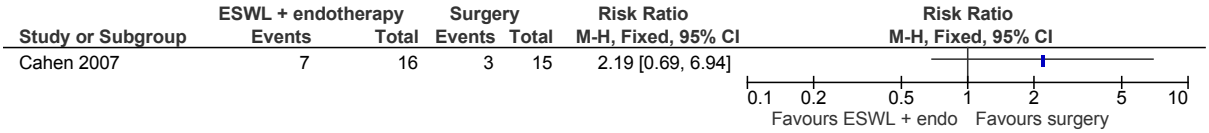
1

Figure 231: Pancreatic function (Endocrine insufficiency developed at 2 years)



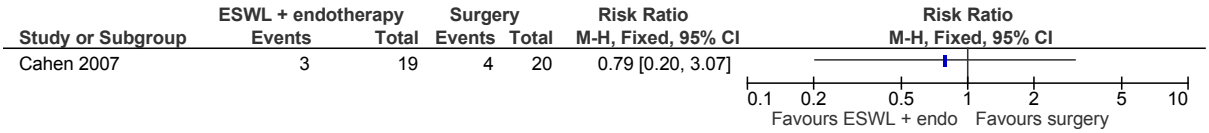
2

Figure 232: Pancreatic function (Endocrine insufficiency developed at 7 years)



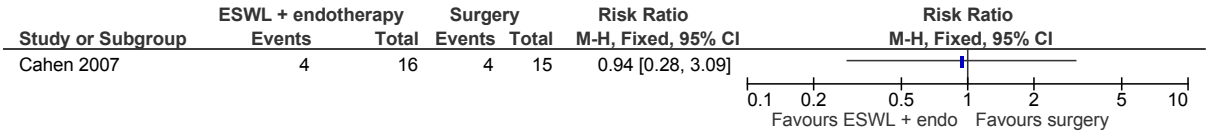
3

Figure 233: Pancreatic function (Endocrine insufficiency persisted at 2 years)



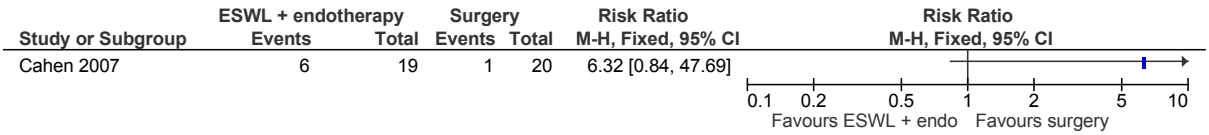
4

Figure 234: Pancreatic function (Endocrine insufficiency persisted at 7 years)



5

Figure 235: Pancreatic function (Exocrine insufficiency developed at 2 years)



6

Figure 236: Pancreatic function (Exocrine insufficiency developed at 7 years)

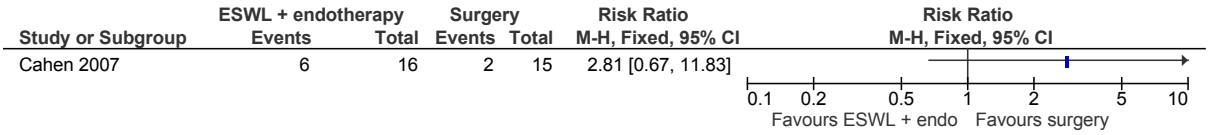


Figure 237: Pancreatic function (Exocrine insufficiency persisted at 2 years)

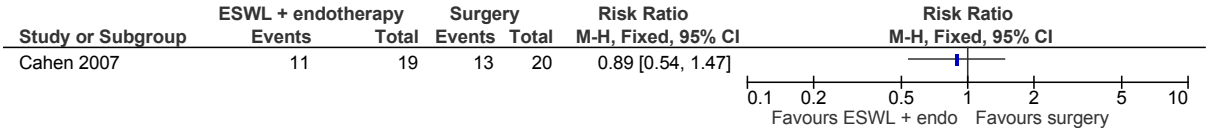
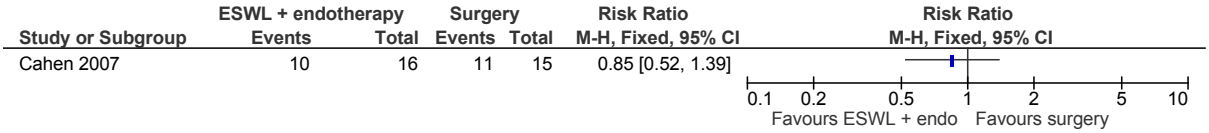


Figure 238: Pancreatic function (Exocrine insufficiency persisted at 7 years)



K.15.2 Endotherapy versus surgery

Figure 239: Pain (Complete absence of pain) at 5 years

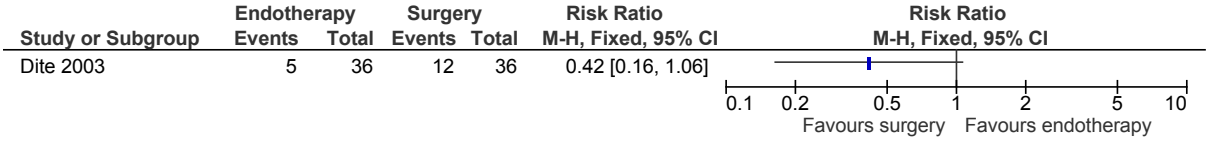


Figure 240: Pain (Partial relief of pain) at 5 years

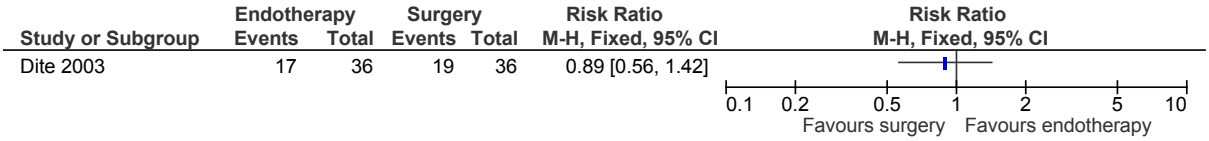
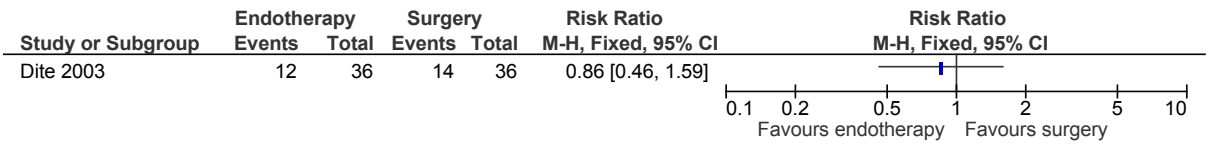


Figure 241: Pancreatic function (New onset diabetes)



K.15.3 ESWL versus ESWL and endotherapy

Figure 242: Pain (Pain relapse) at 2 years

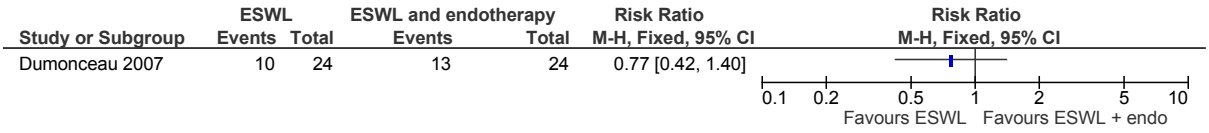


Figure 243: Pain (Pain intensity; VAS score) at 2 years

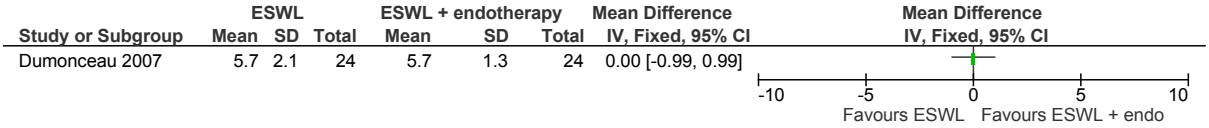


Figure 244: Length of hospital stay at 2 years

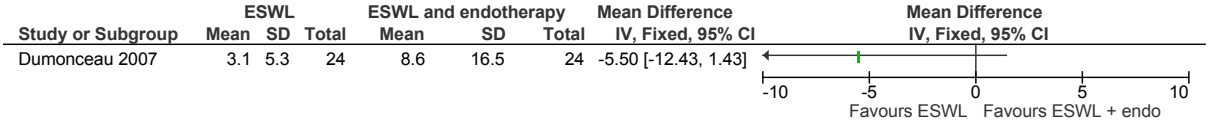
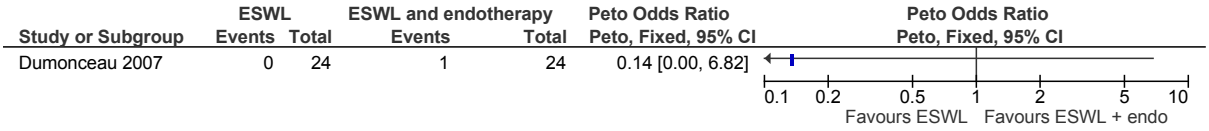


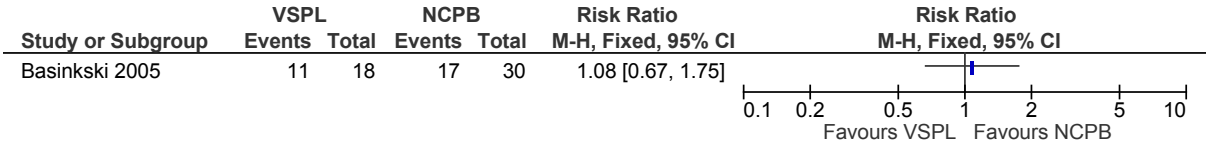
Figure 245: Procedure related complications at 1 month



K.16 Management of small-duct disease in people with chronic pancreatitis

K.16.1 VSPL versus NCPB

Figure 246: Pain (Use of opioids); timepoint unclear



K.17 Management of pseudocysts

K.17.1 Endoscopic drainage versus open surgical drainage or resection

Figure 247: Complications at ≤12 months and >12 months

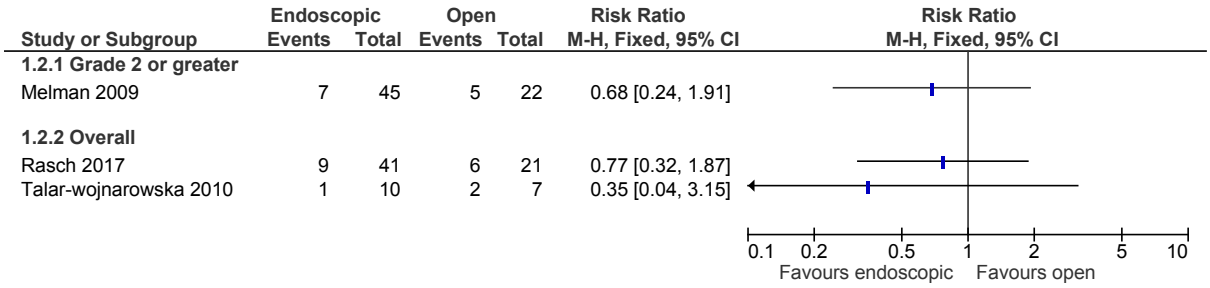
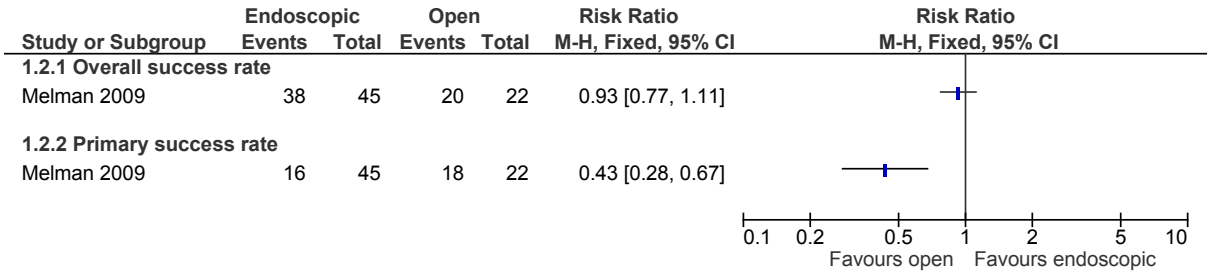
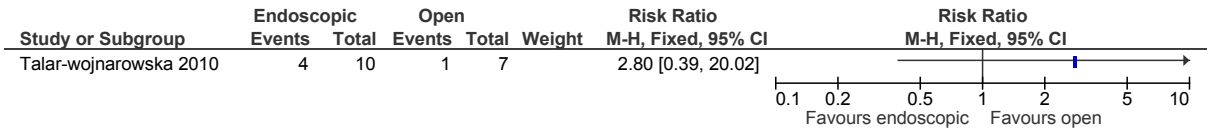


Figure 248: Resolution of presenting symptoms or pseudocysts at >12 months



1

Figure 249: Recurrence of pseudocysts at >12 months



2

Figure 250: Length of hospital stay at ≤12 months

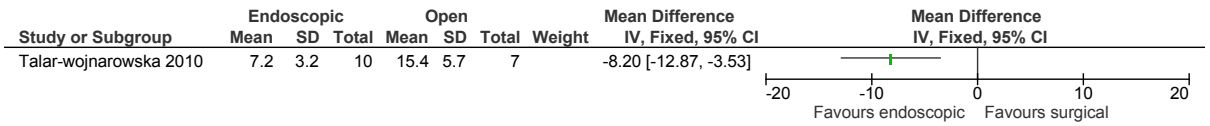
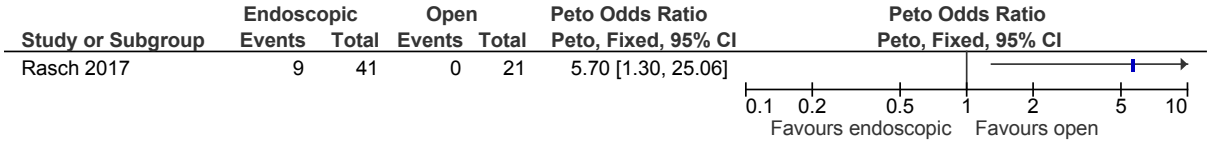
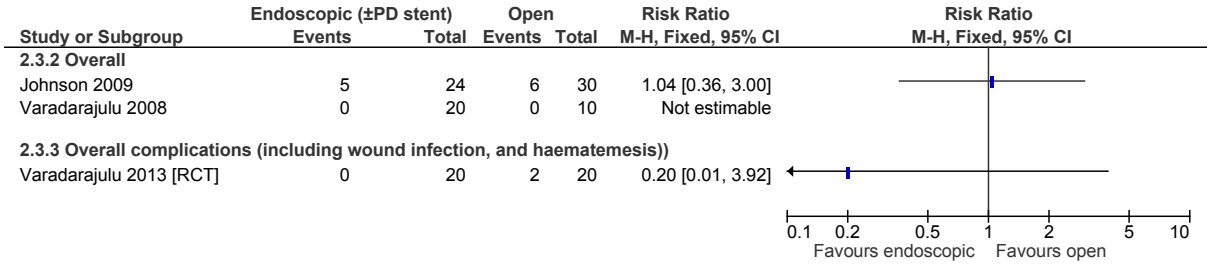


Figure 251: Repeated procedure (re-intervention) at ≤12 months



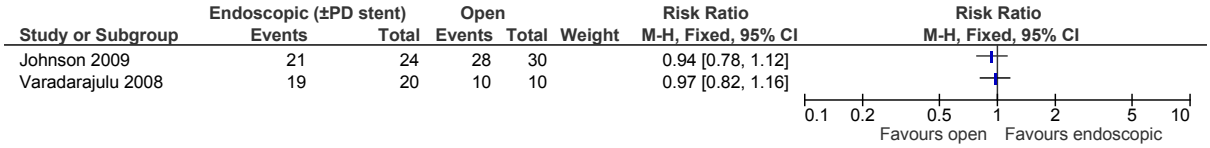
3 ## K.17.2 Combined endoscopic drainage and pancreatic duct stent versus open surgical drainage

Figure 252: Complications at unclear follow-up



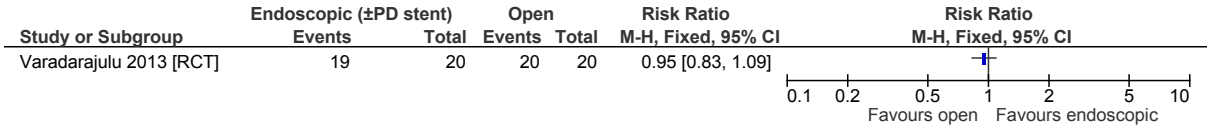
1

Figure 253: Resolution of pseudocysts at unclear follow-up



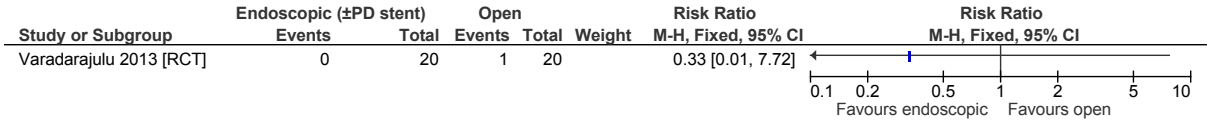
2

Figure 254: Resolution of presenting symptoms (treatment success) at unclear follow-up



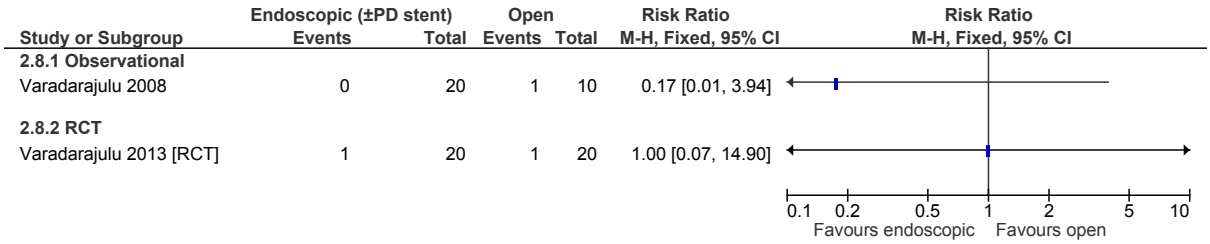
3

Figure 255: Recurrence (new onset abdominal pain in the presence of a pancreatic fluid collection on CT after resolution of the initial presentation) at >12 months



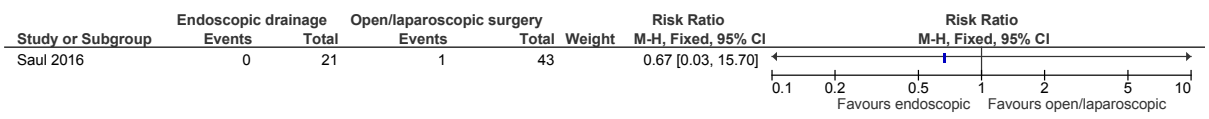
4

Figure 256: Repeated procedures (re-intervention) at ≤12 months or >12 months



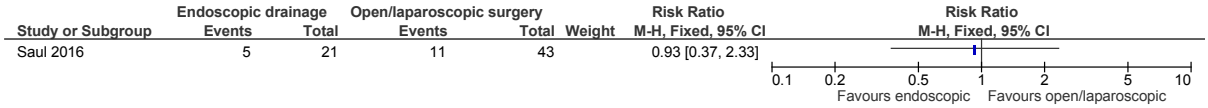
5 ## K.17.3 Endoscopic drainage versus combination of open and laparoscopic surgery

Figure 257: Mortality at ≤12 months



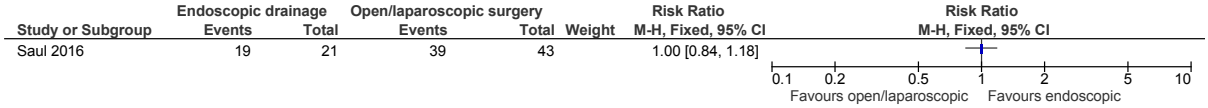
1

Figure 258: Overall complications (including bleeding, infection, stent migration) at >12 months



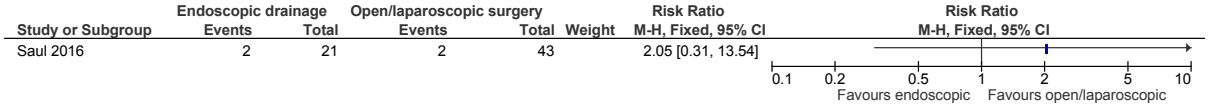
2

Figure 259: Clinical success (complete resolution or decrease in the size of pseudocysts to 2cm or smaller on CT with associated resolution of symptoms) at ≤12 months



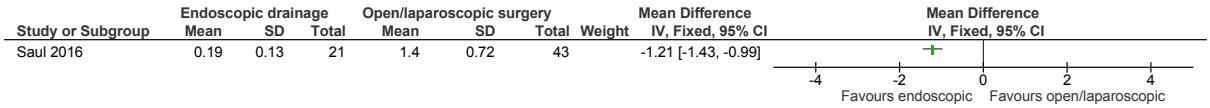
3

Figure 260: Recurrence (pancreatic pseudocyst found on CT in association with symptoms after initial resolution) at >12 months



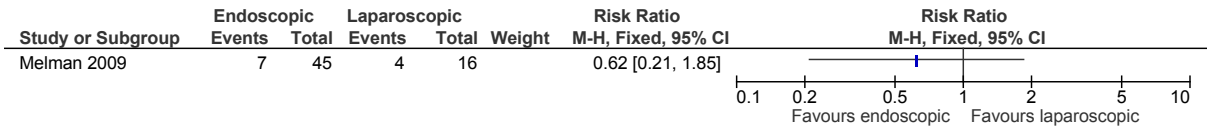
4

Figure 261: Length of CCU stay (days) at >12 months



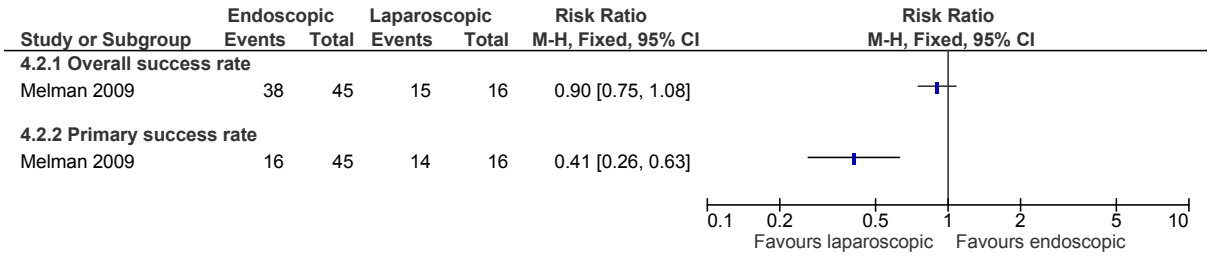
5 **K.17.4 Endoscopic drainage versus laparoscopic drainage**

Figure 262: Complications (grade 2 or greater) at >12 months



6

Figure 263: Resolution of presenting symptoms at >12 months



K.17.5 Endoscopic drainage versus endoscopic pancreatic stent

Figure 264: Significant complications at ≤12 months

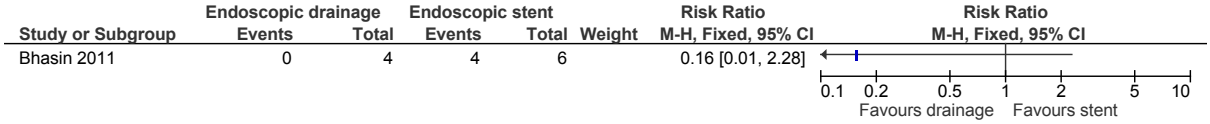
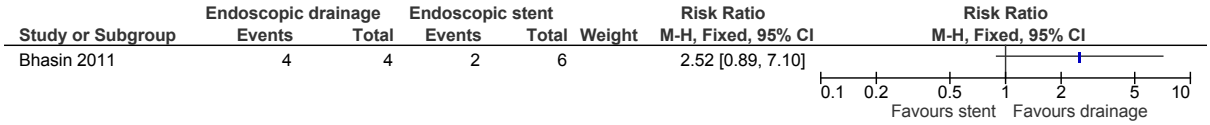


Figure 265: Resolution of pseudocysts at ≤12 months



K.17.6 Endoscopic drainage versus standard treatment (observation)

Figure 266: Complications at ≤12 months

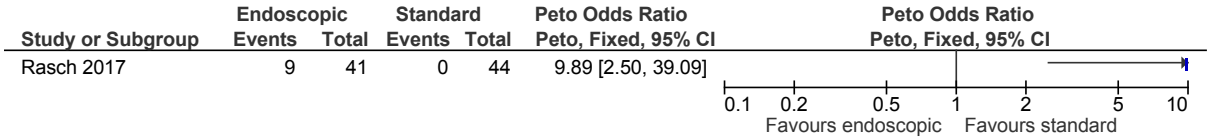
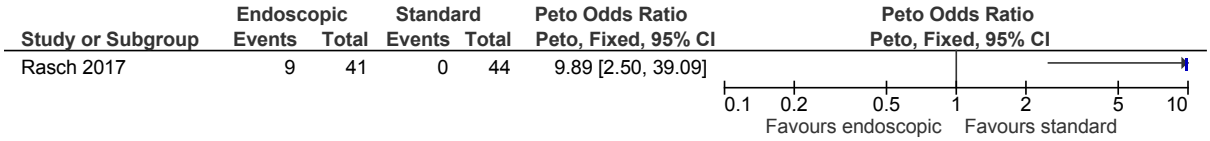


Figure 267: Repeated procedure (re-intervention) at ≤12 months



K.17.7 Percutaneous drainage versus open surgical drainage or resection

Figure 268: Mortality at ≤12 months

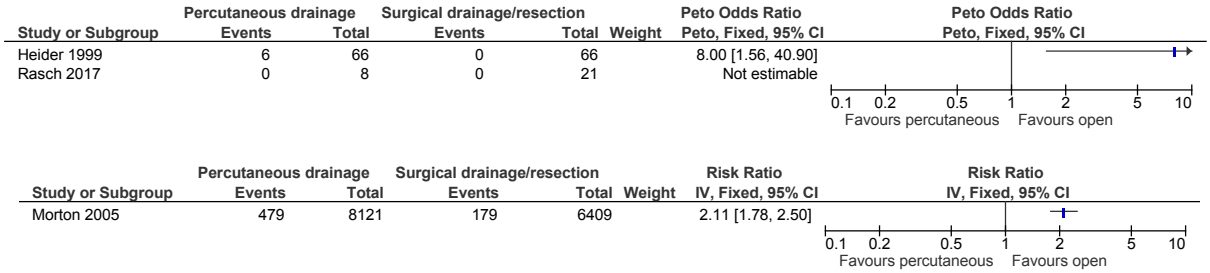
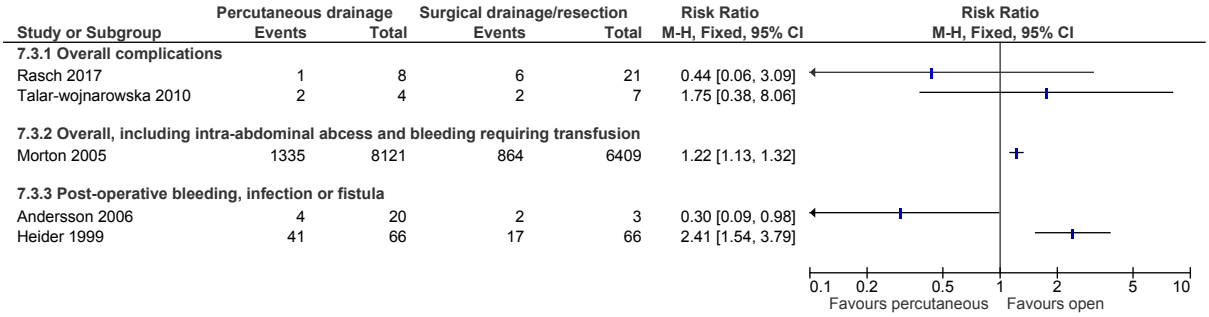
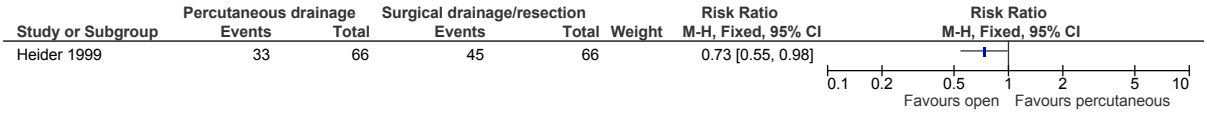


Figure 269: Complications at ≤12 months and >12 months



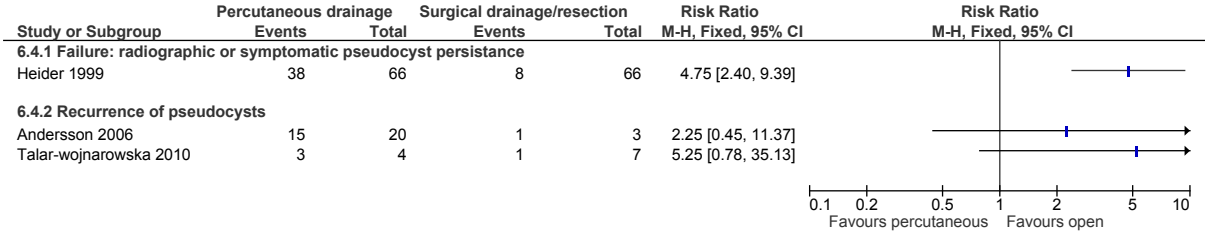
1

Figure 270: Resolution of pseudocyst or symptoms at unclear follow-up



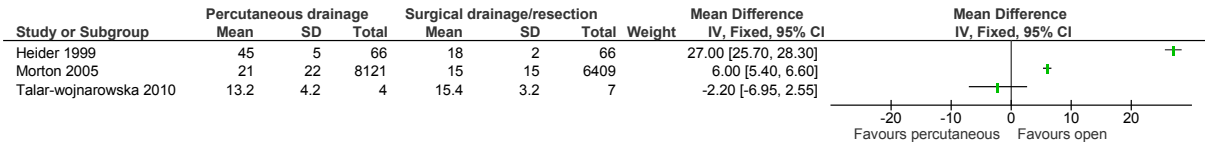
2

Figure 271: Recurrence of pseudocyst at >12 months



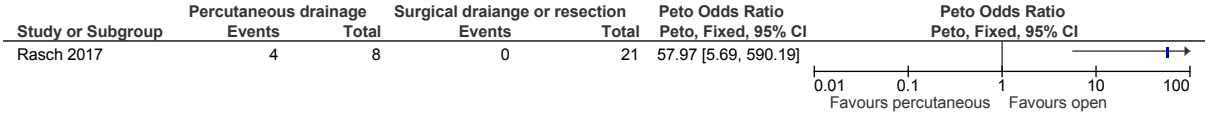
3

Figure 272: Length of hospital stay ≤12 months



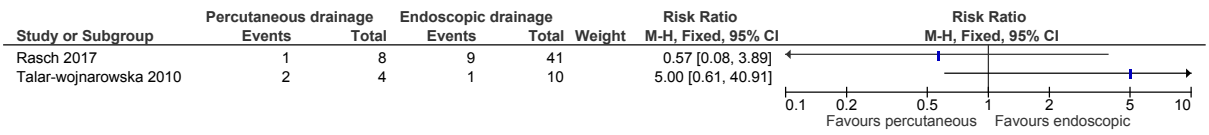
4

Figure 273: Repeated procedure (re-intervention) at ≤12 months



5 **K.17.8 Percutaneous drainage versus endoscopic drainage**

Figure 274: Complications at ≤12 months



6

Figure 275: Procedural adverse events at unclear follow-up

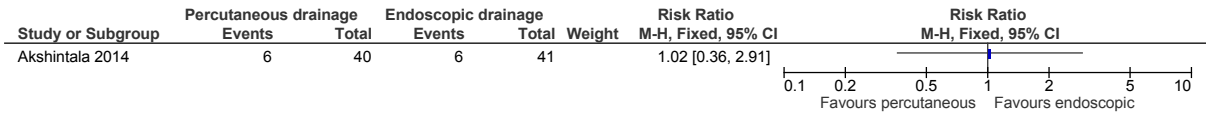


Figure 276: Recurrence of pseudocysts at >12 months

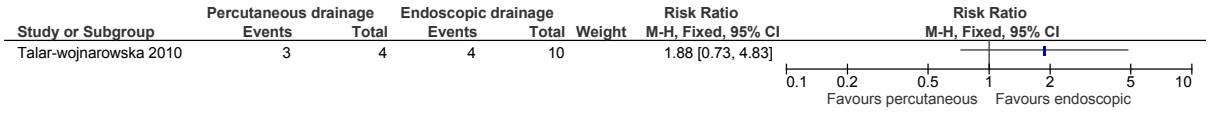


Figure 277: Length of hospital stay (days) at ≤12 months

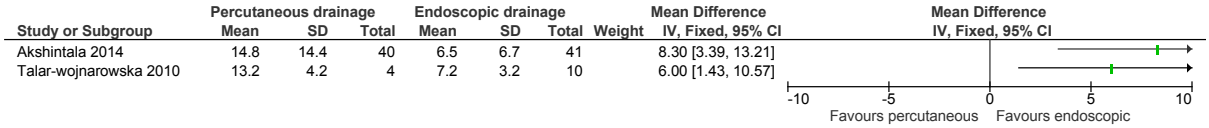
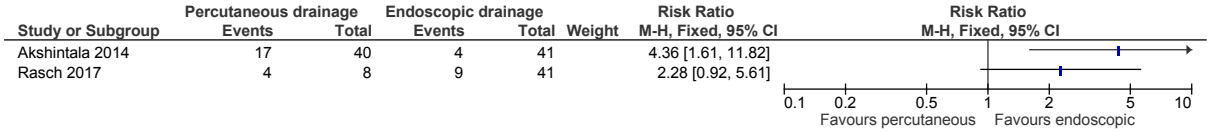


Figure 278: Repeated procedures (re-intervention) at ≤12 months



K.17.9 Percutaneous drainage versus standard treatment (observation)

Figure 279: Mortality at ≤12 months

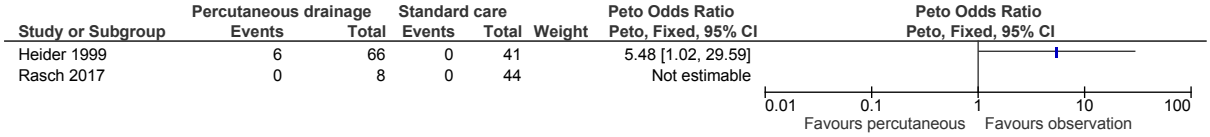
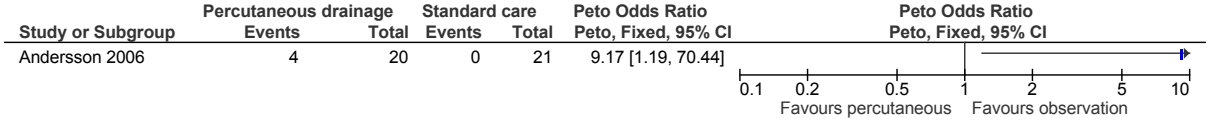


Figure 280: Complications - Post-operative bleeding, infection or fistula at >12 months



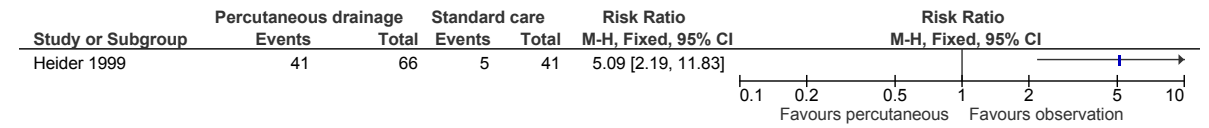
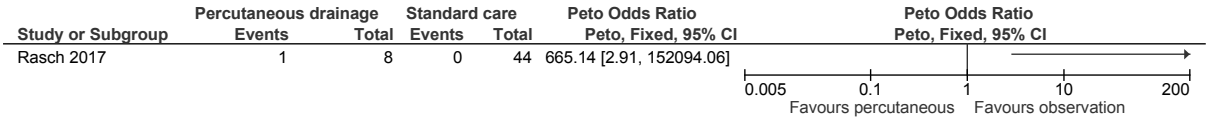
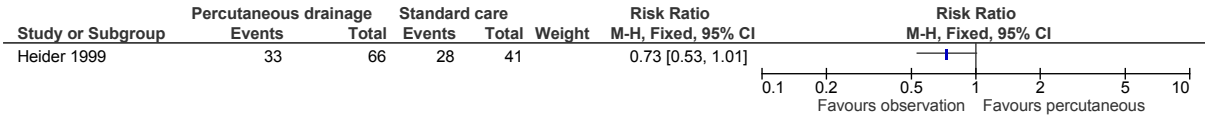


Figure 281: Complications at ≤12 months



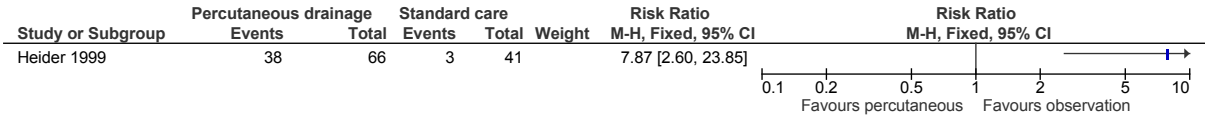
1

Figure 282: Resolution of pseudocysts or symptoms at unclear follow-up



2

Figure 283: Failure (defined as radiographic persistence of a symptomatic pseudocyst in the observed group and a persistent symptomatic pseudocyst requiring a further procedure in the intervention groups) at unclear follow-up



3

Figure 284: Recurrence at >12 months

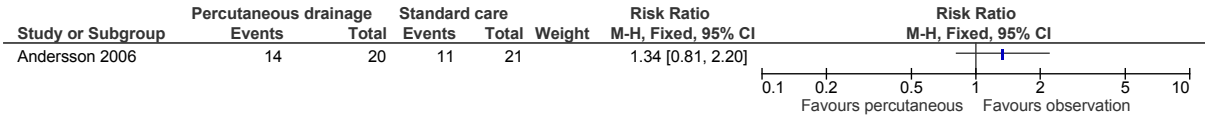
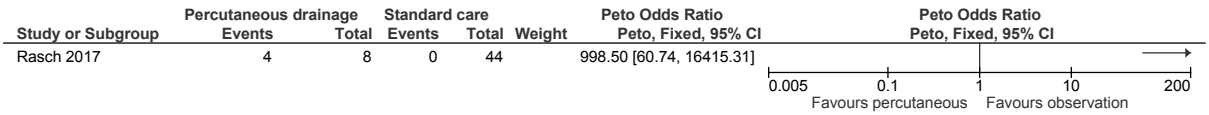
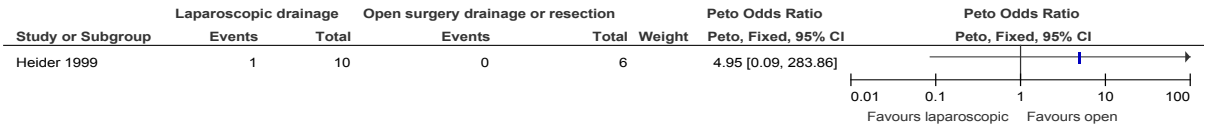


Figure 285: Repeated procedures (re-intervention) at ≤12 months



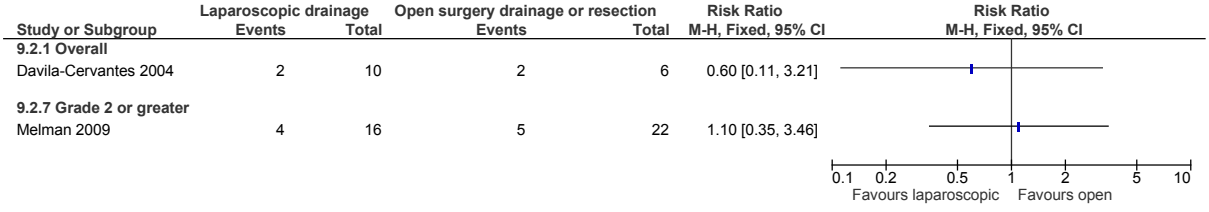
4 **K.17.10 Laparoscopic drainage versus open surgical drainage or resection**

Figure 286: Mortality at ≤12 months



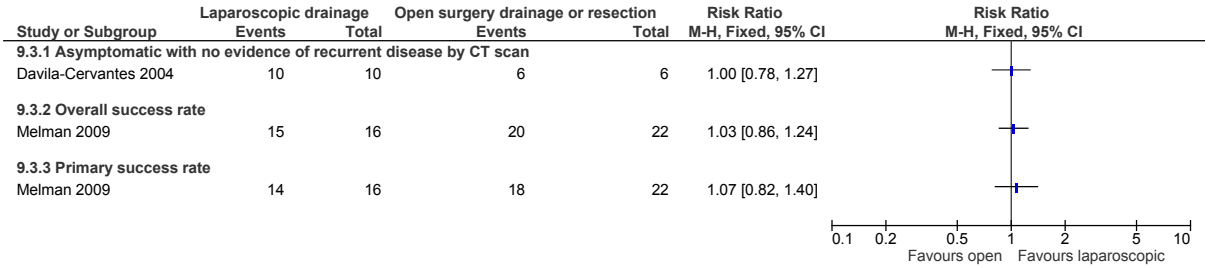
5

Figure 287: Complications at >12 months



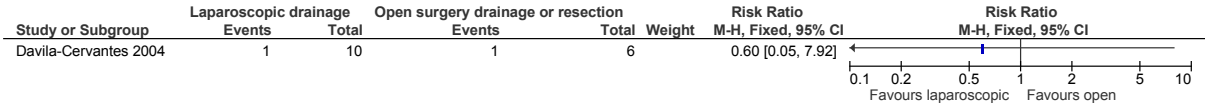
1

Figure 288: Resolution of presenting symptoms at >12 months



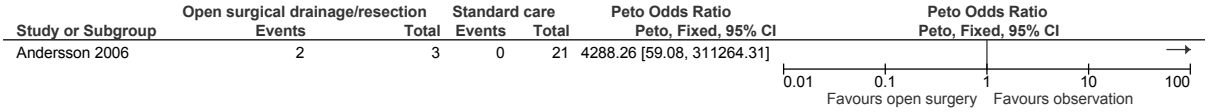
2

Figure 289: Residual pseudocyst at unclear follow-up



3 **K.17.11 Open surgical drainage or resection versus standard treatment (observation)**

Figure 290: Complications – Post-operative bleeding, infection or fistula at >12 months



4

Figure 291: Complications – Post-operative bleeding, infection or fistula at unclear follow-up

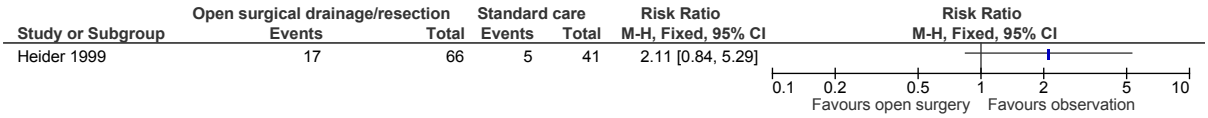
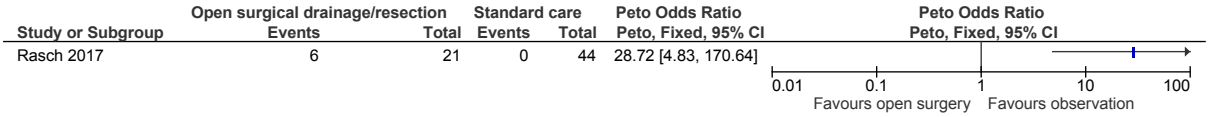
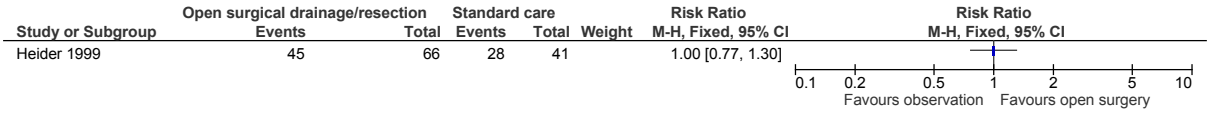


Figure 292: Complications at ≤12 months



5

Figure 293: Resolution of pseudocyst and symptoms (after hospital discharge; defined as recurrent cyst, recurrent pancreatitis, fistula, infection) at unclear follow-up



6

Figure 294: Failure (radiographic persistence of a symptomatic pseudocyst) at unclear follow-

up

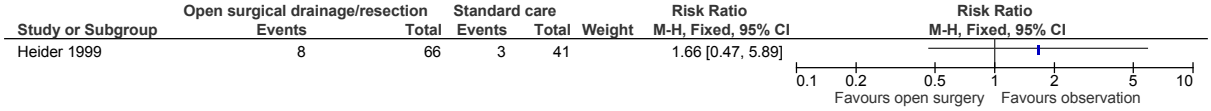
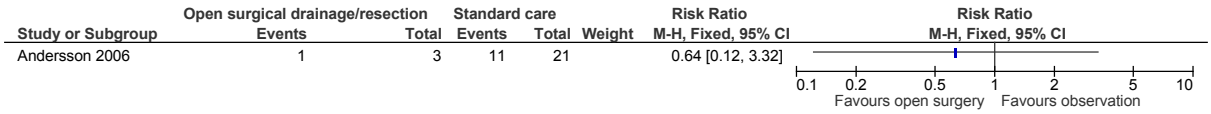


Figure 295: Recurrence at >12 months



K.18 Management of pancreatic ascites and pleural effusion secondary to pancreatitis

None.

K.19 Management of biliary obstruction in people with chronic pancreatitis

K.19.1 Metal stents versus plastic stents

Figure 296: Mortality at 2 years

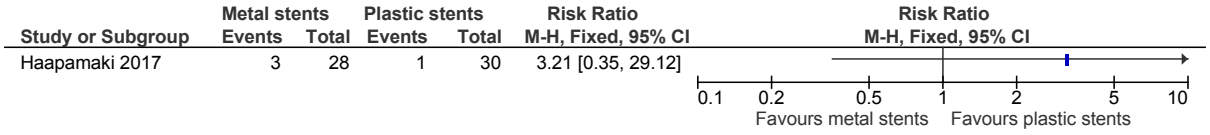


Figure 297: Recurrence of biliary obstruction (Recurrent strictures) at 2 years

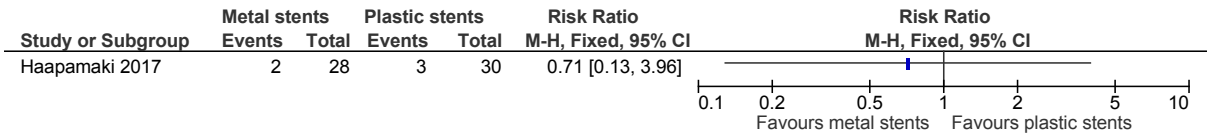
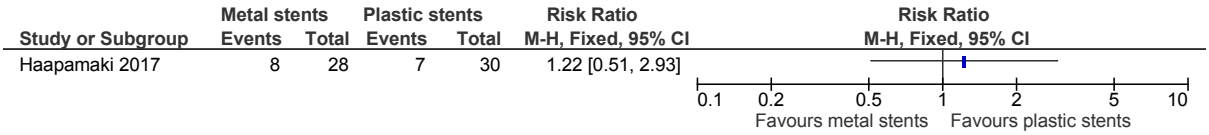
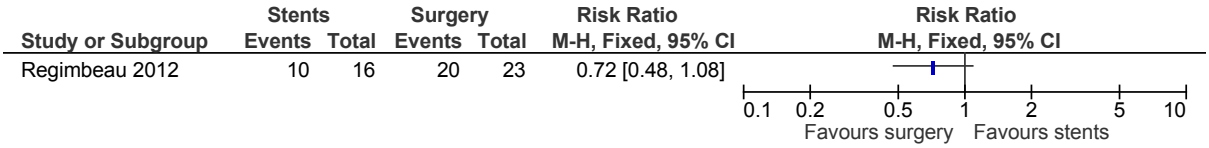


Figure 298: Complications (Adverse events) at 2 years



K.19.2 Stenting versus surgery

Figure 299: Recurrence of biliary obstruction (Successful treatment) at 1 year



K.20 Management of type 3c diabetes secondary to pancreatitis

None.

K.21 Receiving specialist input in people with acute pancreatitis

None.

K.22 Follow-up of pancreatic exocrine function in people with chronic pancreatitis

None.

K.23 Follow-up to identify diabetes in people with chronic pancreatitis

None.

K.24 Follow-up to identify pancreatic cancer in people with chronic pancreatitis

None.

Appendix L: Excluded clinical studies

L.1 Patient information

Reference	Reason for exclusion
Duggan 2011[316]	Abstract only
Haritha 2015[441]	Incorrect study design (questionnaire on patients' knowledge of smoking)
Nordeen 2012[807]	Abstract only
Wlochal 2015[1154]	Incorrect study design (survey on patients' knowledge of nutrition)

L.2 Lifestyle interventions: stopping or reducing alcohol consumption

Study	Exclusion reason
Ammann 1994[37]	Incorrect interventions
Apte 1998[47]	Inappropriate study design (narrative review)
Conway 2005[242]	Inappropriate study design (narrative summary review)
Estruch 1993[347]	Not review population
Haber 2001[431]	Inappropriate study design (proceedings of a workshop)
Hanck 2004[438]	Inappropriate study design (narrative review)
Jaakkola 1994[515]	Inappropriate study design (no control group)
Kume 2015[625]	Not review population. Inappropriate study design (case-control)
Lang 2012[634]	Inappropriate study design (before and after study with no control group)
Maejima 1996[693]	Inappropriate study design (non-comparative)
Mayerle 2007[724]	Inappropriate study design (narrative review)
Nikkola 2013[799]	Inappropriate study design
Nordback 2005[804]	Inappropriate study design (non-comparative). Inappropriate comparison. Incorrect interventions
Pezzilli 2015[861]	Inappropriate study design (narrative review)
Piette 1998[868]	Inappropriate study design (case-control)
Samokhvalov 2015[944]	Systematic review is not relevant to review question or unclear PICO

Study	Exclusion reason
Sand 2007[947]	Inappropriate study design (narrative review)
Sarles 1990[952]	Inappropriate study design (narrative review)
Schenker 1998[957]	Inappropriate study design (narrative review)
Schneider 2005[963]	Inappropriate study design (narrative review)
Strum 1995[1033]	Inappropriate study design (case series)

L.3 Aetiology of acute pancreatitis

Study	Exclusion reason
Ansari 1996[42]	Incorrect interventions
Chak 1999[203]	Incorrect study design
Chen 2017[215]	Incorrect study design
Choudhary 2016[224]	Incorrect study design
Cimen 2015[227]	Incorrect study design
Di Leo 2017[293]	Incorrect study design. Incorrect population
Easler 2016[326]	Incorrect study design
Gaitch 2016[381]	Incorrect population
Gasiorowska 2011[393]	Not review population
Giefer 2017[398]	Incorrect study design
Jalaly 2017[522]	Incorrect study design
Ma 2017[690]	Incorrect study design
Mariani 2009[712]	Incorrect study design
Nitsche 1995[801]	Incorrect interventions
Park 2016[842]	Incorrect study design
Poddar 2017[871]	Incorrect population
Raizner 2013[891]	Not review population
Reid 2017[907]	Incorrect study design

Repiso Ortega 2011[908]	Incorrect study design
Safari 2016[931]	Narrative review
Shimizu 2001[992]	Incorrect study design
Sisman 2015[1002]	Not review population
Smith 2015[1006]	Narrative review
Stabuc 2008[1022]	Incorrect study design
Sugiyama 1998[1039]	Incorrect study design
Wilcox 2016[1143]	Inappropriate comparison
Zhan 2011[1182]	Incorrect study design

L.4 Aetiology of chronic pancreatitis

Study	Exclusion reason
Al-Haddad 2008[21]	Incorrect study design
Ammann 2007[38]	Incorrect study design
Aoun 2008[43]	Incorrect study design
Aoun 2010[44]	Incorrect study design
Aparisi 2005[45]	Incorrect study design
Applebaum-Shapiro 2001[46]	Incorrect study design
Aspinwall 2013[55]	Not guideline condition
Avanthi 2015[58]	Incorrect study design
Ballard 2015[77]	Incorrect study design
Bang 2008[81]	Inappropriate comparison
Buechter 2017[167]	Incorrect population
Buijs 2015[170]	Incorrect study design
Buijs 2016[169]	Incorrect population
Camara 2015[188]	Incorrect study design

Campa 2013[189]	Incorrect study design
Cohn 2002[237]	Incorrect study design
Cohn 2003[236]	Incorrect study design
Conwell 2017[243]	Incorrect study design
Derikx 2010[283]	Incorrect study design
Detlefsen 2015[284]	Incorrect interventions
Ellis 2001[341]	Incorrect study design
Ellis 2004[340]	Incorrect study design
Hara 2015[439]	Incorrect study design
Hart 2013[444]	Inappropriate comparison
Ito 2014[505]	Incorrect study design
Jiaming 2001[531]	Unavailable
Joergensen 2010[538]	Inappropriate comparison
Joergensen 2010[539]	Incorrect study design
Lerch 2010[648]	Incorrect study design
Li 2011[655]	Incorrect study design
Liu 2017[668]	Incorrect study design
Lowenfels 1997[681]	Incorrect study design
Lucidi 2011[684]	Incorrect study design
Maes 1999[694]	Not review population
Masson 2013[716]	Incorrect study design
Mayerle 2013[723]	Systematic review is not relevant to review question or unclear PICO
Midha 2010[738]	Incorrect study design
Palermo 2016[829]	Incorrect study design
Pandya 1997[832]	Incorrect study design
Pezzilli 2009[860]	Incorrect study design

Poddar 2017[872]	Incorrect study design
Poddar 2017[871]	Incorrect study design
Rolston 2001[920]	Incorrect study design
Romagnuolo 2008[921]	Incorrect study design
Romagnuolo 2016{Romagnuolo, 2016 #1643}	Incorrect study design
Sherman 2004[991]	Not review population
Spanier 2008[1015]	Incorrect study design
Strate 2003[1031]	Incorrect study design
Tazelaar 2003[1066]	Incorrect study design
Testoni 2014[1070]	Incorrect study design
Vue 2016[1122]	Incorrect population
Wang 2009[1131]	Inappropriate comparison
Wang 2013[1132]	Incorrect interventions
Wilcox 2016[1143]	Incorrect study design

L.5 Diagnosing chronic pancreatitis

Reference	Reason for exclusion
Akisik 2009[19]	Inappropriate study design (two-gate study)
Alkaade 2008[28]	Inappropriate reference test
Amann 1996[35]	Inappropriate population
Ashkar 2014[53]	SR not relevant to pico
Balci 2006[75]	Inappropriate population
Balci 2008[76]	Inappropriate population
Bang 2008[81]	Inappropriate population
Benini 1992[120]	Inappropriate population
Benini 2013[119]	Inappropriate population

Reference	Reason for exclusion
Bhutani 2009[131]	Inappropriate index test
Bian 2013[132]	Inappropriate study design and population
Boedeker 1999[144]	Inappropriate study design
Brugge 1990[163]	Inappropriate population
Buscail 1995[172]	Inappropriate population
Cappellex 2000[192]	Inappropriate population
Casellas 2004[198]	Inappropriate target condition
Catalano 1998[202]	Inappropriate population
Catalano 2007[201]	Inappropriate study design
Chen 2007[216]	Inappropriate population
Chowdhury 2005[225]	Inappropriate reference standard
Chowdhury 2016[226]	Inappropriate population
Coenegrachts 2004[233]	Inappropriate study design; inappropriate population
Conwell 2002[245]	Inappropriate study design
Conwell 2007[246]	Inappropriate population
Conwell 2007[247]	Inappropriate study design
Conwell 2014[244]	Inappropriate study design
Czako 2007[259]	Inappropriate study design
Dancygier 1991[266]	Inappropriate study design
De Backer 2002[273]	Inappropriate study design
Detlefsen 2015[284]	Inappropriate population
Diakowska 2005[294]	Inappropriate study design
Dietrich 2009[295]	Inappropriate population
Dominguez-Munoz 1993[306]	Inappropriate population
Dominguez-Munoz 1995[304]	Inappropriate population
Dominguez-Munoz 1998[305]	Inappropriate population
Dominguez-Munoz 2012[303]	Inappropriate population
Draganov 2004[309]	Inappropriate gold standard
Draganov 2005[311]	Inappropriate reference standard

Reference	Reason for exclusion
Duggan 2016[317]	Inappropriate study design
Dominguez-Munoz 2012[303]	Inappropriate population
Fritscher-Ravens 2002[371]	Inappropriate population
Furuya 1996[378]	Inappropriate population
Gardner 2010[388]	Inappropriate study design
Girish 2009[401]	Inappropriate population
Glasbrenner 1996[403]	Inappropriate population
Glaser 1994[404]	Inappropriate study design
Gleeson 2007[405]	Inappropriate study design
Gonzalez-Sanchez 2017 [409]	Incorrect population
Gredal 2003[414]	Inappropriate population
Gullo 1990[418]	Inappropriate study design
Gullo 1996[417]	Inappropriate population
Gullo 1999[419]	Inappropriate study design
Hardt 2002[440]	Inappropriate population
Hernandez 2010[453]	Inappropriate study design
Hocke 2012[460]	Inappropriate population
Hoki 2009[462]	Inappropriate population
Hollerbach 2001[464]	Inappropriate population
Iglesias-Garcia 2013[489]	Inappropriate population
Iglesias-Garcia 2015[490]	Inappropriate study design
Ishii 2007[501]	Inappropriate study design
Issa 2017[502]	Systematic review: references checked
Jensen 2008[528]	Inappropriate study design
Jung 2015[552]	Inappropriate population
Kahl 2002[558]	Inappropriate population
Kamisawa 2007[569]	Inappropriate population
Kamisawa 2008[571]	Inappropriate population
Kamisawa 2014[570]	Inappropriate study design

Reference	Reason for exclusion
Kanno 2015[575]	Inappropriate study design
Kanno 2016[574]	Inappropriate population
Kataoka 1997[583]	Inappropriate population
Kataoka 1999[581]	Inappropriate reference test
Keim 2003[589]	Inappropriate reference test
Keller 2011[590]	Inappropriate study design
Ketwaroo 2015[592]	Inappropriate study design
Kitagawa 1997[603]	Inappropriate population
Kothari 2017[615]	Incorrect reference standard
Kothari 2017[614]	Incorrect reference standard
Kuwahara 2017[629]	Incorrect reference standard
Kuwahara 2017[630]	Incorrect reference standard
Lankisch 1993[635]	Inappropriate study design
Lankisch 1998[636]	Inappropriate population
Lara 2017[637]	Incorrect reference standard
Lei 2000[646]	Inappropriate study design
Liu 2016[670]	SR not relevant to PICO
Llamoza-Torres 2016[671]	Inappropriate index test
Lock 1997[672]	Inappropriate reference test
Loser 1997[676]	Inappropriate study design
Loser 1998[677]	Inappropriate study design; population
Maeshiro 2007[695]	Inappropriate study design
Mahajan 2016[698]	Inappropriate study design
Miyakawa 2007[746]	Inappropriate population
Mizuno 2009[747]	Inappropriate population
Morishima 2016[759]	Inappropriate population
Pelley 2012[848]	Inappropriate study design
Pezzilli 2000[863]	Inappropriate comparison
Poddar 2017[872]	Inappropriate population

Reference	Reason for exclusion
Poddar 2017[871]	Inappropriate population
Pungpapong 2007[882]	Inappropriate population
Pungpapong 2007[881]	Inappropriate population
Saftoiu 2011[933]	Inappropriate population
Sahai 1998[936]	Inappropriate population
Sai 2008[938]	Inappropriate design; Inappropriate population
Sainani 2015[939]	Inappropriate study design
Sato 2017[953]	Incorrect reference standard
Schlaudraff 2008[960]	Inappropriate population
Seicean 2010[975]	Inappropriate study design
Sheridan 2002[990]	Inappropriate study design
Songur 2000[1011]	Inappropriate population; Inappropriate reference test
Stevens 2009[1027]	Inappropriate population
Stevens 2010[1026]	Inappropriate reference test
Sugiyama 2007[1040]	Inappropriate population
Sugumar 2011[1041]	Inappropriate design
Trikudanathan 2015[1080]	Inappropriate population
Trikudanathan 2016[1079]	Inappropriate population
Uskudar 2009[1089]	Inappropriate study design, Inappropriate population
Wejnarska 2016[1140]	Inappropriate population
Yanagisawa 2017[1170]	Inappropriate population
Yanling 2001[1175]	Inappropriate study design
Zhang 2003[1185]	Inappropriate study design

L.6 Type of intravenous fluid for resuscitation in people with acute pancreatitis

Study	Exclusion reason
Abu-El-Haija 2017[7]	Systematic review is not relevant to review question or unclear PICO

Aggarwal 2014[13]	Inappropriate study design (narrative review)
Bolado 2016[146]	Not in English
Bortolotti 2014[148]	Inappropriate study design
Brown 2002[160]	Inappropriate comparison
Buxbaum 2014[177]	Not guideline condition
Caraceni 2013[194]	Incorrect study design
Choi 2016[222]	Not review population
De-Madaria 2011[272]	Inappropriate comparison
De-Madaria 2014[270]	Incorrect study design
Dimagno 2014[297]	Not review population
Dimagno 2015[296]	Incorrect study design
Eckerwall 2006[331]	Incorrect interventions
Gardner 2008[390]	Inappropriate study design
Haydock 2013[447]	Inappropriate study design
Haydock 2013[448]	Systematic review is not relevant to review question or unclear PICO
Kuwabara 2011[628]	Inappropriate study design
Lipinski 2015{Lipinski, 2015 #290}	Inappropriate intervention
Mao 2009[710]	Inappropriate comparison
Maurer 2015[721]	Inappropriate study design
Mok 2016[752]	Not review population
Mole 2011[753]	No relevant outcomes
Mosztbacher 2017 [764]	Inappropriate study design
Nakamura 2014[781]	Not guideline condition
Niederau 2006[795]	Inappropriate study design
Platell 2001[870]	Systematic review is not relevant to review question or unclear PICO
Pupelis 2008[886]	Incorrect interventions

Sagi 2014[934]	Inappropriate comparison
Schepers 2013[959]	Inappropriate study design
Sharma 2016[983]	Incorrect interventions
Shaygan-Nejad 2015[985]	Incorrect interventions. Not review population
Shen 2014[987]	Systematic review is not relevant to review question or unclear PICO
Sun 2015[1046]	Incorrect interventions
Szabo 2015[1049]	Inappropriate comparison
Szczygiel 1991[1050]	Incorrect interventions
Talukdar 2011[1059]	Inappropriate study design
Tenner 2013[1069]	Inappropriate study design
Trikudanathan 2012[1078]	Systematic review is not relevant to review question or unclear PICO
Wall 2011[1126]	Incorrect interventions
Wang 2013[1130]	Incorrect interventions
Warndorf 2011[1134]	Incorrect interventions
Weinberg 2014[1138]	Not guideline condition
Weitz 2014[1139]	Inappropriate study design
Wu 2011[1159]	Inappropriate study design
Wyncoll 1999[1163]	Inappropriate study design
Zhao 2013[1188]	Incorrect interventions

L.7 Speed of intravenous fluid for resuscitation in people with acute pancreatitis

Study	Exclusion reason
Aboelsoud 2016[4]	Incorrect interventions
Aggarwal 2014[13]	Inappropriate study design (narrative review)
Bortolotti 2014[148]	Inappropriate study design

Brown 2002[160]	Incorrect interventions
Buxbaum 2014[177]	Not review population
Caraceni 2013[194]	Inappropriate study design
Choi 2016[222]	Not guideline condition
De-Madaria 2014[270]	Inappropriate study design
Dimagno 2014[297]	Not review population
Dimagno 2015[296]	Inappropriate study design
Du 2011[313]	Inappropriate comparison
Gardner 2008[390]	Inappropriate study design (narrative review)
Haydock 2013[447]	Inappropriate study design (survey)
Haydock 2013[448]	Systematic review is not relevant to review question or unclear PICO
Kuwabara 2011[628]	Inappropriate study design
Lipinski 2015[664]	Incorrect interventions
Mao 2009[710]	Inappropriate intervention
Maurer 2015[721]	Inappropriate study design
Mok 2016[752]	Not guideline condition
Mole 2011[753]	No relevant outcomes
Nakamura 2014{Nakamura, 2014 #266}	Not guideline condition
Niederau 2006[795]	Inappropriate study design
Platell 2001[870]	Systematic review is not relevant to review question or unclear PICO
Pupelis 2008[886]	Incorrect interventions
Sagi 2014[934]	Inappropriate comparison
Schepers 2013[959]	Inappropriate study design
Sharma 2016[983]	Incorrect interventions
Shaygan-Nejad 2015[985]	Incorrect interventions. Not review population
Shen 2014[987]	Systematic review is not relevant to review question or unclear PICO

Sun 2015[1046]	Incorrect interventions
Szczygiel 1991[1050]	Incorrect interventions
Talukdar 2014[1056]	Inappropriate study design
Tenner 2013[664]	Inappropriate study design
Trikudanathan 2012[1078]	Systematic review is not relevant to review question or unclear PICO
Warndorf 2011[939]	Incorrect interventions
Weinberg 2014[1138]	Not guideline condition
Weitz 2014[1139]	Inappropriate study design
Wu 2011[983]	Inappropriate study design
Wyncoll 1999[1163]	Inappropriate study design
Zhao 2013[1188]	Incorrect interventions

L.8 Route of feeding in people with severe acute pancreatitis

Study	Exclusion reason
Abou-Assi 2002[6]	Abstract only
Abu-El-Haija 2016[8]	Inappropriate comparison
Al Samaraee 2010[23]	Systematic review: references checked
Alsolaiman 2003[32]	Incorrect study design: comment article
Buxbaum 2017[178]	Not Severe acute pancreatitis. Incorrect interventions
Cao 2008[191]	Systematic review: references checked
Chang 2013[208]	Systematic review: references checked
Cui 2013[258]	Not in the English language
Davies 2011[267]	Incorrect study design: survey
Eatock 2000[328]	Incorrect study design: non-comparative
Eckerwall 2007[333]	Not Severe acute pancreatitis. Not Moderately severe acute pancreatitis. Incorrect interventions
Erstad 2000[345]	Narrative review: references checked
Gianotti 2009[396]	Guideline report: references checked

Study	Exclusion reason
Horibe 2016[469]	Systematic review: references checked
Jafari 2015[517]	Systematic review: references checked
Jeejeebhoy 2007[526]	Narrative review: references checked
Jiang 2007[532]	Systematic review: references checked
Kahl 2014[559]	Not Severe acute pancreatitis. Not Moderately severe acute pancreatitis. Incorrect interventions
Kale-Pradhan 1999[564]	Narrative review: references checked
Kalfarentzos 1991[566]	Incorrect study design: narrative review
Karamitsios 1997[578]	Narrative review: references checked
Kaushik 2004[584]	Incorrect study design: narrative review
Krishnan 2017[618]	Narrative review: references checked
Kuwabara 2011[627]	Incorrect study type
Larino-Noia 2014[638]	Majority had mild acute pancreatitis
Li 2013[656]	Systematic review: references checked
Li 2013[654]	Majority had mild acute pancreatitis
Li 2014[659]	Systematic review: references checked
Ma 2016[689]	Incorrect interventions
Makola 2007[702]	Systematic review: references checked
Marik 2004[713]	Systematic review: references checked
Marta 2016[714]	Systematic review: references checked
McClave 1997[729]	Majority had mild acute pancreatitis
McClave 1998[730]	Systematic review: references checked
McClave 2006[728]	Systematic review: references checked
Mirtallo 2012[742]	Guideline report: references checked
Nakad 1998[779]	Incorrect study design: non-comparative
Navaneethan 2010[789]	Narrative review: references checked
Olah 2002[816]	Majority had mild acute pancreatitis
Olah 2010[817]	Systematic review: references checked
Olah 2014[818]	Narrative review: references checked
Pandey 2004[831]	Incorrect outcomes

Study	Exclusion reason
Pendharkar 2016[849]	Incorrect interventions
Petrov 2007[859]	Systematic review: references checked
Petrov 2008[855]	Systematic review: references checked
Petrov 2008[857]	Systematic review: references checked
Petrov 2009[856]	Systematic review: references checked
Petrov 2010[858]	Systematic review: references checked
Petrov 2013[854]	Incorrect interventions
Piciucchi 2010[867]	Incorrect study design: observational (sufficient randomised data for this comparison)
Pisters 1992[869]	Incorrect study design: narrative review
Powell 2000[877]	Incorrect interventions
Pupelis 2000[883]	Incorrect interventions
Pupelis 2006[885]	Incorrect study design: non-comparative
Quan 2011[888]	Systematic review: references checked
Shen 2017[986]	Incorrect outcomes
Singh 2012[996]	Incorrect study design: observational (sufficient randomised data for this comparison)
Siow 2008[1000]	Systematic review: references checked
Spanier 2008[1014]	Not review population
Stimac 2016[1028]	Incorrect interventions
Sun 2004[1043]	Inappropriate comparison
Sun 2013[1044]	Inappropriate comparison
Sun 2013[1045]	Inappropriate comparison
Szabo 2015 [1049]	Incorrect population and comparisons
Tao 2016[1063]	Incorrect study design: observational (sufficient randomised data for this comparison)
Targarona Modena 2006[1065]	Incorrect study design: observational (sufficient randomised data for this comparison)
Teich 2010[1068]	Not Severe acute pancreatitis. Not Moderately severe acute pancreatitis. Incorrect interventions
Thomson 2006[1071]	Review: references checked

Study	Exclusion reason
Vaughn 2017[1110]	Systematic review: references checked
Windsor 1998[1149]	Majority had mild acute pancreatitis
Wu 2015[1162]	Inappropriate comparison
Yi 2012[1177]	Systematic review: references checked
Zhang 2011[1186]	Not in the English language
Zhang 2014[1184]	Inappropriate comparison
Zhao 2003[1187]	Inappropriate comparison
Zhu 2016[1196]	Systematic review: references checked
Zou 2014[1197]	Not review population

L.9 Early versus late nutritional intervention in people with chronic pancreatitis

Reference	Reason for exclusion
Kataoka 2014[582]	Incorrect intervention
Makola 2006[701]	Incorrect intervention
Mizushima 2004[748]	Incorrect intervention
Skipworth 2011[1003]	Incorrect intervention
Stanga 2005[1023]	Incorrect intervention

L.10 Specialist versus non-specialist nutritional assessment in people with chronic pancreatitis

Reference	Reason for exclusion
Avanesov 2017[57]	Incorrect study design
Issa 2017[503]	Incorrect study design
Kaushik 2004[584]	Incorrect study design; incorrect population
Kumar 2013[624]	Incorrect study design; incorrect population
McClave 1998[730]	Incorrect study design
Mirtallo 2012[742]	Incorrect study design

L.11 Prophylactic antimicrobial agents to prevent infection in people with acute pancreatitis

Study	Exclusion reason
Abu-El-Haija 2017[7]	Incorrect study design
Arlt 2014[50]	Incorrect study design
Bai 2008[66]	Systematic review: References checked. Systematic review: methods are not adequate/unclear
Baltatzis 2016[79]	Incorrect study design
Baltatzis 2016[78]	Incorrect study design
Bartholomew 1996[92]	Incorrect study design
Bassi 1992[95]	Incorrect study design
Bassi 1992[101]	Incorrect study design
Bassi 1996[97]	Incorrect study design
Bassi 2004[96]	Incorrect study design
Beger 2009[112]	Inappropriate study design (narrative review)
Besselink 2008[125]	Incorrect study design
Calandra 2004[187]	Not guideline condition. Not review population
Dambrauskas 2007[265]	Systematic review: references checked. Systematic review: methods are not adequate/unclear
da Silveira 2002[264]	Incorrect study design
De Campos 2006[274]	Incorrect study design
De Waele 2003[277]	Incorrect study design
De Waele 2014[276]	Incorrect study design
Eggimann 2006[334]	Incorrect study design
Galeiras 2016[382]	Incorrect study design
Hart 2008[443]	Systematic review: References checked. Systematic review: methods are not adequate/unclear
Ho 1997[459]	Incorrect study design

Howard 2002[475]	Incorrect study design
Hubaczová 2000[480]	Order cancelled (abstract)
Ignatavicius 2012[491]	Incorrect study design
Jafri 2009[518]	Systematic review: references checked. Systematic review: methods are not adequate/unclear
Jiang 2012[533]	Systematic review: References checked. Systematic review: methods are not adequate/unclear
Johnson 1996[546]	Incorrect study design
Lim 2015[662]	Systematic review: References checked. Systematic review: methods are not adequate/unclear
Luiten 1999[685]	Incorrect study design
Mandal 2017[706]	Incorrect study design
Manes 2006[708]	Inappropriate comparison
Maraví-Poma 2003[711]	Incorrect interventions. Inappropriate comparison
Marusic 2008[715]	Incorrect study design
Mazaki 2006[727]	Systematic review: References checked
Mcclelland 1992[731]	Incorrect study design
Moggia 2017[750]	Incorrect intervention
Mourad 2017[766]	Incorrect study design
Moyshenyat 2006[767]	Systematic review: References checked. Systematic review: methods are not adequate/unclear
Nicholson 2011[794]	Incorrect study design
Oldach 1995[821]	Incorrect study design
Papakostas 2000[834]	Systematic review: References checked. Systematic review: methods are not adequate/unclear
Piascik 2004[866]	Incorrect study design
Piascik 2010[865]	Incorrect interventions
Powell 1998[876]	Incorrect study design
Powell 1999[875]	Incorrect study design

Rada 2015[890]	Systematic review: references checked. Systematic review: methods are not adequate/unclear
Rao 2012[897]	Unavailable
Schwarz 1997[969]	Not in English
Segarra-Newnham 1998[973]	Systematic review: references checked. Systematic review: methods are not adequate/unclear
Segarra-Newnham 2009[974]	Systematic review: references checked. Systematic review: methods are not adequate/unclear
Sharma 2001[984]	Incorrect study design
Slavin 2001[1005]	Incorrect study design
Spicak 2002[1018]	Not in English
Spicak 2003[1017]	Not in English
Spicak 2004[1016]	Abstract only
Swidnicka-Siergiejko 2007[1047]	Incorrect study design
Talukdar 2014[1056]	Incorrect study design
Ukai 2015[1087]	Systematic review: References checked. Systematic review: methods are not adequate/unclear
Villatoro 2003[1114]	Systematic review: not latest version
Villatoro 2010[1115]	Systematic review: methods are not adequate/unclear. Systematic review: references checked
Vries 2007[1121]	Systematic review: References checked. Systematic review: methods are not adequate/unclear
Wang 2012[1133]	Unavailable
Wittau 2008[1151]	Systematic review is not relevant to review question or unclear PICO
Wittau 2011[1152]	Systematic review: References checked. Systematic review: methods are not adequate/unclear
Xiong 2006[1164]	Systematic review: References checked. Systematic review: methods are not adequate/unclear
Xu 2008[1165]	Systematic review: References checked
Yang 2009[1174]	Unavailable

Yao 2010[1176]	Systematic review: References checked. Systematic review: methods are not adequate/unclear
Zainutdinov 2016[1179]	Incorrect comparison
Zhang 2010[1183]	Systematic review is not relevant to review question or unclear PICO
Zhou 2005[1194]	Incorrect study design

L.12 Methods of management of infected necrosis in people with acute pancreatitis

Study	Exclusion reason
Abdelhafez 2013[3]	Inappropriate comparison
Ai 2010[17]	Not review population
Ala-Kokko 2001[24]	Narrative article
Albers 2016[25]	Not in English
Alsfasser 2012[31]	Not review population
Alvarez-Sanchez 2014[33]	Systematic review is not relevant to review question or unclear PICO
Alvi 2011[34]	Not review population
Ang 2013[41]	Inappropriate comparison
Ashley 2001[54]	Not review population
Aultman 1997[56]	Not review population
Babu 2009[64]	Systematic review is not relevant to review question or unclear PICO
Babu 2010[63]	Inappropriate comparison
Bakker 2009[72]	Narrative review
Bakker 2012[68]	Incorrect interventions
Bala 2009[74]	Inappropriate comparison
Bang 2014[80]	Not review population
Baril 2000[86]	Incorrect study design

Baron 2002[88]	Incorrect study design
Barreda 2015[89]	Not review population
Baudin 2012[102]	Inappropriate study design
Bausch 2012[103]	Not review population
Beck 2012[105]	Incorrect study design
Beenen 2011[108]	No relevant outcomes
Beger 1986[110]	Incorrect interventions
Beger 1988[111]	Not review population
Beger 1989[109]	Narrative article
Beger 1995[113]	Narrative review
Bello 2012[117]	Systematic review is not relevant to review question or unclear PICO
Berzin 2008[122]	Inappropriate comparison
Besselink 2007[126]	Incorrect interventions
Boland 2010[147]	Inappropriate comparison
Bosscha 2001[150]	Not review population
Bradley 1991[155]	No relevant outcomes
Bradley 2008[156]	Systematic review is not relevant to review question or unclear PICO
Branum 1998[158]	Inappropriate study design
Bruennler 2008[162]	Inappropriate comparison. Incorrect interventions
Bucher 2008[164]	Inappropriate comparison
Buchler 2000[165]	Incorrect study design
Busse 2015[175]	Inappropriate comparison
Carter 2000[195]	Inappropriate comparison
Castellanos 2005[200]	Inappropriate comparison
Castellanos 2013[199]	Inappropriate comparison

Chang 2006[207]	Inappropriate comparison
Chang 2014[206]	Systematic review is not relevant to review question or unclear PICO
Charnley 2006[210]	Incorrect study design
Chaudhary 1997[211]	Inappropriate comparison
Cheung 2005[219]	Inappropriate comparison
Cheung 2010[220]	Not review population
Cirocchi 2013[228]	Systematic review is not relevant to review question or unclear PICO
Coelho 2008[232]	Inappropriate comparison
Connor 2003[239]	Not review population
Connor 2005[240]	Not review population
Connor 2006[241]	Narrative review
Cresswell 2015[256]	Inappropriate comparison
Dhingra 2015[291]	Incorrect interventions
Doctor 2011[300]	Incorrect interventions
Doglietto 1994[301]	Not review population
Dominioni 1997[307]	Paper not available
Dong 2008[308]	Incorrect study design
Easler 2012[327]	Narrative review
Easler 2014[325]	Not review population
Echenique 1998[330]	Inappropriate comparison
Eggink 1984[335]	Inappropriate comparison
Endlicher 2003[342]	Inappropriate comparison
Escourrou 2008[346]	Inappropriate comparison
Farkas 2006[352]	Inappropriate comparison
Foitzik 1995[361]	Not review population

Fotoohi 1999[364]	Not review population
Fotoohi 2007[365]	Narrative review
Freeny 1998[366]	Inappropriate comparison
Fugger 1995[372]	Inappropriate comparison
Gambiez 1998[383]	Not review population
Gardner 2009[386]	Incorrect interventions
Gardner 2011[387]	Inappropriate comparison
Gentile 1998[394]	Inappropriate comparison
Gomatos 2016[408]	Not review population
Gou 2013[412]	Paper not available
Guo 2001[421]	Not in English
Guo 2013[423]	Incorrect interventions
Guo 2014[422]	Incorrect interventions
Gurusamy 2016[428]	Review protocol
Haghshenasskashani 2011[432]	Systematic review is not relevant to review question or unclear PICO
Harris 2004[442]	Inappropriate comparison
Hocke 2008[461]	Not in English
Hollemans 2016[463]	Not review population
Hookey 2006[467]	Incorrect study design
Horvath 2001[471]	Inappropriate comparison
Horvath 2010[470]	Incorrect study design
Howard 1989[473]	Narrative article
Huang 1993[479]	Not review population
Huggett 2015[481]	Inappropriate comparison
Hughes 2007[482]	Narrative review
Hungness 2002[485]	Incorrect interventions

Jagielski 2015[520]	Incorrect study design
Jiang 2016[535]	Not guideline condition
Kalfarentzos 1999[567]	Inappropriate comparison
Karjula 2015[580]	Inappropriate comparison
Ke 2016[586]	Systematic review is not relevant to review question or unclear PICO
Khreiss 2015[593]	Not review population
Kulkarni 2014[620]	Not review population
Lee 2006[645]	Inappropriate study design
Lee 2007[643]	Inappropriate comparison
Li 2016[657]	Incorrect interventions
Lopes 2007[674]	Inappropriate comparison
Loveday 2008[680]	Systematic review is not relevant to review question or unclear PICO
Madenci 2014[691]	Inappropriate comparison
Mathew 2014[717]	Inappropriate comparison
Mier 1997[739]	Inappropriate comparison
Mikami 2005[740]	Narrative review
Mortele 2009[760]	Not review population
Mouli 2013[765]	Systematic review is not relevant to review question or unclear PICO
Mukai 2014[771]	Not review population
Mukai 2015[769]	Not review population
Mukai 2015[770]	Not review population
Munene 2011[773]	Not review population
Navalho 2006[788]	Inappropriate comparison
Nieuwenhuijs 2003[798]	Systematic review: methods are not adequate/unclear
Papachristou 2007[833]	Inappropriate comparison

Parekh 2006[835]	Inappropriate comparison
Pascual 2013[843]	Paper not available
Raraty 2010[899]	Not review population
Rau 1997[903]	Narrative review
Rische 2013[913]	Inappropriate comparison
Rocha 2009[916]	Not review population
Rosenberg 2015[923]	Narrative review
Schrover 2008[967]	Inappropriate comparison
Seewald 2005[972]	Incorrect study design
Seifert 2009[976]	Incorrect study design
Shenvi 2016[989]	Incorrect interventions
Solanki 2013[1010]	Outcomes not fully reported
Tong 2012[1074]	No relevant outcomes
Vallance 2014[1090]	No relevant outcomes
Van Baal 2011[1091]	Systematic review is not relevant to review question or unclear PICO
Van Brunschot 2012[1094]	Narrative review
Van Brunschot 2013[1098]	Review protocol
Van Brunschot 2014[1095]	Systematic review is not relevant to review question or unclear PICO
Van Grinsven 2016[1100]	Incorrect interventions
Van Santvoort 2011[1101]	Not review population
Voermans 2007[1119]	Incorrect study design
Wronski 2013[1157]	Inappropriate comparison
Zerem 2011[1181]	Incorrect study design

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L.13 Timing of management of infected necrosis in people with acute pancreatitis

Study	Exclusion reason
Abdelhafez 2013[3]	Inappropriate comparison
Ai 2010[17]	Not review population
Ala-Kokko 2001[24]	Narrative article
Albers 2016[25]	Not in English
Alsfasser 2012[31]	Not review population
Alvarez-Sanchez 2014[33]	Systematic review is not relevant to review question or unclear PICO
Alvi 2011[34]	Not review population
Ang 2013[41]	Inappropriate comparison
Arlt 2014[50]	Inappropriate comparison. Incorrect interventions
Ashley 2001[54]	Not review population
Aultman 1997[56]	Not review population
Babu 2009[64]	Systematic review is not relevant to review question or unclear PICO
Babu 2010[63]	Inappropriate comparison
Bakker 2009[72]	Narrative review
Bakker 2012[68]	Inappropriate comparison
Bala 2009[74]	Inappropriate comparison
Bang 2014[80]	Not review population
Baril 2000[86]	Incorrect study design
Baron 2002[88]	Incorrect study design
Barreda 2015[89]	Not review population
Baudin 2012[102]	Inappropriate study design
Beattie 2002[104]	Incorrect study design
Beck 2012[105]	Incorrect study design
Becker 2009[106]	Incorrect study design

Beenen 2011[108]	Inappropriate comparison
Beger 1986[110]	Incorrect interventions
Beger 1988[111]	Not review population
Beger 1989[109]	Narrative review
Beger 1995[113]	Narrative review
Bello 2012[117]	Systematic review is not relevant to review question or unclear PICO
Berzin 2008[122]	Inappropriate comparison
Besselink 2006[124]	Inappropriate comparison. Not review population. Incorrect interventions
Besselink 2006[123]	Inappropriate comparison
Besselink 2007[126]	Systematic review is not relevant to review question or unclear PICO
Boland 2010[147]	Inappropriate comparison
Bosscha 2001[150]	Not review population
Bradley 1991[155]	Inappropriate comparison
Bradley 2008[156]	Systematic review is not relevant to review question or unclear PICO
Branum 1998[158]	Inappropriate study design
Brunschot 2014[1095]	Systematic review is not relevant to review question or unclear PICO
Bucher 2008[164]	Inappropriate comparison
Buchler 2000[165]	Incorrect study design
Busse 2015[175]	Inappropriate comparison
Castellanos 2005[200]	Inappropriate comparison
Castellanos 2013[199]	Inappropriate comparison
Chang 2006[207]	Inappropriate comparison
Chang 2014[206]	Systematic review is not relevant to review question or unclear PICO
Chaudhary 1997[211]	Inappropriate comparison
Cheung 2005[219]	Inappropriate comparison
Cheung 2010[220]	Not review population

Cirocchi 2013[228]	Systematic review is not relevant to review question or unclear PICO
Connor 2003[239]	Not review population
Connor 2005[240]	Not review population
Connor 2005[238]	Incorrect study design
Connor 2006[241]	Narrative review
Cresswell 2015[256]	Inappropriate comparison
Dhingra 2015[291]	Incorrect interventions
Doctor 2011[300]	Incorrect study design
Doglietto 1994[301]	Not review population
Dominioni 1997[307]	Paper not available
Dong 2008[308]	Incorrect study design
Easler 2012[327]	Narrative review
Easler 2014[325]	Not review population
Echenique 1998[330]	Inappropriate comparison
Eggink 1984[335]	Inappropriate comparison
Endlicher 2003[342]	Inappropriate comparison
Farkas 1998[353]	Incorrect interventions
Farkas 2006[352]	Inappropriate comparison
Fernandez-del Castillo 1998[358]	Not review population
Foitzik 1995[361]	Not review population
Fotoohi 2007[365]	Narrative review
Fugger 1995[372]	Inappropriate comparison
Gambiez 1998[383]	Not review population
Gardner 2009[386]	Incorrect interventions
Gardner 2011[387]	Inappropriate comparison
Garg 2010[391]	Inappropriate comparison

Gentile 1998[394]	Inappropriate comparison
Gluck 2012[406]	Inappropriate comparison
Gomatos 2016[408]	Not review population
Gotzinger 2003[411]	Not review population
Gou 2013[412]	Paper not available
Guo 2001[421]	Not in English
Guo 2013[423]	Incorrect interventions
Gurusamy 2016[428]	Review protocol
Haghshenasskashani 2011[432]	Systematic review is not relevant to review question or unclear PICO
Harris 2004[442]	Inappropriate comparison
Hocke 2008[461]	Not in English
Hollemans 2016[463]	Not review population
Horvath 2001[471]	Incorrect study design
Howard 1989[473]	Narrative review
Huang 1993[479]	Not review population
Huggett 2015[481]	Not review population
Hughes 2007[482]	Narrative review
Hungness 2002[485]	Not review population
Jagielski 2015[520]	Incorrect study design
Jiang 2016[535]	Not review population
Kalfarentzos 1999[567]	Inappropriate comparison
Karjula 2015[580]	Inappropriate comparison
Ke 2016[586]	Systematic review is not relevant to review question or unclear PICO
Khreiss 2015[593]	Not review population
Kulkarni 2014[620]	Not review population
Kumar 2014[622]	Inappropriate comparison

Lee 2006[645]	Inappropriate study design
Lee 2007[643]	Inappropriate comparison
Li 2016[657]	Inappropriate comparison
Loveday 2008[680]	Systematic review is not relevant to review question or unclear PICO
Madenci 2014[691]	Inappropriate comparison
Mathew 2014[717]	Inappropriate comparison
Mier 1997[739]	Not review population
Mikami 2005[740]	Narrative review
Moggia 2017[750]	Not review population
Mortele 2009[760]	Not review population
Mouli 2013[765]	Systematic review is not relevant to review question or unclear PICO
Mukai 2014[771]	Not review population
Mukai 2015[769]	Not review population
Mukai 2015[770]	Not review population
Munene 2011[773]	Not review population
Nieuwenhuijs 2003[798]	Systematic review: methods are not adequate/unclear
Pascual 2013[843]	Paper not available
Pupelis 2015[884]	Inappropriate comparison
Raraty 2010[899]	Not review population
Rasch 2016[901]	Inappropriate comparison
Rau 1997[903]	Narrative review
Rau 2005[902]	Incorrect interventions
Rosenberg 2015[923]	Narrative review
Ross 2014[924]	Incorrect study design
Shenvi 2016[989]	Incorrect interventions
Szeliga 2014[1051]	Inappropriate comparison

Vallance 2014[1090]	Inappropriate comparison
Van Baal 2011[1091]	Systematic review is not relevant to review question or unclear PICO
Van Brunschot 2012[1094]	Narrative review
Van Brunschot 2013[1098]	Review protocol
Van Grinsven 2016[1100]	Narrative review
Van Grinsven 2017[1099]	Inappropriate comparison
Wronski 2013[1157]	Inappropriate comparison
Zerem 2011[1181]	Incorrect study design

L.14 Management of pain in people with chronic pancreatitis

Study	Exclusion reason
Adamek 1999[10]	Incorrect study design
Ahmed Ali 2012[15]	Inappropriate comparison
Ahmed Ali 2015[16]	Not review population
Aimoto 2013[18]	Inappropriate comparison
Aljebreen 2014[27]	Inappropriate comparison
Amornyotin 2015[39]	Incorrect interventions
Arendt 1999[49]	Unavailable
Armbrecht 1986[51]	No relevant outcomes
Bachmann 2014[65]	Inappropriate comparison
Banks 1991[83]	Incorrect study design
Basinski 2005[93]	Not review population
Bassi 1999[98]	Incorrect study design
Beckingham 1997[107]	Systematic review is not relevant to review question or unclear PICO
Behrns 2008[115]	Incorrect study design
Bejanin 1993[116]	Unavailable
Bergman 2012[121]	Not review population
Bhardwaj 2013[128]	Incorrect study design

Bilton 1994[133]	Not review population
Binmoeller 1995[134]	Incorrect study design
Bliss 2015[139]	Not review population
Bloechle 1995[142]	Unavailable
Bloechle 1996[140]	Incorrect study design
Bloechle 2001[141]	Unavailable
Bouwense 2012[153]	No relevant outcomes
Brand 2000[157]	Incorrect study design
Brown 1997[161]	Systematic review is not relevant to review question or unclear PICO
Buchler 1996[166]	Incorrect study design. Not in English
Buhler 1999[168]	Not review population
Burton 2011[171]	Incorrect study design
Buscher 2002[173]	Incorrect study design
Buscher 2007[174]	Incorrect study design
Butorova 2007[176]	Unavailable
Byrne 2009[179]	Not review population
Cahen 2007[183]	Unavailable
Cahen 2007[182]	Not review population
Cai 2013[186]	Incorrect interventions
Capurso 2012[193]	Incorrect study design
Cartmell 2004[196]	No extractable outcomes
Chan 2001[204]	Not review population
Chauhan 2010[212]	Incorrect study design
Chauhan 2012[213]	Incorrect study design
Chen 2015[214]	Unavailable
Chiang 2007[221]	Inappropriate comparison
Classen 1990[230]	Incorrect study design
Cremer 1989[255]	Incorrect study design
Davies 1996[268]	Incorrect study design
De las Heras Castano 2000[275]	Incorrect study design

D'Egidio 1991[260]	Incorrect study design
Delhaye 2004[279]	Incorrect study design
Deprez[282]	Abstract only
D'Haese 2014[262]	Incorrect study design
Dhingra 2013[290]	No extractable outcomes
Dhir 2015[292]	Incorrect study design
Dite 2003[299]	Not review population
Duffas 2005[315]	Inappropriate comparison
Dumonceau 2007[319]	Not review population
Duvnjak 1998[324]	Inappropriate comparison
Eisenach 2003[338]	Incorrect interventions
Fan 1993[350]	Not review population
Fitzsimmons 1999[359]	Incorrect study design
Fitzsimmons 2005[360]	Incorrect study design
Folsch 1997[362]	Not review population
Fujisawa 2014[374]	Inappropriate comparison
Fuller 1981[375]	Incorrect interventions
Funnell 1994[376]	Incorrect study design
Gabbrielli 2005[380]	Incorrect study design
Garzya 1985[392]	Not in English
Giovannini 2016[400]	Incorrect study design
Gooshe 2015[410]	Systematic review is not relevant to review question or unclear PICO
Gooshe 2015[410]	Incorrect interventions
Gress 2001[415]	Incorrect study design
Guda 2005[416]	Systematic review is not relevant to review question or unclear PICO
Gupta 2007[424]	Incorrect study design
Gurusamy 2016[429]	Inappropriate comparison. Systematic review is not relevant to review question or unclear PICO
Halder 2015[433]	Inappropriate comparison
Halgreen 1986[434]	Study prior to search cut-off date

Heider 1999[451]	Incorrect study design
Hernandez 2011[454]	Systematic review is not relevant to review question or unclear PICO
Herrerías 1989[455]	Unavailable
Heyries 2010[456]	Conference abstract
Hirota 2010[457]	Systematic review is not relevant to review question or unclear PICO
Hoogerwerf 2005[466]	Incorrect study design
Horibe 2015[468]	Not review population. Systematic review is not relevant to review question or unclear PICO
Howell 1993[476]	Incorrect study design
Hu 2016[478]	Unavailable
Inui 2005[494]	Incorrect study design
Irani 2012[497]	Not review population
Isaksson 1983[498]	Study prior to study cut-off date
Itoi 2009[507]	Inappropriate comparison
Izbicki 1994[513]	Inappropriate comparison
Izbicki 1995[514]	Not in English
Izbicki 1996[511]	Incorrect study design
Izbicki 1997[512]	Unavailable
Izbicki 1998[510]	Incorrect study design
Izbicki 1998[509]	Inappropriate comparison
Jacobson 2005[516]	Incorrect study design
Jagielski 2017[519]	Incorrect study design
Jazrawi 2011[525]	Incorrect study design
Jeppe 2011[530]	Conference abstract
Jeppe 2013[529]	Incorrect study design
Jiang 2014[534]	Not in English
Jimenez 2000[536]	Inappropriate comparison
Johanns 1996[540]	Incorrect study design
John 2014[541]	Conference abstract
John 2014[542]	Conference abstract

John 2016[543]	Conference abstract
Joliat 2017[548]	Inappropriate comparison
Jouannaud 2006[551]	Not review population
Junming 2015[553]	Conference abstract
Kandiah 2014[572]	Conference abstract
Kapural 2010[576]	Conference abstract
Kapural 2011[577]	Incorrect interventions
Karasawa 2002[579]	Incorrect study design
King 2010[600]	Systematic review is not relevant to review question or unclear PICO. Not review population
Kirk 2006[601]	Incorrect interventions
Klapdor 2012[604]	Incorrect study design Not review population
Klempa 1995[605]	Unavailable
Knill-Jones 1973[606]	Not in English
Knop 2010[607]	Incorrect study design
Kocher 2008[608]	Systematic review is not relevant to review question or unclear PICO
Kocher 2011[609]	Systematic review is not relevant to review question or unclear PICO
Koninger 2004[612]	Unavailable
Kozarek 1985[617]	Incorrect study design
Kwek 2014[631]	Incorrect study design
Lang 1991[633]	Not review population
Larvin 1991[640]	Incorrect study design
Leksowski 2007[647]	Incorrect study design
Lerch 2009[649]	Incorrect study design
Levy 1989[650]	Unavailable
Li 2006[653]	Unavailable
Li 2015[658]	Incorrect interventions
Li 2016[651]	Inappropriate comparison
Liu 1997[667]	Incorrect study design

Lorenz 1988[675]	Unavailable
Lu 2013[682]	Inappropriate comparison
Madsen 1985[692]	Study prior to search cut-off date
Magyar 1997[696]	No relevant outcomes
Makin 2012[700]	Incorrect study design
Malhotra 2007[705]	Review protocol
Mayyas 2010[726]	Not review population. Systematic review is not relevant to review question or unclear PICO
McCloy 1998[732]	Incorrect study design
McMahon 1991[733]	Incorrect study design
Melman 2009[734]	Not review population
Mergener 2005[737]	Incorrect study design
Milek 2014[741]	Inappropriate comparison
Mobius 2007[749]	Inappropriate comparison
Mohseni Salehi Monfared 2009[751]	Incorrect study design
Monkemuller 2004[754]	Incorrect study design
Moole 2016[755]	Systematic review is not relevant to review question or unclear PICO
Morgan 2003[757]	Incorrect study design
Mossner 1993[762]	Incorrect study design
Muhl 2009[768]	Incorrect study design
Muller 2008[772]	Inappropriate comparison
Nakahara 2013[780]	Incorrect study design
Nakamura 2012[782]	Not review population
Nandi 2002[784]	Abstract only
Ni 2015[793]	Incorrect study design
Niemann 2000[797]	Inappropriate comparison
Noda 1994[802]	Incorrect interventions
Nussinson 1991[808]	Incorrect study design
Ohwada 1997[813]	Not review population
O'Keefe 2001[811]	Not review population

Olazabal 1978[820]	Not review population
Oracz 2010[823]	Not in English
Paisley 2014[827]	Incorrect study design
Paris 1993[837]	Not review population
Park 2009[840]	Not in English
Puli 2009[880]	Not review population. Systematic review is not relevant to review question or unclear PICO
Puylaert 2011[887]	Incorrect study design
Ramesh 2013[892]	Incorrect study design
Riediger 2007[912]	Inappropriate comparison
Rubenstein 2002[925]	Incorrect study design
Rupasinghe 2017[926]	Incorrect study design
Rustagi 2015[928]	Incorrect study design
Rustagi 2015[928]	Systematic review is not relevant to review question or unclear PICO. Incorrect interventions
Safdi 2006[932]	Not review population
Sahai 2010[935]	Incorrect study design
Sahel 1987[937]	Incorrect study design
Salim 1991[942]	Incorrect population
Samuelson 2016[945]	Unavailable
Santosh 2009[949]	Inappropriate comparison
Sarfeh 1988[950]	Inappropriate comparison
Sawai 2006[955]	Not review population
Schofield 1994[965]	Abstract only
Shah 2010[980]	Incorrect study design
Shah 2013[979]	Incorrect interventions
Shao 2012[981]	Unavailable
Shen 2014[988]	Inappropriate comparison
Shrikhande 2006[993]	Incorrect study design
Siriwardena 2012[1001]	Incorrect interventions
Slaff 1984[1004]	Results not fully reported

Staahl 2007[1021]	No extractable outcomes
Stefaniak 2008[1024]	Incorrect interventions
Stevens 2012[1025]	Inappropriate comparison
Strate 2005[1032]	Unavailable
Strate 2006[1030]	Unavailable
Strate 2008[1029]	Inappropriate comparison
Sukharamwala 2015[1042]	Systematic review is not relevant to review question or unclear PICO. Inappropriate comparison
Talukdar 2015[1058]	Systematic review is not relevant to review question or unclear PICO
Talukdar 2016[1057]	Incorrect intervention
Tandan 2010[1062]	Not review population
Thorat 2012[1072]	Not review population
Trespi 1997[1076]	Unavailable
Uden 1989[1085]	Abstract only
Usatoff 2000[1088]	Incorrect study design
Vantini 1990[1105]	Incorrect interventions
Varadarajulu 2011[1108]	Not review population
Verhaegh 2013[1113]	Incorrect study design
Vitkomb 2010[1118]	Unavailable
Wilder-Smith 1999[1144]	Inappropriate comparison
Will 2006[1147]	Incorrect study design
Will 2011[1146]	Not review population
Winstead 2009[1150]	Systematic review is not relevant to review question or unclear PICO
Witzigmann 2003[1153]	Inappropriate comparison
Wolf 1995[1155]	Incorrect study design
Yaghoobi 2016[1168]	Systematic review is not relevant to review question or unclear PICO
Yang 2014[1172]	Not in English
Zambudio 2014[1180]	Incorrect study design
Zhou 2015[1191]	Systematic review is not relevant to review question or unclear

	PICO. Incorrect interventions
Zhu 2017[1195]	Unavailable

L.15 Management of pancreatic duct obstruction in people with chronic pancreatitis

Study	Exclusion reason
Adamek 1999[10]	Incorrect study design
Ahmed Ali 2012[15]	Inappropriate comparison
Ahmed Ali 2014[14]	Incorrect interventions
Ahmed Ali 2015[16]	Not review population
Aimoto 2013[18]	Inappropriate comparison
Aljebreen 2014[27]	Inappropriate comparison
Amornyotin 2015[39]	Incorrect interventions
Arendt 1999[49]	Unavailable
Armbrecht 1986[51]	No relevant outcomes
Bachmann 2014[65]	Inappropriate comparison
Banks 1991[83]	Incorrect study design
Basinski 2005[93]	Not review population
Bassi 1999[98]	Incorrect study design
Beckingham 1997[107]	Systematic review is not relevant to review question or unclear PICO
Bergman 2012[121]	Not review population
Binmoeller 1995[134]	Incorrect study design
Bloechle 1996[140]	Not in English
Bouwense 2012[153]	No relevant outcomes
Brand 2000[157]	Incorrect study design
Brown 1997[161]	Systematic review is not relevant to review question or unclear PICO
Buchler 1996[166]	Not in English

Buhler 1999[168]	Not review population
Buscher 2002[173]	Incorrect study design
Buscher 2007[174]	Incorrect study design
Byrne 2009[179]	Not review population
Cai 2013[186]	Incorrect interventions
Cartmell 2004[196]	No relevant outcomes
Chauhan 2010[212]	Incorrect study design
Chauhan 2012[213]	Incorrect study design
Chiang 2007[221]	Inappropriate comparison
Classen 1990[230]	Incorrect study design
Cremer 1989[255]	Incorrect study design
Davies 1996[268]	Incorrect study design
D'Egidio 1991[260]	Incorrect study design
Delhaye 2004[279]	Incorrect study design
D'Haese 2014[262]	Incorrect study design
Dhir 2015[292]	Incorrect study design
Duffas 2005[315]	Inappropriate comparison
Eisenach 2003[338]	Incorrect interventions
Fan 1993[350]	Not review population
Folsch 1997[362]	Not review population
Fujisawa 2014[374]	Inappropriate comparison
Fuller 1981[375]	Incorrect interventions
Funnell 1994[376]	Incorrect study design
Gabbrielli 2005[380]	Incorrect study design
Garzya 1985[392]	Not in English
Giovannini 2016[400]	Incorrect study design

Gooshe 2015[410]	Incorrect interventions
Gress 2001[415]	Incorrect study design
Guda 2005[416]	Systematic review is not relevant to review question or unclear PICO
Gupta 2007[424]	Incorrect study design
Gurusamy 2016[429]	Inappropriate comparison
Halder 2015[433]	Inappropriate comparison
Halgreen 1986[434]	Not review population
Heider 1999[451]	Incorrect study design
Heyries 2010[456]	Conference abstract
Hirota 2010[457]	Systematic review is not relevant to review question or unclear PICO
Hoogerwerf 2005[466]	Incorrect study design
Horibe 2015[468]	Not review population
Howell 1993[476]	Incorrect study design
Inui 2005[494]	Incorrect study design
Irani 2012[497]	Not review population
Isaksson 1983[498]	Not review population
Itoi 2009[507]	Inappropriate comparison
Izbicki 1994[513]	Inappropriate comparison
Izbicki 1995[514]	Not in English
Izbicki 1996[511]	Incorrect study design
Izbicki 1998[510]	Incorrect study design
Izbicki 1998[509]	Inappropriate comparison
Jacobson 2005[516]	Incorrect study design
Jagielski 2017[519]	Incorrect study design
Jazrawi 2011[525]	Incorrect study design
Jeppe 2011[530]	Conference abstract

Jeppe 2013[529]	Incorrect study design
Jiang 2014[534]	Not in English
Jimenez 2000[536]	Inappropriate comparison
Johanns 1996[540]	Incorrect study design
John 2014[541]	Conference abstract
John 2014[542]	Conference abstract
John 2016[543]	Conference abstract
Joliat 2017[548]	Inappropriate comparison
Jouannaud 2006[551]	Not review population
Junming 2015[553]	Conference abstract
Kaido 2006[563]	Inappropriate comparison
Kandiah 2014[572]	Conference abstract
Kapural 2010[576]	Conference abstract
Kapural 2011[577]	Incorrect interventions
Karasawa 2002[579]	Incorrect study design
King 2010[600]	Not review population
Kirk 2006[601]	Incorrect interventions
Knill-Jones 1973[606]	Not in English
Knop 2010[607]	Incorrect study design
Kocher 2008[608]	Systematic review is not relevant to review question or unclear PICO
Kocher 2011[609]	Systematic review is not relevant to review question or unclear PICO
Kozarek 1985[617]	Incorrect study design
Kwek 2014[631]	Incorrect study design
Lang 1991[633]	Not review population
Larvin 1991[640]	Incorrect study design
Leksowski 2007[647]	Incorrect study design

Lerch 2009[649]	Incorrect study design
Li 2015[658]	Incorrect interventions
Li 2016[651]	Inappropriate comparison
Liu 1997[667]	Incorrect study design
Lu 2013[682]	Inappropriate comparison
Madsen 1985[692]	Not review population
Magyar 1997[696]	No relevant outcomes
Makin 2012[700]	Incorrect study design
Malesci 1995[704]	Not review population
Malhotra 2007[705]	Review protocol
Mayyas 2010[726]	Not review population
McMahon 1991[733]	Incorrect study design
Melman 2009[734]	Not review population
Mergener 2005[737]	Incorrect study design
Milek 2014[741]	Inappropriate comparison
Monkemuller 2004[754]	Incorrect study design
Moole 2016[755]	Systematic review is not relevant to review question or unclear PICO
Morgan 2003[757]	Incorrect study design
Mossner 1992[763]	Not review population
Muhl 2009[768]	Incorrect study design
Nakahara 2013[780]	Incorrect study design
Nakamura 2012[782]	Not review population
Ni 2015[793]	Incorrect study design
Niemann 2000[797]	Inappropriate comparison
Noda 1994[802]	Incorrect interventions
Nussinson 1991[808]	Incorrect study design

Ohwada 1997[813]	Not review population
O'Keefe 2001[811]	Not review population
Olazabal 1978[820]	Not review population
Oracz 2010[823]	Not in English
Paris 1993[837]	Not review population
Puli 2009[880]	Not review population
Puylaert 2011[887]	Incorrect study design
Ramesh 2013[892]	Incorrect study design
Riediger 2007[912]	Inappropriate comparison
Rubenstein 2002[925]	Inappropriate comparison
Rustagi 2015[928]	Incorrect interventions
Safdi 2006[932]	Not review population
Sahai 2010[935]	Incorrect study design
Sahel 1987[937]	Incorrect study design
Santosh 2009[949]	Inappropriate comparison
Sarfeh 1988[950]	Inappropriate comparison
Sawai 2006[955]	Not review population
Seza 2011[978]	Not review population
Shah 2013[979]	Incorrect interventions
Shen 2014[988]	Inappropriate comparison
Shrikhande 2006[993]	Incorrect study design
Siriwardena 2012[1001]	Incorrect interventions
Staahl 2007[1021]	No relevant outcomes
Stefaniak 2008[1024]	Incorrect interventions
Stevens 2012[1025]	Inappropriate comparison
Sukharamwala 2015[1042]	Inappropriate comparison

Talukdar 2016[1057]	Not review population
Thorat 2012[1072]	Not review population
Usatoff 2000[1088]	Incorrect study design
Vantini 1990[1105]	Incorrect interventions
Varadarajulu 2011[1108]	Not review population
Verhaegh 2013[1113]	Incorrect study design
Wilder-Smith 1999[1144]	Inappropriate comparison
Will 2006[1147]	Incorrect study design
Will 2011[1146]	Not review population
Winstead 2009[1150]	Systematic review is not relevant to review question or unclear PICO
Witzigmann 2003[1153]	Inappropriate comparison
Wolf 1995[1155]	Incorrect study design
Yaghoobi 2016[1168]	Systematic review is not relevant to review question or unclear PICO
Yang 2014[1172]	Not in English
Zambudio 2014[1180]	Incorrect study design
Zhou 2015[1191]	Incorrect interventions

L.16 Management of small-duct disease in people with chronic pancreatitis

Study	Exclusion reason
Akshintala 2014[20]	Not review population
Andersson 2006[40]	Not review population
Ardengh 2014[48]	Not review population
Azeem 2012[60]	Not review population
Barthet 1993[91]	Not review population
Bhasin 2011[129]	Not review population

Boerma 2002[145]	Not review population
Boutros 2010[151]	Not review population
Bouwense 2011[152]	Not review population
Chen 2017[217]	Not review population
Clarke 2012[229]	Not review population
Davila-Cervantes 2004[269]	Not review population
D'Egidio 1992[261]	Not review population
Epelboym 2014[344]	Not review population
Farkas 2004[351]	Not review population
Farnbacher 2002[355]	Not review population
Giovannini 2012[399]	Not review population
Howard 2002[474]	Not review population
Huizinga 1992[483]	Not review population
Iqbal 2009[495]	Not review population
John 2015[545]	Not review population
John 2017[544]	Not review population
Jordan 2001[549]	Not review population
Keck 2010[588]	Not review population
Kondo 2014[611]	Not review population
Lu 2014[683]	Not review population
Naoum 2003[785]	Not review population
Rosch 2002[922]	Not review population
Saul 2016[954]	Not review population
Sharma 2002[982]	Not review population
Teh 2006[1067]	Not review population
Trevino 2010[1077]	Not review population

Varadarajulu 2007[1109]	Not review population
Varadarajulu 2008[1107]	Not review population
Vitas 1992[1117]	Not review population
Will 2007[1145]	Not review population
Yang 2016[1171]	Not review population

L.17 Management of pseudocysts

Study	Exclusion reason
Adams 1992[11]	Incorrect interventions
Aljarabah 2007[26]	Systematic review: study designs inappropriate
Ardengh 2014[48]	Not review population: cysts not pseudocysts
Azeem 2012[60]	Not review population
Barthet 1993[91]	Not review population
Binmoeller 1995[135]	Incorrect study design
Boerma 2002[145]	Not review population
Boutros 2010[151]	Inappropriate comparison
Bouwense 2011[152]	Not review population
Chen 2017[217]	Not review population
Clarke 2012[229]	Incorrect study design
D'Egidio 1992[261]	Inappropriate comparison
Epelboym 2014[344]	Not review population
Farkas 2004[351]	Not review population
Farnbacher 2002[355]	Not review population
Giovannini 2012[399]	Systematic review: methods are not adequate/unclear
Howard 2002[474]	Not review population
Huizinga 1992[483]	Inappropriate comparison
Iqbal 2009[495]	Not review population
John 2015[545]	Not review population
John 2017[544]	Not review population

Study	Exclusion reason
Jordan 2001[549]	Not review population
Kahaleh 2006[557]	Inappropriate comparison
Keck 2010[588]	Not review population
Kondo 2014[611]	Not pseudocysts. Not review population
Lu 2014[683]	Not review population
Naoum 2003[785]	Confounding by indication: severity of pseudocysts dictated which treatment was received
Rosch 2002[922]	Inappropriate comparison. Not review population
Russell 2013[927]	Incorrect interventions
Seven 2012[977]	Not review population
Sharma 2002[982]	Inappropriate comparison
Smits 1995[1007]	Inappropriate comparison
Teh 2006[1067]	Inappropriate comparison
Trevino 2010[1077]	Not review population: Peripancreatic fluid collections not just pseudocysts
Varadarajulu 2007[1109]	Not review population: Peripancreatic fluid collections not just pseudocysts
Vitas 1992[1117]	All procedures performed prior to 1990
Will 2007[1145]	Not review population
Williams 1992[1148]	Incorrect interventions
Yang 2016[1171]	Inappropriate comparison.

L.18 Management of pancreatic ascites and pleural effusion secondary to pancreatitis

Study	Exclusion reason
Abadia 2010[1]	Conference abstract
Adler 1990[12]	Incorrect study design
Allen 2014[29]	Incorrect population
Alonso Ordas 2017[30]	Abstract only

Azoulay 2003[61]	Incorrect study design
Bakker 2011[69]	Incorrect study design
Banimahd 2009[82]	Incorrect study design
Bassi 2000[94]	Incorrect study design
Bassi 2000[99]	Incorrect study design
Bhasin 2006[130]	Incorrect study design
Bintcliffe 2016[136]	Incorrect study design
Bracher 1999[154]	Incorrect study design
Cabay 1998[180]	Incorrect study design
Cheng 2017[218]	Incorrect population
Closset 2000[231]	Incorrect study design
Cohen 2001[234]	Incorrect study design
Cohen 2007[235]	Incorrect study design
Cope 2001[248]	Incorrect study design
Coronel 2017[249]	Incorrect study design
Costamagna 2001[252]	Incorrect study design
Da Cunha 1995[263]	Incorrect study design
Dhar 1996[289]	Incorrect study design
Falconi 2002[348]	Incorrect study design
Feig 1992[356]	Not review population
Felix 2014[357]	Incorrect population
Fotoohi 1999[364]	Incorrect study design
Friess 1994[370]	Incorrect study design
Friess 1996[369]	Incorrect study design
Futagawa[379]	Incorrect population
Gjorup 1992[402]	Incorrect population

Gumaste 1992[420]	Incorrect study design
Halttunen 2005[436]	Incorrect study design
Halttunen 2007[435]	Incorrect study design
Hassenpflug 2012[445]	Incorrect study design
Heo 2017[452]	Incorrect study design
Holst 1998[465]	Not in English
Houlihan 2013[472]	Incorrect study design
Igami 2009[487]	Incorrect study design
Ihse 1994[492]	Incorrect study design
Irani 2012[497]	Incorrect study design
Jain 2009[521]	Incorrect study design
Jenkins 1995[527]	Incorrect study design
Jiang 2016[535]	Incorrect study design
Jorge 1991[550]	Incorrect study design
Kaman 2001[568]	Incorrect study design
Kanneganti 2009[573]	Incorrect study design
Karjula 2015[580]	Incorrect study design
Kawakatsu 2016[585]	Incorrect study design
King 2010[600]	Incorrect study design
Koizumi 2005[610]	Incorrect study design
Kozarek 1991[616]	Incorrect study design
Kurumboor 2009[626]	Incorrect study design
Larsen 2014[639]	Incorrect study design
Le Moine 2004[641]	Incorrect study design
Lee 2014[644]	Incorrect study design
Liang 2007[660]	Incorrect study design

Lipsett 1992[665]	Incorrect study design
Lipsett 1998[666]	Incorrect study design
Liu 2015[669]	Inappropriate comparison
Mattison 1997[720]	Incorrect study design
Mithofer 1997[744]	Incorrect study design
Mittal 2007[745]	Incorrect study design
Moorthy 2007[756]	Incorrect study design
Morgan 2007[758]	Incorrect study design
Munoz-Bongrand 2004[775]	Inappropriate comparison
Nabi 2017[777]	Incorrect study design
Nair 2007[778]	Incorrect study design
Nakamura 2014[781]	Incorrect population
Niedergethmann 2010[796]	Incorrect intervention
Nikou 2004[800]	Incorrect intervention
Nordback 1996[805]	Incorrect study design
Nwariaku 1995[809]	Not review population
Okabayashi 2004[814]	Incorrect study design
Okamoto 2008[815]	Incorrect intervention
Olakowski 2009[819]	Not in English
Ondrejka 2000[822]	Not in English
O'Toole 2007[812]	Incorrect study design
Pai 2009[826]	Incorrect study design
Palani Velu 2014[828]	Incorrect comparator
Pandey 2014[830]	Incorrect study design
Parekh 1992[836]	Incorrect study design
Park 2011[839]	Incorrect study design

Patil 2016[844]	Abstract only
Pearson 2012[846]	Incorrect study design
Pericleous 2016[850]	Incorrect study design
Phillips 2000[864]	Incorrect study design
Prabhudesai 1993[878]	Incorrect study design
Pratt 2008[879]	Incorrect intervention
Ramesh 2013[893]	Incorrect study design
Ramos-de la Medina 2006[894]	Incorrect population
Rana 2010[895]	Incorrect study design
Rana 2017[896]	Incorrect study design
Raptis 1994[898]	Not review condition
Reszetow 2006[909]	Incorrect study design
Ridgeway 1996[910]	Incorrect study design
Ridolfi 2014[911]	Incorrect study design
Roberts 2012[914]	Incorrect study design
Rockey 1990[917]	Incorrect study design
Sanchez 2016[946]	Not in English
Santos 2017[948]	Incorrect study design
Schmidt 2009[962]	Incorrect comparator
Schweigert 2013[971]	Incorrect study design
Schweigert 2013[970]	Incorrect study design
Sikora 2005[994]	Incorrect study design
Simmons 1997[995]	Incorrect study design
Singh 2013[998]	Incorrect study design
Smoczynski 2007[1009]	Incorrect study design
Sorrentino 2017[1013]	Incorrect population

Srikanth 2002[1019]	Incorrect population
Suc 2004[1035]	Incorrect population
Sugimoto 2015[1037]	Incorrect study design
Tahir 2011[1052]	Incorrect study design
Tajima 2006[1053]	Incorrect study design
Tanaka 2013[1061]	Incorrect study design
Tsiotos 1995[1082]	Incorrect population
Tsiotos 1999[1081]	Incorrect study design
Uchikov 2000[1083]	Incorrect study design
Vansonnenberg 1997[1104]	Incorrect study design
Velamati 2006[1111]	Incorrect study design
Voss 2003[1120]	Incorrect study design
Wakefield 1996[1124]	Incorrect study design
Wang 2017[1129]	Incorrect population
Weniger 2016[1141]	Incorrect study design
Wolfsen 1992[1156]	Incorrect study design
Wronski 2011[1158]	Incorrect study design
Xu 2014[1166]	Incorrect study design
Yokoi 2016[1178]	Incorrect study design
Zhou 2016[1192]	Incorrect study design

L.19 Management of biliary obstruction in people with chronic pancreatitis

Study	Exclusion reason
Abdallah 2007[2]	Incorrect study design
Acosta 2006[9]	Incorrect comparison

Arslanlar 2007[52]	Systematic review is not relevant to review question or unclear PICO
Ayub 2010[59]	Unavailable
Azzopardi 2012[62]	Incorrect study design
Bakhru 2011[67]	Unavailable
Baron 2009[87]	Incorrect study design
Baron 2010{Baron, 2010 #847}	Incorrect study design
Barthet 1994[90]	Incorrect study design
Behm 2009[114]	Incorrect study design
Blero 2015[138]	Incorrect study design
Boskoski 2016[149]	Unavailable
Brijbassie 2016[159]	Unavailable
Cahen 2005[185]	Incorrect study design
Cahen 2008[184]	Incorrect study design
Cantu 2005[190]	Incorrect study design
Chang 2016[205]	Incorrect study design
Chaput 2016[209]	Incorrect study design
Choo 2012[223]	Incorrect study design
Costamagna 2007[251]	Incorrect study design
Costamagna 2013[250]	Incorrect study design
Coté 2016[253]	Not review population
Cremer 1992[254]	Incorrect study design
Deviere 1990[287]	Incorrect study design
Deviere 1992[285]	Unavailable
Deviere 1994[286]	Incorrect study design
Deviere 2014[288]	Incorrect study design
Deviere 2015[292]	Incorrect study design

Ding 2012[298]	Incorrect comparison
Draganov 2002[310]	Incorrect study design
Dubravcsik 2012[314]	Incorrect comparison
Dumonceau 1999[320]	Incorrect study design
Dumonceau 1999[321]	Incorrect study design
Dumonceau 2010[318]	Incorrect study design
Dumonceau 2011[322]	Systematic review is not relevant to review question or unclear PICO
Eickhoff 2001[336]	Incorrect study design
Eickhoff 2003[337]	Not in English
Eisendrath 1999[170]	Incorrect study design
Enya 2004[343]	Incorrect study design
Familiari 2013[349]	Systematic review is not relevant to review question or unclear PICO
Farnbacher 2000[354]	Incorrect study design
French 2003[367]	Incorrect study design
Frey 1990[368]	Systematic review is not relevant to review question or unclear PICO
Fujino 2009[373]	Inappropriate comparison
Garcia-Cano 2010[385]	Not in English
Giacino 2012[395]	Incorrect study design
Gibbons 1998[397]	Systematic review is not relevant to review question or unclear PICO
Goenka 1997[407]	Incorrect study design
Gouma 2007[413]	Incorrect study design
Gupta 2006[426]	Incorrect study design
Gupta 2007[424]	Incorrect study design
Gupta 2011[427]	Incorrect study design
Hammel 2001[437]	Incorrect study design
Hausegger 1996[446]	Incorrect study design

Hu 2014[477]	Incorrect study design
Huizinga 1992[484]	Incorrect study design
Igarashi 2004[488]	Incorrect study design
Ikeda 2010[493]	Incorrect interventions
Irani 2014[496]	Incorrect study design
Isayama 2009[499]	Incorrect study design
Ito 2012[504]	Not review population
Itoi 2012[508]	Incorrect study design
Jang 2010[523]	Incorrect study design
Kaffes 2013[555]	Incorrect study design
Kaffes 2015[554]	Incorrect study design
Kahaleh 2008[209]	Incorrect study design
Kahaleh 2013[556]	Incorrect study design
Kahl 2002[562]	Incorrect study design
Kahl 2003[560]	Incorrect study design
Kahl 2004[561]	Incorrect study design
Kianicka 2013[594]	Incorrect study design
Kiehne 2000[595]	Incorrect study design
Kikuyama 2009[597]	Incorrect interventions
Kikuyama 2009[596]	Incorrect study design
Kim 1998[599]	Inappropriate comparison
Kim 2015[598]	Incorrect study design
Kulkarni 2015[619]	Incorrect study design
Kumar 2004[623]	Incorrect study design
Kwon 2016[632]	Incorrect study design
Lee 2011[642]	Unavailable

Li 2014[652]	Incorrect study design
Lillemoe 1992[661]	Incorrect study design
Lin 2010[663]	Incorrect interventions
Long 1990[673]	Incorrect study design
Lytras 2011[688]	Not review population
Mahajan 2009[697]	Incorrect study design
Mangiavillano 2014[709]	Incorrect study design
Matlock 2005[718]	Incorrect study design
Matsubayashi 2016[719]	Not review population
Mauri 2013[722]	Incorrect study design
Menon 2001[735]	Incorrect study design
Merdrignac 2016[736]	Incorrect study design
Mitchell 2003[743]	Incorrect study design
Muniraj 2013[774]	Systematic review is not relevant to review question or unclear PICO
Myburgh 1993[776]	Inappropriate comparison
Nakanuma 2010[783]	Incorrect study design
Nealon 1996[790]	Incorrect study design
O'Brien 1998[810]	Incorrect study design
Oria 2007[825]	Incorrect comparison
Park 2003[873]	Incorrect study design
Park 2008[841]	Incorrect study design
Park 2016[842]	Incorrect study design
Pausawasadi 2012[845]	Incorrect study design
Pearson 2012[846]	Not review population
Perri 2011 [852]	Unavailable
Perri 2012[851]	Incorrect study design

Poincloux 2015[873]	Incorrect interventions
Poley 2012[874]	Incorrect interventions
Ray 2015[904]	Incorrect study design
Rebibo 2013[905]	Incorrect study design
Rocca 2006[915]	Incorrect study design
Ryu 2013[930]	Incorrect study design
Sakai 2009[941]	Incorrect study design
Saluja 2014[943]	Incorrect study design
Sarkaria 2014[951]	Incorrect study design
Saxena 2015[956]	Incorrect study design
Schepers 2017[958]	Review protocol
Schlosser 2001[961]	Incorrect study design
Schnelldorfer 2003[964]	Incorrect study design
Schutz 1995[968]	Incorrect study design
Smits 1996[1008]	Incorrect study design
Suc 1998[1034]	Incorrect population
Targarona 1996[1064]	Incorrect population. Incorrect intervention
Van Berkel 2004[1092]	Incorrect study design
Van Boeckel 2009[1093]	Incorrect study design
Velanovich 2009[1112]	Systematic review is not relevant to review question or unclear PICO
Vitale 2000[1116]	Incorrect study design
Wagh 2013[1123]	Incorrect study design
Waldthaler 2013[1125]	Inappropriate comparison
Walter 2015[1127]	Incorrect study design
Walter 2015[1128]	Incorrect population
Wasan 2005[1135]	Not review population

Weber 2014[1136]	Incorrect study design
Weigt 2016[1137]	Incorrect interventions
Yamaguchi 2006[1169]	Incorrect study design
Yang 2012[1173]	Incorrect intervention
Zheng 2015[1190]	Incorrect interventions
Zhou 2002[1193]	Incorrect comparison

L.20 Management of type 3c diabetes secondary to pancreatitis

None.

L.21 Receiving specialist input in people with acute pancreatitis

Study	Exclusion reason
Avanesov 2017[57]	Incorrect study design
Banks 2006[84]	Incorrect study design
Issa 2017[503]	Incorrect study design
Loser 1993[678]	Incorrect study design
Mayumi 2002[725]	Incorrect study design
Park 2009[838]	No relevant outcomes
Pezzilli 2006[862]	Incorrect study design
Soran 2001[1012]	Incorrect interventions
Sriskandarajah 2016[1020]	Incorrect interventions
Toh 2000[1073]	Incorrect interventions
Toouli 2002[1075]	Incorrect study design
Working Group IAP/APA APG 2013[486]	Incorrect study design
Wyncoll 1999[1163]	Incorrect study design

L.22 Follow-up of pancreatic exocrine function in people with chronic pancreatitis

Study	Exclusion reason
Adamek 1999[10]	Inappropriate study design
Ammann 1996[36]	Incorrect interventions
Belyaev 2013[118]	Inappropriate comparison
Dranka-Bojarowska 2015[312]	Incorrect interventions
Ekbom 1994[339]	Incorrect interventions
Endlicher 2003[342]	Inappropriate study design
Furuya 1997[377]	Incorrect interventions
Maire 2011[699]	Inappropriate comparison
Sudo 2014[1036]	Incorrect interventions
Sugito 2012[1038]	Inappropriate study design
Symersky 2006[1048]	Incorrect interventions
Takuma 2011[1054]	Not review question
Tanaka 2014[1060]	Incorrect interventions

L.23 Follow-up to identify diabetes in people with chronic pancreatitis

Study	Exclusion reason
Bittner 1994 [137]	Inappropriate comparison. Incorrect interventions
Hiroyoshi 1999 [458]	Incorrect interventions.
Ito 2007 [506]	Non-comparative study; not follow-up tests
Malecka-Panas 2002 [703]	Not review population: healthy controls
Quartuccio 2017 [889]	Incorrect interventions.
Roeyen 2016 [918]	Inappropriate comparison. Incorrect interventions. Non-comparative study
Ruxer 2012 [929]	Not English language

Schrader 2010 [966]	Inappropriate comparison. Incorrect interventions

L.24 Follow-up to identify pancreatic cancer in people with chronic pancreatitis

Study	Exclusion reason
Keane 2014[587]	Not relevant to review question
Kirkegard 2017[602]	Incorrect comparison
Konzen 1993[613]	Not relevant to review question

Appendix M: Excluded health economic studies

M.1 Patient information

None.

M.2 Lifestyle interventions: stopping or reducing alcohol consumption

None.

M.3 Aetiology of acute pancreatitis

None.

M.4 Aetiology of chronic pancreatitis

None.

M.5 Diagnosing chronic pancreatitis

None.

M.6 Type of intravenous fluid for resuscitation in people with acute pancreatitis

None.

M.7 Speed of intravenous fluid for resuscitation in people with acute pancreatitis

None.

M.8 Route of feeding in people with severe acute pancreatitis

None.

M.9 Early versus late nutritional intervention in people with chronic pancreatitis

None.

M.10 Specialist versus non-specialist nutritional assessment in people with chronic pancreatitis

None.

M.11 Prophylactic antimicrobial agents to prevent infection in people with acute pancreatitis

None.

M.12 Methods of management of infected necrosis in people with acute pancreatitis

None.

M.13 Timing of management of infected necrosis in people with acute pancreatitis

None.

M.14 Management of pain in people with chronic pancreatitis

None.

M.15 Management of pancreatic duct obstruction in people with chronic pancreatitis

None.

M.16 Management of small-duct disease in people with chronic pancreatitis

None.

M.17 Management of pseudocysts

None.

M.18 Management of pancreatic ascites and pleural effusion secondary to pancreatitis

None.

M.19 Management of biliary obstruction in people with chronic pancreatitis

None.

M.20 Management of type 3c diabetes secondary to pancreatitis

None.

M.21 Receiving specialist input in people with acute pancreatitis

None.

M.22 Follow-up of pancreatic exocrine function in people with chronic pancreatitis

None.

M.23 Follow-up to identify diabetes in people with chronic pancreatitis

None.

M.24 Follow-up to identify pancreatic cancer in people with chronic pancreatitis

None.

Appendix N: Unit costs

N.1 Patient information

None.

N.2 Lifestyle interventions: stopping or reducing alcohol consumption

None.

N.3 Aetiology of acute pancreatitis

None.

N.4 Aetiology of chronic pancreatitis

None.

N.5 Diagnosing chronic pancreatitis

None.

N.6 Type of intravenous fluid for resuscitation in people with acute pancreatitis

Table 2: Unit costs of fluids for resuscitation

Fluid regimen	Volume	Unit cost
0.9% Sodium Chloride (saline)	1 litre bag	£2.50
Ringer's lactate solution	1 litre bag	£0.70

Source: NICE CG174 Intravenous fluid therapy in adults in hospital[786]

N.7 Speed of intravenous fluid for resuscitation in people with acute pancreatitis

None.

N.8 Route of feeding in people with severe acute pancreatitis

None.

N.9 Early versus late nutritional intervention in people with chronic pancreatitis

None.

N.10 Specialist versus non-specialist nutritional assessment in people with chronic pancreatitis

None.

N.11 Prophylactic antimicrobial agents to prevent infection in people with acute pancreatitis

Table 3: UK costs of antimicrobials

Drug	Dose	Unit cost	Cost per week
Quinolones			
Ciprofloxacin	250 mg, 2 times a day	£0.75 per 10 tablets	£1.04
Carbapenem			
Imipenem IV (with cilastatin	500 mg, 3 times a day	£75.45 per 10 vials	£158.45
	1 g, 3 times a day		£316.89
Meropenem IV	500 mg, 3 times a day	£76.90 per 10 vials	£161.49
	1 g, 3 times a day	£153.50 per 10 vials	£322.35
Chephalosporin			
Ceftazidime IV	2 g, 3 times a day	£27.70 per 10 vials	£58.17
Cefuroxime IV	1.5 g, per day	£4.70 per vial	£32.90
Aminoglycoside			
	500 mg, twice a day	£60 per 5 vials	£168.00
Imidazole			
Metronidazole IV	500 mg, 3 times a day	£62 per 20 bags	£65.10
Fluconazole IV	100 mg, once a day	£12.60 per 5 bottles	£88.20

Sources: NHS Drug Tariff, September 2016;[791], BNF, November 2016[143]

N.12 Methods of management of infected necrosis in people with acute pancreatitis

None.

N.13 Timing of management of infected necrosis in people with acute pancreatitis

None.

N.14 Management of pain in people with chronic pancreatitis

None.

N.15 Management of pancreatic duct obstruction in people with chronic pancreatitis

Table 4: UK costs of interventions for treating pancreatic duct disease

HRG code	Procedure	Mean cost per procedure
Surgery		
GA04, GA05, GA06	Elective Major to Complex open Hepatobiliary or Pancreatic Procedures	£7,547
Endotherapy		
GB05, GB06, GB09	Elective Major to Complex Therapeutic Endoscopic Retrograde Cholangiopancreatography	£1,840
Extracorporeal shock wave lithotripsy (ESWL)		
LB36Z	Extracorporeal Lithotripsy (all organs, not pancreas-specific), Day cases (all cases)	£470 (£405)

Source: NHS Reference costs 2015/16[281]

N.16 Management of small-duct disease in people with chronic pancreatitis

None.

N.17 Management of pseudocysts

Table 5: UK costs of interventions for treating pseudocysts

HRG code	Procedure	Number of cases[(a)]	Mean cost per procedure
Pancreatic endoscopic stent by ERCP		**29,987**	**£1,996**
GB06E	Intermediate Therapeutic Endoscopic Retrograde Cholangiopancreatography with CC Score 6+	3,084	£4,121
GB06F	Intermediate Therapeutic Endoscopic Retrograde Cholangiopancreatography with CC Score 4–5	3,162	£2,708
GB06G	Intermediate Therapeutic Endoscopic Retrograde Cholangiopancreatography with CC Score 2–3	7,160	£2,048
GB06H	Intermediate Therapeutic Endoscopic Retrograde Cholangiopancreatography with CC Score 0–1	16,581	£1,442
EUS guided pseudocyst drainage[(b)]		**5,898**	**£4,903**
GB09D	Complex Therapeutic Endoscopic Retrograde Cholangiopancreatography with CC Score 5+	794	£5,530
GB09E	Complex Therapeutic Endoscopic Retrograde Cholangiopancreatography with CC Score 2–4	1,187	£2,961
GB09F	Complex Therapeutic Endoscopic Retrograde Cholangiopancreatography with CC Score 0–1	1,295	£1,811
GA05C	Very Major Open, Hepatobiliary or Pancreatic Procedures, with CC Score 3+	725	£9,337
GA05D	Very Major Open, Hepatobiliary or Pancreatic Procedures, with CC Score 0–2	1,897	£6,273
Percutaneous drainage of pseudocyst[(c)]		**1,300**	**£5,431**

HRG code	Procedure	Number of cases[a]	Mean cost per procedure
GA06C	Major Open, Hepatobiliary or Pancreatic Procedures, with CC Score 2+	579	£7,301
GA06D	Major Open, Hepatobiliary or Pancreatic Procedures, with CC Score 0–1	721	£3,930
Laparoscopic pseudocyst drainage[d]		**3,922**	**£6,560**
GA06C	Major Open, Hepatobiliary or Pancreatic Procedures, with CC Score 2+	579	£7,301
GA06D	Major Open, Hepatobiliary or Pancreatic Procedures, with CC Score 0–1	721	£3,930
GA05C	Very Major Open, Hepatobiliary or Pancreatic Procedures, with CC Score 3+	725	£9,337
GA05D	Very Major Open, Hepatobiliary or Pancreatic Procedures, with CC Score 0–2	1,897	£6,273
Pseudocyst drainage by open surgery[e]		**3,922**	**£6,560**

Source: NHS Reference costs 2015/16[281]

(a) 'Number of cases' refers to annual number of cases classified to these codes, this will include other procedures coded in the same category, not only the procedure of interest in this review

(b) GB09 if coded to J611 + Y76 – cystogastrotomy of pancreas or GA05 if coded to K614 + Y76 - drainage of cyst of pancreas

(c) GA06 if coded to J611 + Y752 – cystogastrotomy of pancreas

(d) Same 4 codes used as for laparoscopic pseudocyst drainage; GA06 if coded to J611 + Y53 – cystogastrotomy of pancreas or GA05 coded to K614 + Y53 – drainage of cyst of pancreas

(e) Same 4 codes used as for laparoscopic pseudocyst drainage; GA06 if coded to J611 – cystogastrotomy of pancreas or GA05 coded to K614 – drainage of cyst of pancreas

N.18 Management of pancreatic ascites and pleural effusion secondary to pancreatitis

None.

N.19 Management of biliary obstruction in people with chronic pancreatitis

Table 6: UK costs of interventions for treating biliary obstruction

Procedure	Unit cost
Therapeutic Endoscopic Retrograde Cholangiopancreatography[a]	£2,177
Very Major Open Hepatobiliary or Pancreatic Procedures[b]	£7,120

Source: NHS reference costs 2015/16[281]

(a) Weighted cost of intermediate, major and complex intervention based on activity (GB05F, GB05G, GB05H, GB06E, GB06F, GB06G, GB06H, GB09D, GB09E, GB09F)

(b) Weighted cost of very major open procedures based on activity (GA05C, GA05D)

Table 7: UK costs of stents

Stent	Unit cost
Endoscopic Retrograde Cholangiopancreatography 7fr 11cm biliary plastic stent 9cm between flaps	£21
Endoscopic Retrograde Cholangiopancreatography dual platform (short or long wire) biliary metal stent	£688
Endoscopic Retrograde Cholangiopancreatography dual platform (short or long wire)	£150

Stent	Unit cost
biliary dilatation fusion titan balloon	

Source: NHS Supply Chain Catalogue 2015[792]

N.20 Management of type 3c diabetes secondary to pancreatitis

None.

N.21 Receiving specialist input in people with acute pancreatitis

None.

N.22 Follow-up of pancreatic exocrine function in people with chronic pancreatitis

None.

N.23 Follow-up to identify diabetes in people with chronic pancreatitis

None.

N.24 Follow-up to identify pancreatic cancer in people with chronic pancreatitis

None.

Appendix O: Research Recommendations

O.1 Priority research recommendations

O.1.1 Research recommendation: In people with suspected (or under investigation for) chronic pancreatitis, whose diagnosis has not been confirmed by the use of 'first-line' tests (for example, CT scan, ultrasound scan, upper GI endoscopy or combinations of these), what is the most accurate diagnostic test to identify whether chronic pancreatitis is present?

Why this is important:

People with chronic pancreatitis usually present with chronic abdominal pain. However, there are many other causes of chronic abdominal pain (for example, peptic ulcer disease, gallstone disease, gastric cancer, pancreatic cancer and abdominal aortic aneurysm). First-line tests to exclude these other causes include abdominal ultrasound, upper GI endoscopy and abdominal CT scan. Where the diagnosis has still not been confirmed following these first-line tests, it is important to have a clinical algorithm of specialist tests to be able to identify people with chronic pancreatitis. Appropriate management options can then be offered. A diagnostic cohort study is needed to determine the accuracy of magnetic resonance cholangiopancreatography (MRCP) with or without sectretin and endoscopic ultrasound in diagnosing chronic pancreatitis.

Criteria for selecting priority research recommendations

Question framework	Population: people with suspected (or under investigation for) chronic pancreatitis, whose diagnosis has not been confirmed by the use of 'first-line' tests Target condition: Chronic pancreatitis in people presenting with chronic abdominal pain, and normal or uncertain CT or ultrasound scan or upper GI endoscopy Index tests: • Combination of MRCP plus or minus secretin with EUS (cut-off: Rosemont criteria: presence of chronic pancreatitis if >5) (including elastography) • MRCP with or without secretin • EUS (cut-off: Rosemont criteria: presence of chronic pancreatitis if >5) (including elastography) Reference standard: Biopsy, clinical follow-up or subsequent CT scan Outcome measures: Diagnostic accuracy of the test or combination of tests
Importance to patients or the population	Delayed diagnosis of chronic pancreatitis is very common and has been repeatedly highlighted as a concern by patient support groups. Identification of chronic pancreatitis in its early stages before complications occur will potentially slow down the progression of the disease and reduce complications.
Relevance to NICE guidance	When the guideline is updated this will enable more definitive diagnosis of chronic pancreatitis.
Relevance to the NHS	Accurate diagnosis will lead to better and earlier treatment for people with chronic pancreatitis. This will result in reduced resource use by preventing complications, which leads to lower downstream costs.
National priorities	None.
Current evidence base	The systematic review in the NICE guideline identified only 1 study, with the evidence rated as very low quality. This was not sufficient to inform a recommendation.
Equality	None.

Study design	Diagnostic accuracy study using a prospective cohort design.
Feasibility	The proposed research can be carried out in a realistic timescale and at an acceptable cost. There are no ethical or technical issues.
Other comments	None.
Importance	• High: the research is essential to inform future updates of key recommendations in the guideline.

O.1.2 Research recommendation: What is the most clinically effective and cost-effective speed of administration of intravenous fluid for resuscitation in people with acute pancreatitis?

Why this is important:

There is clinical uncertainty about the optimal rate of fluid for resuscitation in severe acute pancreatitis. Severe acute pancreatitis causes the depletion of body fluids and reduction of the intravascular volume severe enough to cause hypotension, acute renal failure and pancreatic hypoperfusion aggravating the damage to the pancreas. In addition, there is conflicting evidence about the effect of aggressive or conservative fluid management on outcomes in other conditions with a pathophysiology.

Current guidelines recommend aggressive fluid therapy during the first 24 hours of hospital admission guided by central venous pressure monitoring or the intrathoracic blood volume index. The use of central venous pressure monitoring to guide fluid resuscitation has little evidence to support it. A randomised controlled trial is needed to determine whether aggressive rates of intravenous fluid administration for the initial period of fluid resuscitation are more clinically or cost-effective than conservative rates in people with acute pancreatitis.

Criteria for selecting priority research recommendations

PICO question	Population: People with acute pancreatitis enrolled shortly after admission to the emergency department Intervention(s): • conservative IV fluid management using a balanced solution for resuscitation (for example, Hartmann's solution), defined as 40 ml/kg/hour for 6–12 hours then 10–20 ml/kg/hour. • Moderate IV fluid management using a balanced solution for resuscitation (for example, Hartmann's solution) defined as 60 ml/kg/hour for 6–12 hours. then 30 ml/kg/hour • Aggressive IV fluid management using a balanced solution for resuscitation (for example, Hartmann's solution) defined as 80 ml/kg/hour for 6–12 hours then 40 ml/kg/hour. Comparison: to each other Outcome(s): mortality (at 90 days and 12 months), hospital mortality, CCU admissions, rates of severe pancreatitis, multiple organ failure, necrotising pancreatitis and rates of surgical and non-surgical intervention in adult patients with acute pancreatitis (all grades of severity), length of hospital stay, quality of life. Follow-up: 90 days
Importance to patients or the population	Identifying the most appropriate speed of early fluid administration may reduce the proportion of patients with acute pancreatitis who go on to develop severe disease, which would reduce mortality and improve quality of life.
Relevance to NICE guidance	The answer to this question will allow NICE to make a strong recommendation about the optimal speed of IV fluid resuscitation in acute pancreatitis.
Relevance to the NHS	Acute pancreatitis is a common condition with an annual incidence of 150–420

	cases per million. About a-third of patients will develop severe acute pancreatitis, which has a significant risk of mortality and morbidity, and requires prolonged and resource-intensive hospital care. It is feasible that the appropriate use of early fluid administration may reduce the proportion of patients with acute pancreatitis who go on to develop severe disease. This would have a significant impact on the resource consumption of people with acute pancreatitis.
National priorities	None.
Current evidence base	The NICE committee was unable to find enough evidence to make a strong recommendation. The body of evidence was limited to 3 randomised trials and 6 non-randomised studies, all with small sample sizes. The evidence was low to very low quality and there was no consistent evidence of benefit of either aggressive or conservative fluid resuscitation strategies.
Equality	None. All patients presenting with acute pancreatitis will be included.
Study design	A randomised-controlled trial should be undertaken to determine whether aggressive or conservative rates of intravenous fluid administration for the initial period of fluid resuscitation are more clinically or cost-effective at reducing 90-day mortality, hospital mortality, CCU admissions, rates of severe pancreatitis, multiple organ failure, and necrotizing pancreatitis in adult patients with acute pancreatitis (all grades of severity). The study population should include adult patients (aged more than 16 years old) with all grades of severity of acute pancreatitis enrolled shortly after admission to the Emergency Department. Acute pancreatitis should be defined as at least two of: (1) Characteristic abdominal pain (2) Serum amylase or lipase more than three times the upper limit of normal (3) Cross-sectional imaging showing changes consistent with acute pancreatitis. The study should also consider the impact of different fluid rates of administration on quality of life.
Feasibility	Patients will need to be recruited from the Accident and Emergency department following emergency admissions and recruitment will need to take place 24-hours a day, which is a technical issue for research. All patients presenting with acute pancreatitis will be included in the study. However, it would be beneficial to stratify mild, moderate and severe acute pancreatitis although this may be difficult to achieve as the disease severity is not known at presentation and fluid administration should be started promptly.
Other comments	It would be important to attempt to begin fluid administration within 3–6 hours of admission as there is evidence to suggest that patients admitted to hospital with acute pancreatitis are under-hydrated.
Importance	• High: the research is essential to inform future updates of key recommendations in the guideline.

O.1.3 Research recommendation: Is the long-term use of opioids more clinically effective and cost effective than non-opioid analgesia (including non-pharmacological analgesia) in people with chronic pain due to chronic pancreatitis?

Why this is important:

Chronic pancreatitis is a complex condition needing biopsychosocial management. The pain is varied in nature, intensity, duration and severity, along with acute exacerbations. It is also multifactorial, making it difficult to have a standard regimen that can work for everyone. Some people also develop psychosocial factors such as reduction in quality of life, relationship issues, addiction to painkillers and financial difficulties.

Chronic pancreatitis is usually managed pharmacologically with a combination of opioids and other interventions. However, the use of opioids in managing chronic pancreatitis is known to cause serious side-effects – including tolerance, addiction, tiredness and constipation. These side-effects are frequently worse than the disease itself. Therefore, the whole rationale for the use of opioids in chronic pancreatitis is questionable. A cohort study is needed to determine how effective long-term opioid use is in this population compared with non-opiate pain management strategies, including analgesia and psychological therapies.

Criteria for selecting priority research recommendations

PICO question	Population: People with painful chronic pancreatitis Intervention(s): non-opiate pain management strategies, including analgesia and psychological therapies Comparison: Opioids Outcomes: Quality of life, pain, tolerance, addiction, tiredness, constipation, breakthrough pain, flare ups, hospital admissions, amount of rescue analgesia being used. Follow-up: at least 12 months
Importance to patients or the population	Clear evidence on the benefits and harms of opioids in chronic pancreatitis should enable more appropriate use of this intervention, which could prevent overuse of opioids and the related harms of, for example, opioid tolerance and addiction. Therefore, quality of life could be improved by targeting opioid use to those who are likely to benefit through successful pain management.
Relevance to NICE guidance	Clarification of the role of opioids in managing pain in chronic pancreatitis would allow the NICE guideline on pancreatitis to make firm recommendations regarding their use in clinical practice. Pain management is one of the most important aspects of care for people with chronic pancreatitis as it is often the most troublesome symptom.
Relevance to the NHS	Opioids are commonly used in both acute and chronic pancreatitis. The side effects of opioids are extensive including addiction, tolerance, and constipation. This also reduces quality of life for patients. With little evidence to support their use, they might even cause harm at high doses such as reduced systemic hormone levels, reduced immunity and death. Clinicians widely use the WHO analgesic ladder to guide escalation of pharmacological therapy, which is also included in the SIGN 2013 chronic pain guidance. Whilst the guidance does accept that the analgesic ladder was not devised for use in chronic pain, it advocates its use for non-specialists in chronic pain management. Therefore, new evidence specific to chronic pain may be more cost effective if some therapies are proven to have a positive effect.
National priorities	None
Current evidence base	The evidence review in this guideline did not identify any studies for either short- or long-term use of opioids in chronic pancreatitis. Although it is known that opioids are good analgesics for acute pain and for pain at the end of life there is little evidence of their use for long-term pain. The recent opioid awareness campaign clearly highlights the long-term harm in using opioids at high doses over long periods.
Equality	Not applicable
Study design	Appropriately designed and powered cohort studies.
Feasibility	Most pancreatitis patients will require analgesia and opioids are commonly used for their acute episodes. Enrolling an opioid-naïve patient in chronic pancreatitis might be difficult. This can lead to challenges in the design, but could be addressed by the active treatment arm showing reduction in opioid use with better quality of life.
Other comments	None

Importance	• High: the research is essential to inform future updates of key recommendations in the guideline.

O.1.4 Research recommendation: What is the most clinically effective and cost-effective intervention for managing small-duct disease (in the absence of pancreatic duct obstruction, inflammatory mass or pseudocyst) in people with chronic pancreatitis presenting with pain?

Why this is important:

People who have chronic pancreatitis with small duct disease are more difficult to treat than those without the disease because they do not have an anatomically correctable pancreatic abnormality – for example, pancreatic duct obstruction, inflammatory mass or pseudocysts. A randomised controlled trial study is needed to determine what the most effective intervention is for treating small duct disease. The following interventions should be compared with each other and with no treatment: surgery (partial resection, total resection with or without islet transplant, or drainage), endoscopic treatment, or standard care (for example, pharmacological treatment only, enzyme replacement therapy, nerve blocks).

Criteria for selecting priority research recommendations

PICO question	Population: People with chronic pancreatitis presenting with pain, without pancreatic duct obstruction, inflammatory mass or pseudocyst Intervention(s): Surgery (partial resection, total resection with or without islet transplant, or drainage), endoscopic treatment, or standard care (for example, pharmacological treatment only, enzyme replacement therapy, nerve blocks). Comparison: Compared with each other and with no treatment Outcome(s): Quality of life, mortality, complications, pain, length of hospital stay Follow-up: 12–24 months
Importance to patients or the population	Chronic pancreatitis is a difficult disease to treat and patients become extremely frustrated because of the variation in treatments that are available or not available in different centres. Patients with small duct disease are particularly affected by this lack of consistency.
Relevance to NICE guidance	The answer to this question will allow NICE to make a strong recommendation about the management of small-duct disease when the guideline is updated.
Relevance to the NHS	Reduction in pain and complications will improve quality of life and overall patient care and reduce hospital length of stay and, therefore, should be cost effective.
National priorities	None.
Current evidence base	Only a single small, non-randomised study was identified by the systematic review within this NICE guideline. Therefore, more robust evidence is required to inform evidence-based practice.
Equality	None.
Study design	Appropriately designed and powered multicentre randomised controlled trials or cohort studies.
Feasibility	The proposed research can be carried out in a realistic timescale and at an acceptable cost. There are no ethical or technical issues.
Other comments	None.
Importance	• High: the research is essential to inform future updates of key recommendations in the guideline.

O.1.5 Research recommendation: What is the most clinically effective and cost-effective insulin regimen for type 3c diabetes secondary to pancreatitis?

Why this is important:

Type 3c diabetes is associated with metabolic instability and risk of decompensation leading to severe hypoglycaemia and ketoacidosis, in addition to poor quality of life. However, there is no evidence available in this population to inform practice. Therefore, research specifically on type 3c diabetes is essential to inform future updates of key recommendations in this guideline. National adoption of evidence-based insulin management in type 3c diabetes has the potential to cost-effectively improve health and well-being, reducing the incidence of acute and long-term complications of poorly controlled glucose levels in chronic pancreatitis. A randomised controlled trial is needed to determine the most effective insulin therapy regimen in this population, comparing twice daily insulin injections, an insulin analogue multiple daily dose basal bolus regimen, and insulin pump therapy.

Criteria for selecting priority research recommendations

PICO question	Population: Adults with insulin-treated type 3c diabetes. Intervention(s): • Twice daily insulin injections • insulin analogue multiple daily dose basal bolus regimen, • insulin pump (CSII) therapy Comparison: To each other Outcome(s): Glucose variability and time in rage, HbA1c, hypoglycaemia, episodes of ketoacidosis, mortality, nutritional status and quality of life. Follow-up: 6 months
Importance to patients or the population	Recommendations for insulin management specifically in type 3c diabetes could improve the ability to control glucose levels, reducing the incidence of acute and long-term complications.
Relevance to NICE guidance	The answer to this question will allow NICE to make an evidence-based recommendation in an important type of diabetes not adequately addressed by existing guidelines, which is essential to inform future updates of key recommendations in the guidance.
Relevance to the NHS	National adoption of evidence-based insulin management in type 3c diabetes has the potential to cost-effectively improve health and well-being, reducing incidence of acute and long-term complications of poorly controlled glucose levels in chronic pancreatitis.
National priorities	None
Current evidence base	The guideline found no relevant studies and could only recommended following type 1 diabetes guidelines.
Equality	People with type 3c diabetes have been potentially disadvantaged in terms of equity of access to interventions provided to those with insulin-requiring type 1 diabetes, including structured education, multiple daily dose insulin regimens and insulin pump therapy.
Study design	Appropriately designed and powered randomised controlled trials comparing glycaemic control attained with twice daily insulin injections with an insulin analogue multiple daily dose basal bolus regimen and with insulin pump (CSII) therapy. Studies should last at least 6 months and should assess glucose variability and time within range (3–10 mmol/litre) in addition to HbA1c and hypoglycaemia. Hypoglycaemia awareness in addition to severe events requiring assistance in treatment and episodes of diabetic ketoacidosis should be compared. Nutritional

	status should be assessed. Patient reported outcomes should include validated treatment satisfaction, hypoglycaemia fear and quality of life measures (including improved independence). Data collected should enable health economic analysis. The study should also stratify participants by residual insulin (C-peptide) status to determine whether this influences requirement for and impact of a more complex insulin regimen.
Feasibility	Through appropriate multidisciplinary involvement in trial design and completion, together with carefully structured patient education and support, this research should not raise additional feasibility, ethical, safety or technical issues.
Other comments	This research will necessitate a multidisciplinary approach, facilitating enhanced evidence-based diabetes management for type 3c diabetes.
Importance	• High: the research is essential to inform future updates of key recommendations in the guideline.

O.2 Other research recommendations

O.2.1 What is the most clinically effective and cost-effective type of intravenous fluid for resuscitation in people with acute pancreatitis?

O.2.2 What is the most clinically effective and cost-effective intervention for managing pancreatic duct obstruction, with or without an inflammatory mass, in children with chronic pancreatitis presenting with pain?

O.2.3 What is the clinical effectiveness and cost effectiveness of metal stents compared to surgery for treating biliary obstruction in adults with chronic pancreatitis?

Appendix P: NICE technical team

Name	Role
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