Surveillance proposal consultation document

2018 surveillance of Gallstone disease: diagnosis and management (NICE guideline CG188)

Proposed surveillance decision

We propose to not update the NICE guideline on <u>Gallstone disease</u>: <u>diagnosis and management</u> at this time.

Reasons for the proposal to not update the guideline

New evidence was identified during the surveillance review which supports the current recommendations for the use of particular diagnostic interventions and management strategies for gallstone disease.

New evidence was also identified concerning investigations for the diagnosis of gallbladder disease that are not currently recommended, the benefits of single-stage versus two-stage surgery in the management of common bile duct (CBD) stones, the timing of endoscopic retrograde cholangiopancreatography (ERCP) in the management of CBD stones and the timing of cholecystectomy following a diagnosis of gallstone pancreatitis. However, it was concluded that in the absence of further evidence synthesis or additional published evidence, this evidence would not be sufficient to trigger an update at this time.

We will request that Cochrane consider undertaking a review to consider the new evidence on timings of surgical procedures in the management of CBD stones and following diagnosis of gallstone pancreatitis. Once completed we will undertake an exceptional surveillance review to consider the results and any impact on the guideline.

For further details and a summary of all evidence identified in surveillance, see <u>appendix A</u> below.

Overview of 2018 surveillance methods

NICE's surveillance team checked whether recommendations in Gallstone disease: diagnosis and management (NICE guideline CG188) remain up to date.

The surveillance process consisted of:

- Initial feedback from topic experts via a questionnaire.
- Literature searches to identify relevant evidence.
- Assessment of new evidence against current recommendations.

- Deciding whether or not to update sections of the guideline, or the whole guideline.
- Consultation on the decision with stakeholders (this document).

After consultation on the decision we will consider the comments received and make any necessary changes to the decision. We will then publish the final surveillance report containing the decision, the summary of the evidence used to reach the decision, and responses to comments received in consultation.

For further details about the process and the possible update decisions that are available, see <u>ensuring that published guidelines are current and accurate</u> in developing NICE guidelines: the manual.

See <u>appendix A: summary of evidence from surveillance</u> below for details of all evidence considered, with references.

Evidence considered in surveillance

Search and selection strategy

We searched for new evidence related to the whole guideline.

We found 54 studies in a search that included systematic reviews, meta-analyses, randomised controlled trials, economic evaluations, and observational studies on the diagnosis and management of gallstone disease published between 1 February 2014 and 3 April 2018.

Selecting relevant studies

The standard surveillance review process of using RCT's, full economic evaluations of relevance to the UK and systematic reviews was used for this search.

The only deviation from this was the inclusion of observational studies for patient, family member and carer information and for the diagnosis of gallstone disease.

Ongoing research

We checked for relevant ongoing research. Of the ongoing studies identified, 2 UK based RCT's were assessed as having the potential to change recommendations. We plan to check the publication status regularly, and evaluate the impact of the results on current recommendations as quickly as possible. These studies are:

- A randomised controlled trial comparing laparoscopic cholecystectomy with observation/conservative management for preventing recurrent symptoms and complications in adults with uncomplicated symptomatic gallstones.
- A randomised controlled trial to establish the clinical and cost effectiveness of expectant management versus pre-operative imaging with MRCP in patients with

symptomatic gallstones undergoing laparoscopic cholecystectomy at low or moderate risk of common bile duct stones: The Sunflower Study

Intelligence gathered during surveillance

Views of topic experts

We considered the views of topic experts, including those who helped to develop the guideline. For this surveillance review, topic experts completed a questionnaire about developments in evidence, policy and services related to NICE guideline CG188.

Six experts responded: 3 indicated that the guideline should be updated and 3 indicated that the guideline did not need updating. The following issues were raised:

One topic expert questioned whether conservative management is better than surgery for some patients with an episode of acute cholecystitis, as the expert highlighted that these patients may not have a further attack of gallstone symptoms. However evidence identified during this surveillance review indicates that acute cholecystitis patients receiving conservative management have a significantly greater likelihood of gallstone-related complications and, if they ended up requiring surgery, they have more surgery-related complications compared to patients receiving planned laparoscopic cholecystectomy. As such the evidence supports recommendation 1.2.4 which says to 'offer early laparoscopic cholecystectomy (to be carried out within 1 week of diagnosis) to people with acute cholecystitis'. A topic expert also suggested that recommendation 1.3.2 should be updated to include postoperative ERCP for clearing the bile duct, however evidence identified during this surveillance review did not support the use of postoperative ERCP.

Topic experts highlighted papers on the timing of laparoscopic cholecystectomy after ERCP and the cost effectiveness of early cholecystectomy, which have been included as evidence in this surveillance review.

Other sources of information

We considered all other correspondence received since the guideline was published, including correspondence received based on a coroner's report. This formed the basis of a decision to consider the timing of surgery following the diagnosis of gallstone pancreatitis, which is currently out of scope for NICE guideline CG188. We will keep abreast of research in this area to assess whether operation intervals can be more clearly defined and any implications for NICE guideline CG188.

Views of stakeholders

Stakeholders are consulted on all surveillance decisions except if the whole guideline will be updated and replaced. Because this surveillance decision is to not update the guideline, we are consulting on the decision.

See <u>ensuring that published guidelines are current and accurate</u> in developing NICE guidelines: the manual for more details on our consultation processes.

Equalities

No equalities issues were identified during the surveillance process.

Overall decision

After considering all evidence and other intelligence and the impact on current recommendations, we propose that no update is necessary at this time.

Appendix A: Summary of evidence from surveillance

2018 surveillance of Gallstone disease: diagnosis and management (2014) NICE guideline CG188

Summary of evidence from surveillance

Studies identified in searches are summarised from the information presented in their abstracts.

Feedback from topic experts who advised us on the approach to this surveillance review, was considered alongside the evidence to reach a final decision on the need to update each section of the guideline.

Frequently used abbreviations

AGP	Acute gallstone pancreatitis
CBD	Common bile duct
СТ	Computed tomography
DLC	Delayed laparoscopic cholecystectomy
ELC	Early laparoscopic cholecystectomy
EUS	Endoscopic ultrasound
ERCP	Endoscopic retrograde cholangiopancreatography
HIDA scan	Hepatobiliary iminodiacetic acid scan
LC	Laparoscopic cholecystectomy
IOC	Intraoperative cholangiography
LCBDE	Laparoscopic common bile duct exploration
LFTs	Liver function tests
MRCP	Magnetic resonance cholangiopancreatography

1.1 Diagnosing gallstone disease

Recommendations in this section of the guideline

- 1.1.1 Offer liver function tests and ultrasound to people with suspected gallstone disease, and to people with abdominal or gastrointestinal symptoms that have been unresponsive to previous management.
- 1.1.2 Consider magnetic resonance cholangiopancreatography (MRCP) if ultrasound has not detected common bile duct stones but the:

- bile duct is dilated and/or
- liver function test results are abnormal.
- 1.1.3 Consider endoscopic ultrasound (EUS) if MRCP does not allow a diagnosis to be made.
- **1.1.4** Refer people for further investigations if conditions other than gallstone disease are suspected.

Surveillance decision

This section of the guideline should not be updated.

2018 surveillance summary

Strategies for diagnosing gallstone disease

Liver function tests (LFTs) and ultrasound

A Cochrane review included 5 studies (n=523) assessing the diagnostic accuracy of abdominal ultrasound and LFTs in diagnosing common bile duct (CBD) stones in symptomatic patients. Presence of CBD stones were confirmed by either surgical or endoscopic extraction. Absence of CBD stones were confirmed by either surgical or endoscopic negative exploration of the CBD, or symptom-free follow-up for at least 6 months for a negative test result. The summary sensitivity for ultrasound was 0.73 (95% CI 0.44 to 0.90) and the specificity was 0.91 (95% CI 0.84 to 0.95). At the median pre-test probability of CBD stones of 0.408, the post-test probability associated with positive ultrasound tests was 0.85 (95% CI 0.75 to 0.91), and negative ultrasound tests was 0.17 (95% CI 0.08 to 0.33). One study reported the diagnostic accuracy of LFTs and ultrasound: ultrasound yielded a sensitivity of 0.32 (95% CI 0.15 to 0.54), bilirubin (cut-off greater than 22.23 µmol/L) was 0.84 (95% CI 0.64 to 0.95), and alkaline phosphatase (cut-off greater than 125 IU/L) was 0.92 (95% CI 0.74 to 0.99). The specificity for ultrasound was 0.95 (95% CI 0.91 to 0.97), bilirubin was 0.91 (95% CI 0.86 to 0.94), and alkaline phosphatase was 0.79

(95% CI 0.74 to 0.84). All studies were rated as having poor methodological quality. (1)

One observational study reported on the diagnostic utility of abdominal ultrasound in acute cholecystitis, using the intraoperative diagnosis as a reference standard. The sensitivity and specificity of ultrasound was 73.2% and 85.5% respectively. (2)

Magnetic resonance cholangiopancreatography (MRCP)

A systematic review included 25 studies (n=2,310 patients with suspected CBD stones and n=738 with CBD stones) investigating the diagnostic accuracy of MRCP in the detection of CBD stones. Patients had to be diagnosed with CBD based on endoscopic retrograde cholangiopancreatography (ERCP) and/or intraoperative cholangiography (IOC). Random effects models were used to generate pooled results for MRCP in detecting CBD stones: sensitivity = 0.90 (95% CI 0.88 to 0.92; p<0.001); specificity = 0.95 (95% CI 0.93 to 1.0; p<0.001); positive likelihood ratio = 13.28 (95% CI 8.8 to 19.94; p<0.001); negative likelihood ratio = 0.13 (95% CI 0.09 to 0.18; p<0.001); and diagnostic odds ratio = 143.82 (95% CI 82.42 to 250.95, p<0.001). (3)

Two observational studies reported on both the sensitivity and/or specificity of MRCP in detecting CBD stones, confirmed by ERCP and/or IOC, clinical follow-up. (4,5) In one study MRCP yielded a sensitivity of 97% and specificity of 98% (4) whilst another study reported solely on the sensitivity of MRCP, which was 93.3%. (5)

Endoscopic ultrasound (EUS) and MRCP/ERCP

A Cochrane review included 18 studies (n=976 with CBD stones and n=1,390 without stones) assessing the diagnostic accuracy of EUS and MRCP in detecting CBD stones. Presence of CBD stones were confirmed by either surgical or endoscopic extraction. Absence of CBD stones were confirmed by either surgical or endoscopic negative exploration of the CBD, or symptom-free follow-up for at least 6 months for a negative test result. The pooled values of the 13 studies (n=1,537) which assessed EUS for sensitivity and specificity were 0.95 (95% CI 0.91 to 0.97) and 0.97 (95% CI 0.94 to 0.99) respectively. The pooled sensitivity of the 7 studies (n=996) which assessed MRCP for sensitivity and specificity were 0.93 (95% CI 0.87 to 0.96) and 0.96 (95% CI 0.90 to 0.98) respectively. There were no significant differences in sensitivity and specificity values between MRCP and EUS. At the median pre-test probability of CBD stones of 41%, for EUS the post-test probabilities associated with positive and negative EUS test results were 0.96 (95% CI 0.92 to 0.98) and 0.03 (95% CI 0.02 to 0.06) respectively and for MRCP the post-test probabilities associated with positive and negative MRCP test results were 0.94 (95% CI 0.87 to 0.97) and 0.05 (95% CI 0.03 to 0.09). The authors reported that none of the studies were of high methodological quality. (6)

A meta-analysis included 5 prospective cohort studies assessing the diagnostic accuracy of EUS and MRCP in detecting CBD stones. The reference standards used were ERCP, IOC, or clinical follow-up of more than 3 months for negative cases. The results found that the summary sensitivity and specificity values were 0.97 and 0.90 for EUS and 0.87 and 0.92 for MRCP respectively. The overall diagnostic odds ratio of EUS was significantly higher than for MRCP (162.5 versus 79.0 respectively),

mainly due to a significantly higher sensitivity of EUS compared with MRCP; however specificity values were not significantly different between both interventions. (7)

A model based cost-utility analysis taking a UK National Health Service (NHS) perspective with a 1 year time horizon for costs/outcomes compared the cost effectiveness of initial EUS or MRCP in patients with suspected CBD stones to reduce the risk of unnecessary ERCP. The results from the model found that MRCP was less costly compared to EUS for determining which patients required ERCP (\$1,299 versus \$1,753) and less costly than patients directly undergoing ERCP (\$1,781). Cost-effectiveness measured in qualityadjusted life years (QALYs) was similar for each option: 0.998 for EUS and MRCP and 0.997 for direct ERCP. Initial MRCP was the most cost effective method yielding the highest monetary net benefit, which was not sensitive to model parameters. MRCP was described as having a "61% probability of being costeffective at \$29,000". (8)

Six observational studies assessed the diagnostic value of EUS in detecting CBD stones/sludge with ERCP undertaken in confirmed cases or high/intermediate risk patients. (9–14) The sensitivity of EUS reported in these studies ranged from 93.9% to 100%, and the specificity ranged from 79.5% to 100%.

Computed tomography (CT)

An RCT assessed the value of early abdominal non-enhanced CT in developing strategies for treating patients (n=102) with mild acute gallstone pancreatitis (AGP). All patients underwent non-enhanced CT within 48 hours of symptom onset and were randomised to receive early or delayed laparoscopic cholecystectomy. The study reported that non-enhanced CT had an accuracy of 89.2 % in detecting gallbladder stones and was 87.8% accurate in detecting CBD stones. (15)

An observational study assessed the accuracy of intravenous (IV) contrast-enhanced

multidetector CT in detecting CBD stones, in the presence and absence of positive intraduodenal contrast in patients (n=48) who underwent ERCP. Patients were divided into 2 groups based on the presence (n=17) or absence (n=31) of positive intraduodenal contrast, with independent radiologist assessment of CT results who were blinded to clinical and ERCP results. The positive intraduodenal contrast yielded a sensitivity range of 50-80%, specificity 57-71% and 59-71% accuracy compared with the group without contrast which yielded a sensitivity of 77-88%, 50-71% specificity and 71-74% accuracy. All diagnostic performance parameters (except for the positive predictive value) decreased in the positive intraduodenal contrast group, mostly affecting the negative predictive value (NPV) (71%-78% versus 50%-67%). (16)

An observational study with patients presenting with acute biliary pancreatitis (n=78) assessed the diagnostic value of MRCP in detecting CBD stones. ERCP or, when unavailable, IOC/clinical follow-up was used as the reference standard. All patients underwent MRCP and 30/78 patients had CBD stones. Sensitivity of MRCP in detecting CBD stones was significantly higher than the sensitivity of abdominal CT (93.3% versus 66.7%). The area under the receiver operating characteristic curve (AUC) of MRCP in detecting CBD stones was 0.882, which was significantly more accurate than the AUC for abdominal CT at 0.727. Out of the 38 patients who required ERCP, the dilation of the CBD did not impact the sensitivity and NPV of MRCP in detecting CBD stones, which were both 100%. (5)

Other investigative procedures

A Cochrane review included 5 studies (n=318) assessing the diagnostic accuracy of ERCP and IOC for diagnosing CBD stones (IOC is not included as a diagnostic tool in the scope of the guideline). Presence of CBD stones were confirmed by either surgical or endoscopic extraction. Absence of CBD stones were confirmed by either surgical or endoscopic

negative exploration of the CBD, or symptomfree follow-up for at least 6 months for a negative test result. The range of sensitivities of ERCP were 0.67 and 0.94, and the pooled sensitivity was 0.83 (95% CI 0.72 to 0.90). The range of specificities were 0.92 and 1.00, and the pooled specificity was 0.99 (95% CI 0.94 to 1.00). At the median pre-test probability of CBD stones of 0.35, for ERCP the post-test probabilities associated with positive test results was 0.97 (95% CI 0.88 to 0.99) and negative test results was 0.09 (95% CI 0.05 to 0.14). (17)

An observational study based on registry data on urgent cholecystectomies performed in acute cholecystitis patients assessed the diagnostic accuracy of CT and ultrasound for diagnosing acute cholecystitis. Patients were divided into 2 groups: ultrasound only (n=NR) or CT and ultrasound (n=101). CT was significantly more sensitive than ultrasound for the diagnosis of acute cholecystitis (92% versus 79%), whereas ultrasound was significantly more sensitive than CT for identification of gallstones (87% versus 60%). (18)

An observational study with patients (n=412) who underwent cholecystectomy evaluated the sensitivity of sonographic, hepatobiliary iminodiacetic acid scan (HIDA) scan and CT examination of acute cholecystitis to the pathology result. The following sensitivity values were reported: for HIDA scan: 84.2%, CT: 67.3%, and sonography: 59.8% with all differences between methods being significant. In samples with pathology results indicative of complicated acute cholecystitis, CT was significantly more sensitive than sonography in detecting acute cholecystitis (100% and 63.6% respectively) irrespective of whether complications were identified (a HIDA scan was not done). In terms of identifying complications of acute cholecystitis, CT had a sensitivity of 35.71%, whereas sonographic examination was unable to detect any of the complications. (19)

An observational study with patients (n=406) who underwent cholecystectomy for acute cholecystitis, assessed the utility of abdominal ultrasound, HIDA scan or both. One hundred and thirty two patients underwent abdominal ultrasound, 46 patients underwent HIDA scan and 228 patients had both modalities performed, with 214/406 patients having histopathological confirmed acute cholecystitis. The sensitivity values for diagnosing acute cholecystitis were for abdominal ultrasound 73.3% (95% CI 66.3% to 79.5%), HIDA 91.7% (95% CI 86.2% to 95.5%), and for abdominal ultrasound combined with HIDA for acute cholecystitis 97.7% (95% CI 93.4% to 99.5%). During abdominal ultrasound, sonographic Murphy sign, gallbladder distension, and gallbladder wall thickening were associated with a diagnosis of acute cholecystitis. (20)

Intelligence gathering

One topic expert highlighted an ongoing pragmatic RCT known as <u>The Sunflower Study</u> which will compare expectant management (no imaging) versus preoperative imaging with MRCP in patients undergoing laproscopic cholecystectomy or gallstones at low or moderate risk of CBD stones. This ongoing study will be monitored and results considered for impact on the guideline when available. Another topic expert noted that "adoption of and access to diagnostic studies, including endoscopic ultrasound, is widespread".

Regarding specific subgroups of the population, a topic expert asked whether the recommendations apply to pregnant women. No evidence on diagnosis of gallstone disease relating to this subgroup was identified.

Impact statement

A large body of evidence (21 studies consisting of 3 Cochrane reviews, 1 systematic review, 1 meta-analysis, 1 RCT, 1 cost-utility analysis and 14 observational studies) was identified on diagnosis of gallstone disease.

Liver function tests (LFTs) and ultrasound

Evidence was identified on the diagnostic accuracy of liver function tests (LFTs) and abdominal ultrasound in diagnosing gallstone disease that indicates these measures have, overall, good sensitivity and specificity for identifying gallstone disease. There was some indication that abdominal ultrasound may not be as good as other tests for picking up cases of common bile duct (CBD) stones, as reported in a Cochrane review, which highlights the potential need for additional tests. As such, the evidence supports current recommendations to initially offer LFTs and abdominal ultrasound to patients with suspected gallstone disease, but to also consider the use of other diagnostic techniques.

Endoscopic ultrasound (EUS) and MRCP/ERCP

Evidence was identified that indicated endoscopic ultrasound (EUS) and magnetic resonance cholangiopancreatography (MRCP) had high sensitivity and specificity for diagnosing CBD stones. There appears to be no significant differences between investigations in terms of sensitivity and specificity in diagnosing CBD stones as indicated by findings from a Cochrane review. Initial MRCP was found to be more cost effective compared with EUS, based on evidence from one cost-utility analysis. The new evidence supports current recommendations concerning the use of both investigations and highlights that first approach MRCP and EUS can prevent the use of endoscopic retrograde cholangiopancreatography (ERCP) as a diagnostic tool.

There was some indication that ERCP may be of value in diagnosing CBD stones and guiding further invasive treatment as indicated by findings from a Cochrane review. ERCP is currently not included under recommendations for diagnosing gallstone disease but instead under the therapeutic management of CBD stones. As such, it is not anticipated that such

evidence will impact current recommendations. (17)

Other investigative procedures

A small body of evidence (6 studies consisting of 1 RCT and 5 observational studies) was identified on the diagnostic accuracy of computed tomography (CT) and hepatobiliary iminodiacetic acid (HIDA) scans. The evidence indicates that HIDA scans have a higher sensitivity for diagnosing acute cholecystitis compared with ultrasound. There was mixed

evidence concerning the diagnostic performance for CT scans, however two observational studies noted that CT scans were more sensitive in detecting acute cholecystitis compared to ultrasound. At present, there is insufficient consistent evidence in these areas to impact on the recommendation.

New evidence is unlikely to change guideline recommendations.

1.2 Managing gallbladder stones

Recommendations in this section of the guideline

- 1.2.1 Reassure people with asymptomatic gallbladder stones found in a normal gallbladder and normal biliary tree that they do not need treatment unless they develop symptoms.
- 1.2.2 Offer laparoscopic cholecystectomy to people diagnosed with symptomatic gallbladder stones.
- 1.2.3 Offer day-case laparoscopic cholecystectomy for people having it as an elective planned procedure, unless their circumstances or clinical condition make an inpatient stay necessary.
- 1.2.4 Offer early laparoscopic cholecystectomy (to be carried out within 1 week of diagnosis) to people with acute cholecystitis.
- 1.2.5 Offer percutaneous cholecystostomy to manage gallbladder empyema when:
 - surgery is contraindicated at presentation and
 - conservative management is unsuccessful.
- 1.2.6 Reconsider laparoscopic cholecystectomy for people who have had percutaneous cholecystostomy once they are well enough for surgery.

Surveillance decision

This section of the guideline should not be updated.

2018 surveillance summary

Laparoscopic cholecystectomy (LC) versus conservative management

Two systematic reviews included 2 RCT's (n=201) investigating the clinical and cost effectiveness of cholecystectomy compared with observation/conservative management in patients with symptomatic gallstones or acute cholecystitis. Patients randomised to observation/conservative management had a significantly greater likelihood of gallstonerelated complications (RR 6.69, 95% CI 1.57 to 28.51) particularly acute cholecystitis (RR 9.55, 95% CI 1.25 to 73.27), were significantly less likely to have surgery (RR 0.50, 95% CI 0.34 to 0.73) and to have surgery-related complications (RR 0.36, 95% CI 0.16 to 0.81) compared to those patients randomised to cholecystectomy. The cost-analysis based on a Markov model, found that LC was more costly (£1,236 more per patient) and effective compared to observation/conservative management, however there was uncertainty around some of the parameters used in the economic model. A rise in the number of patients who required surgery during conservative treatment, resulted in a reduction in the cost effectiveness of the conservative management strategy. (21,22)

LC compared with LC and Intraoperative cholangiography (IOC)

A randomised trial including symptomatic patients (n=371) with suspected gallstones were randomised to either receive routine LC alone or LC and IOC. The results found no significant differences in the rates of successful LC (98.38% versus 97.85%), CBD stone retainment (0.54% versus 0.00%), CBD injury (0.54% versus 0.53%) and other complications (2.16% versus 2.15%), as well as length of hospital stay (5.10+/-1.41 days versus 4.99+/-1.53 days). The authors reported no fatal complications for either interventions. At 1 year follow-up, 1 case of diarrhoea lasting for 3 months post routine LC and 1 case of intermittent epigastric discomfort post LC and

IOC were reported, however no abnormalities were identified during radiological examination. (23)

LC compared with percutaneous cholecystostomy

A systematic review and meta-analysis included 6 studies (n=337,500) assessing the benefit of percutaneous cholecystostomy compared with LC in the management of critically ill patients with acute cholecystitis. The results, found that LC was significantly superior in terms of mortality (OR 4.28, 95% CI 1.72 to 10.62), length of hospital stay (OR 1.41, 95% CI 1.02 to 1.95) and rate of readmission for biliary complaints (OR 2.16, 95% CI 1.72 to 2.73) compared to percutaneous cholecystostomy. There were no significant differences between both interventions in terms of complications or reinterventions. (24)

Day-case LC versus inpatient LC

A systematic review that undertook a metaanalysis included 12 studies comparing the safety and feasibility of day LC compared to overnight stay LC. The results found no significant differences between both groups in terms of morbidity, prolonged hospitalisation, readmission rate, consultation rate, postoperative nausea and vomiting scale, time to return to activity and work. (25)

An RCT with data from symptomatic gallstone patients (n=65) randomised to undergo daycase LC or routine (conventional) LC procedure compared the feasibility and safety of both procedures. The results found no significant differences between both procedures in terms of complications, quality of life, satisfaction, postoperative nausea and vomiting and pain outcomes. The authors reported that 97% of day-case LC patients were successfully discharged with a lower mean duration of stay of 8.9+/-4.54 hours compared with those patients who underwent routine procedure at 3.33+/-1.45 days. (26)

Timing of interventions in the management of gallbladder disease

A systematic review of RCT's (n=NR) assessed the optimal timing for LC in acute cholecystitis patients. The review reported that there was a preference for early LC in patients with acute cholecystitis although there was a lack of consistency in defining "early". The review indicated that immediate LC within 24 hours after admission is the best approach in American Society of Anesthesiologists physical status classification system (ASA) I-III patients with acute cholecystitis patients compared to delayed LC after initial antibiotic therapy. This was in relation to morbidity, duration of hospital stay and treatment cost outcomes. The authors stated that "concerning critically ill patients suffering from acute calculous or acalculous cholecystitis, there is no consensus in treatment due to missing data in the literature". (27)

A meta-analysis included 15 RCT's comparing outcomes between early and delayed cholecystectomy for acute cholecystitis. The results found no differences in mortality, bile duct injuries, bile duct leaks, risk of conversion to open surgery between both early and delayed groups. A proportion of patients in the delayed group (9.7%) failed initial nonoperative management and underwent emergency LC, whereas early surgery patients had a significantly shorter hospital stay, lower risk of wound infections and lower mean hospital costs when compared with delayed cholecystectomy. Definitions of time periods for early and delayed LC were not provided in the abstract. (28)

A meta-analysis included 16 studies (reporting on 15 RCT's, n=1,625) comparing early laparoscopic cholecystectomy (ELC) performed within 1 week of onset of symptoms with delayed laparoscopic cholecystectomy (DLC) performed at least 1 week after symptoms had subsided for acute cholecystitis. The results found that ELC groups demonstrated significant reductions in days lost from work (MD -11.07, 95% CI -16.21 to -5.94), risk of

wound infection, and length of hospital stay (MD -3.38 days, 95% CI -4.23 to -2.52). ELC was associated with reductions in hospital costs, higher patient satisfaction and quality of life compared with DLC. No significant differences were identified in terms of mortality, bile duct injury, bile leakage, conversion to open surgery or overall complications. (29)

A meta-analysis included 9 RCT's comparing the length of hospital stay between ELC and DLC in patients following acute cholecystitis. Included patients underwent ELC (n= 617) or DLC (n=603) after acute cholecystitis and the mean hospital stay was shorter in the ELC compared with the DLC group (5.4 versus 9.1 days respectively). The results from the metaanalysis showed a significantly shorter mean hospital stay (MD 3.24, 95% CI 1.95 to 4.54) in the ELC group and the rate of major biliary duct injury was 0.8% versus 0.9% for ELC compared to the DLC group respectively. The authors reported no significant differences between both groups. Definitions of time periods for early and delayed LC were not provided in the abstract. (30)

A meta-analysis included 7 RCT's (n=1,106) assessing the safety and outcomes of ELC and DLC in the management of acute cholecystitis. The results found no significant differences in terms of bile duct injury and conversion to open surgery between both groups. The total duration of hospital stay was significantly lower for the ELC group compared with DLC (MD -4.12 days, 95% CI -5.22 to -3.03). Definitions of time periods for early and delayed LC were not provided in the abstract. (31)

An RCT with acute cholecystitis patients (n=62) were randomised to receive either ELC within 72 hours after the onset of symptoms or initial antibiotic treatment followed by DLC after 6-8 weeks. The results found ELC was associated with a lower conversion rate to open surgery, duration of hospital stay,

postoperative recovery and reduced cost of hospitalisation compared with DLC. (32)

An RCT with acute cholecystitis patients (n=86) experiencing more than 72 hours of symptoms were randomised to receive either ELC (performed following hospital admission) or DLC (at least 6 weeks post initial antibiotic treatment). The results found that median length of hospital stay was significantly lower (4 versus 7 days) in the early surgery compared to delayed surgery group. The duration of antibiotic therapy was also significantly lower in the early surgery group at 2 days compared to 10 days in the delayed surgery group. Overall morbidity (6 versus 17 patients) and total hospital costs were also significantly lower in the early surgery group whereas there were no significant differences in postoperative complications between both groups. (33)

An RCT compared either ELC within 24 hours of admission or DLC 6-8 weeks after initial conservative management in people with acute cholecystitis (n=50). The study results found that postoperative complications for ELC were 24% versus 8% for DLC and that ELC had significantly shorter length of hospital stay (4.1 days versus 8.6 days). The conversion rate to open surgery in ELC was 16% and 8% in DLC and blood loss was 159.6 mL in ELC versus 146.8 mL for DLC. The authors concluded that ELC "should be offered to the patients with acute cholecystitis, provided that the surgery is performed within 96hrs of acute symptoms by an experienced surgeon." (34)

An RCT compared either ELC (within 24 hours of admission) or DLC (after 6-8 weeks of conservative treatment) in patients (n=60) with acute cholecystitis. The results found that length of hospital stay (5.2 +/- 1.40 versus 7.8 +/- 1.65 days) and total costs (2,500.97 +/- 755.265 versus 3,713.47 +/- 517.331 Turkish Lira) were both significantly greater in the delayed compared to the early surgery groups. Intraoperative and postoperative complications were significantly greater in the early surgery

group (8 patients) compared to the delayed surgery group where no patients experienced complications. (35)

A cost-utility analysis based on a model with a 5 year time horizon to compare costs and QALYs gained from 3 treatment strategies for acute cholecystitis: early cholecystectomy (within 7 days of presentation), delayed elective cholecystectomy (8 to 12 weeks from presentation), and watchful waiting (surgery is performed urgently only if recurrent symptoms arise). The results found that early cholecystectomy was superior in terms of costs (6,905 Canadian dollars per person) compared to delayed cholecystectomy (8,511) and watchful waiting (7,274). Early cholecystectomy was also more effective in terms of QALYs gained per person at 4.20 compared to delayed surgery at 4.18 and 3.99 for watchful waiting. Uncertainty was evaluated using probability sensitivity analysis which found that early cholecystectomy was the preferred management of acute cholecystitis in 72% of model iterations, based on the cost-effectiveness threshold of 50,000 Canadian dollars per QALY. (36)

A cost-utility analysis (using data from a prospective cohort study from the UK NHS perspective) with a 1 year time horizon for costs/outcomes aimed to determine the cost effectiveness of emergency cholecystectomy (performed during surgical admission) compared to delayed cholecystectomy (performed during surgical admission) for acute gallbladder disease. The results found that emergency surgery was less expensive (£4,570 versus £4,720) and more effective (0.8868 versus 0.8662 QALYs) than delayed surgery. Probabilistic sensitivity analysis demonstrated that emergency cholecystectomy has greater than 60% likelihood of being cost-effective across willingness-to-pay values for the QALY from £0 to £100,000. (37)

An economic evaluation using data from 6 RCT's using a UK NHS perspective aimed to determine the incremental cost effectiveness of ELC compared to DLC in the treatment of acute cholecystitis. The results found that DLC was more costly with an average net present value of £4,565 compared to £3,920 for ELC, which when scaled to a population level may result in potential savings of £30,000,000 per annum for the NHS. Definitions of time periods for early and delayed LC were not provided in the abstract. (38)

An economic evaluation using records of inpatients (n=191,032) who underwent LC for acute cholecystitis assessed the impact on costs in delaying LC. The results found that approximately 65% of subjects underwent LC within 24 hours of admission with the average cost of care for LC at \$11,087 on the day of admission. Costs progressively increased by 22% on the second hospital day, 37% on day 3, 52% on day 4, 64% on day 5, 81% on day 6, and by 100% on day 7, when compared to the cost of care for LC within 24 hours. (39)

Timing of interventions in the management of gallstone-related pancreatitis

A systematic review that undertook a metaanalysis included 13 studies (n=2,291) comparing the safety of ELC and DLC in patients with mild biliary pancreatitis. The results found that rates of readmissions and complications were higher for DLC than ELC group (complication rate 13.45% versus 6.8%; significance not reported). The duration of hospital stay was shorter in ELC compared with the DLC group and no significant differences were identified in terms of conversion to open surgery between both groups. Definitions of time periods for early and delayed LC were not provided in the abstract (40)

A multicentre RCT superiority trial with hospital patients (n=266) recovering from mild gallstone pancreatitis were randomised to receive either interval cholecystectomy (discharge, followed by surgery 25-30 days after randomisation) or same-admission cholecystectomy (within 72 hours of

randomisation); the primary endpoint was a composite of readmission for recurrent gallstone-related complications or mortality within 6 months following randomisation. The primary endpoint occurred in 23/136 patients in the interval group and in 6/128 patients in the same-admission group (RR 0.28, 95% CI 0.12 to 0.66; p=0.002). Four incidences of serious surgery-related adverse events including bile duct leakage and postoperative bleeding occurred for both groups, but did not result in death. (41)

A multicentre RCT with patients (n=264) diagnosed with mild gallstone pancreatitis were randomised before discharge to receive either early cholecystectomy within 72 hours (sameadmission surgery) or delayed cholecystectomy after 25-30 days (interval surgery). The results found that same-admission surgery significantly lowered the risk of acute readmission for recurrent gallstone-related complications from 16.9% to 4.7%. Costeffectiveness analyses from a societal perspective with costs per readmission prevented as the main outcome over a time horizon of 6 months, found that mean costs were €234 (95% CI -1,249 to 738) less per patient in the same-admission group. Sameadmission was less expensive and more effective than interval surgery, with a societal incremental cost-effectiveness ratio of -€1,918 to prevent one readmission for gallstone-related complications. (42)

An RCT with patients (n=72) diagnosed with mild to moderate acute biliary pancreatitis were randomised to receive either early cholecystectomy or delayed cholecystectomy. The results found no significant differences in perioperative complications or conversion to open surgery between groups. The delayed group demonstrated a significantly greater number of recurrent biliary events (44.12% versus 0%) and significantly longer duration of hospital stay compared to the early group (9 days versus 8). Definitions of time periods for early and delayed cholecystectomy were not provided in the abstract. (43)

An RCT assessed the value of early abdominal non-enhanced CT in developing strategies for treating patients (n=102) with mild AGP. All patients underwent non-enhanced CT within 48 hours of symptom onset and were randomised to receive ELC (within 7 days after pancreatitis attack with AGP symptoms) or DLC (performed at or after 7 days following an attack, with the patient being completely free of AGP symptoms). Patients in both groups were successfully treated with no surgeryrelated complications and there were no instances of increased AGP severity postsurgery. The mean duration of hospital stay was significantly less in the early LC group compared with delayed LC group. (15)

A model based cost-utility analysis for mild AGP (from the UK NHS perspective with a 1 year time horizon for costs/outcomes) assessed the cost effectiveness of LC within 72 hours of admission (group A) or during the same-admission but after 72 hours (group B) or electively in another admission (group C). The results found that the mean costs of LC for group A was €2,748 and group B was €3,543, with QALYs per patient for both groups at 0.888, the cost and QALY values for group C were €3,752 and 0.884 respectively. ELC (within 72 hours of admission) showed a 91% probability of being cost-effective at the maximum willingness-to-pay threshold for a QALY commonly used in the UK. The authors reported that hospitals may not have access to certain interventions such as MRCP and ERCP, particularly at certain times/weekends therefore implementing a target timespan for completing LC within 72 hours may not be feasible without the assignment of further resources that would essentially diminish the cost-effectiveness. The investigators concluded "after 3 days there is little financial advantage to same-admission operation." (44)

Intelligence gathering

One topic expert highlighted an ongoing study:

<u>A randomised controlled trial comparing</u>

<u>laparoscopic cholecystectomy with</u>

observation/conservative management for preventing recurrent symptoms and complications in adults with uncomplicated symptomatic gallstones. This topic expert commented "there is evidence that patients with an episode of acute cholecystitis may not have a further attack of gallstone symptoms" and suggested that "the uncertainty on which the [ongoing] study is based on is incorporated into any NICE CG188 update". This ongoing study will be monitored and results considered for impact on the guideline when available. The topic expert also commented that the recommendation to do cholecystectomy within one week of acute cholecystitis "needs updating" based on the reference provided and that there is an increasing rate of cholecystectomies performed in the NHS and the guidance should consider how this could be lessened.

Regarding specific subgroups of the population, a topic expert asked whether the recommendations apply to pregnant women. No evidence on management of gallbladder stones relating to this subgroup was identified.

Correspondence was received based on a coroner's report. This formed the basis of a request to consider the timing of surgery following the diagnosis of gallstone pancreatitis as an additional area in this surveillance review.

Initial intelligence gathering identified NICE clinical knowledge summary (CKS) on the secondary care management of suspected acute pancreatitis (revised in May 2016) caused by suspected or proven gallstones. The CKS includes detail on the timing of cholecystectomy either during the same-admission for uncomplicated cases, or possibly delayed in severe cases until clinically appropriate. It also states that management may include ERCP within 72 hours of the onset of pain in patients with cholangitis.

NICE quality standard <u>QS104 on gallstone</u> <u>disease</u> uses the <u>Commissioning guide:</u> <u>gallstone disease</u> (2013, reviewed October 2016) from the Royal College of Surgeons

(RCOS) as an evidence source. The guide was NICE accredited from September 2012 for a period of 5 years. RCOS guidance provides secondary care management recommendations which may be applicable to the issue raised: AGP patients should undergo definitive treatment within 2 weeks of recovery from the incident episode.

This evidence is also of relevance to <u>Pancreatitis: diagnosis and management</u> NICE guideline currently in development.

Impact statement

Laparoscopic cholecystectomy (LC) versus conservative management

The new evidence indicated that conservative management resulted in poorer outcomes among patients with symptomatic gallstones or acute cholecystitis compared with LC, although LC was more costly. Overall, this evidence supports the current recommendation to offer LC in people diagnosed with symptomatic gallbladder stones.

LC compared with LC and Intraoperative cholangiography (IOC)

One identified study found no difference in outcomes between routine LC alone or LC and IOC in symptomatic patients with suspected gallstones. No impact on the guidelines is anticipated as there is uncertainty about whether the addition of IOC was beneficial or not since there were no significant differences between the groups on any of the outcomes.

LC compared with percutaneous cholecystostomy

A systematic review indicated that LC was significantly superior to percutaneous cholecystostomy in a number of outcomes including mortality and length of hospital stay. As LC is the recommended approach for managing acute cholecystitis, no impact on the guideline is expected.

Day-case LC versus inpatient LC

New evidence comparing day-case with inpatient LC found no significant differences in outcomes including morbidity and complications. However, as none of the studies reported on costs, which was an important consideration in developing the recommendation on day-case LC, it would be pertinent to wait for further evidence before considering this area for update.

Timing of interventions in the management of gallbladder disease

A large body of evidence (13 studies consisting of 1 systematic reviews, 4 meta-analyses, 2 cost-utility analyses, 2 economic evaluation studies and 4 RCT's) was identified regarding the timing of LC in acute cholecystitis. Overall the evidence supports the use of early LC over delayed LC, which is in line with current recommendations to offer early laparoscopic cholecystectomy (to be carried out within 1 week of diagnosis) to people with acute cholecystitis. We will request that Cochrane consider undertaking a review to evaluate the evidence on the timing of surgery in acute cholecystitis and consider any impact on the guideline when results are available.

Timing of interventions in the management of gallstone-related pancreatitis disease

The management of gallstone-related pancreatitis is not within the scope of NICE guideline CG188. However, correspondence was received based on a coroner's report. This formed the basis of a request to consider the timing of surgery following the diagnosis of gallstone pancreatitis as an additional area in this surveillance review.

Six studies (1 systematic review, 4 RCT's, 1 cost-utility analysis) were identified that assessed the optimal timing of cholecystectomy in gallstone pancreatitis patients. Several studies noted the benefits of early surgery on a range of outcomes, however the timing of early surgery differed, including 7

days after onset of symptoms, within 3 days following admission (same-admission), whilst other studies did not specify.

An optimal timing for surgical treatment of gallstone pancreatitis following diagnosis/onset of symptoms was not demonstrated in the evidence identified through surveillance. At present, it would therefore not be feasible to define operation intervals, however the evidence indicates that

performing early surgery within the sameadmission is good for patient outcomes and reduces costs. We will request that Cochrane consider undertaking a review to evaluate the evidence on the timing of surgery in gallstonerelated pancreatitis and consider any impact on the guideline when results are available.

New evidence is unlikely to change guideline recommendations.

1.3 Managing common bile duct stones

Recommendations in this section of the guideline

- 1.3.1 Offer bile duct clearance and laparoscopic cholecystectomy to people with symptomatic or asymptomatic common bile duct stones.
- 1.3.2 Clear the bile duct:
 - surgically at the time of laparoscopic cholecystectomy or
 - with endoscopic retrograde cholangiopancreatography (ERCP) before or at the time of laparoscopic cholecystectomy.
- 1.3.3 If the bile duct cannot be cleared with ERCP, use biliary stenting to achieve biliary drainage only as a temporary measure until definitive endoscopic or surgical clearance.
- 1.3.4 Use the lowest-cost option suitable for the clinical situation when choosing between day-case and inpatient procedures for elective ERCP.

Surveillance decision

This section of the guideline should not be updated.

2018 surveillance summary

Managing common bile duct stones

Pre/post/intra operative ERCP +LC compared with bile duct exploration + LC

A systematic review included 4 studies comparing single-stage surgical management (involving LC with CBD exploration) versus two-stage surgical management (involving LC with pre/postoperative ERCP) in patients with

symptomatic gallstones and concomitant CBD stones. The review included 1 meta-analysis which reported no significant differences in the effectiveness or frequency of complications between management strategies (details of complications recorded not provided in abstract). Three smaller studies also concurred with these findings, however each study found that single-stage management was more cost-effective. (45)

A systematic review that undertook a metaanalysis included 11 studies (n=1,513) comparing single-stage laparoscopic common bile duct exploration (LCBDE) and cholecystectomy with two-stage preoperative endoscopic stone extraction followed by cholecystectomy (ERCP and LC). The results found that LCBDE was associated with a significantly lower rate of technical failure and shorter hospital stay compared with ERCP and LC. There were no significant differences between groups in terms of mortality, morbidity, treatment cost or recurrent/retained stones. (46)

A meta-analysis included 8 RCT's (n=1,130) assessing single-stage (LC and LCBDE) versus two-stage management (preoperative ERCP and LC) in patients with gallstones and concomitant CBD stones. The results found the rate of CBD stone clearance was significantly higher and duration of hospital stay was significantly shorter in the single-stage group compared with the two-stage group. There were no significant differences between management strategies in terms of postoperative morbidity, mortality, and conversion to other procedures. (47)

An RCT with patients (n=104) with CBD stones undergoing emergency laparoscopic cholecystectomy were randomised to either intraoperative ERCP or LCBDE. The results found that clearance rates for intraoperative ERCP was higher at 87% compared to LCBDE at 69%, although this was not significant. The rate of retained stones was significantly less in ERCP patients at 15% compared to 42% in LCBDE and median postoperative length of stay was significantly shorter in ERCP patients at 2 days compared to 3 days for LCBDE patients. (48)

An RCT in people with concomitant gallbladder and CBD stones (n= 168) were randomised to either single-stage LCBDE and LC or two-stage ERCP followed by LC. The results found the success rate of CBD clearance for LCBDE was 91.7% and ERCP was 88.1%. There were no

significant differences between overall success rate for both groups (88.1% in single-stage group and 79.8% in two-stage group). Direct choledochotomy was performed in 83 patients. The overall duration of hospital stay was significantly less in the single-stage group compared with the two-stage group (4.6 +/-2.4 versus 5.3 +/- 6.2 days respectively). The two-stage group had a significantly greater number of procedures per patient and higher cost. There were no significant differences between both management strategies regarding postoperative wound infection rates or major complications. (49)

An RCT in patients (n=221) with gallstones and concomitant CBD stones compared single-stage LC and LCBDE (within the same operation) or two-stage preoperative endoscopic CBD clearance followed by LC 2-5 days later. The results found no significant differences in the rates of successful CBD clearance or complications between both management strategies. During longer term follow-up (time not specified), reoccurrence of CBD stones were significantly more frequent in the two-stage group (9.5%) compared with the single-stage group (2.1%). (50)

Timing of interventions in the management of CBD stones

A systematic review included 14 studies (n=1,930) evaluating the optimal time interval between ERCP and LC in the management of CBD stones. The pooled estimate for conversion to open surgery increased from 4.2% when LC occurred within 24 hours of ERCP to 7.6% when delayed LC occurred (24-72 hours) post ERCP, to 12.3% when delayed LC either occurred within 2 weeks or between 2-6 weeks and 14% when LC occurred after 6 weeks (significance not reported). (51)

An RCT in patients with concomitant gallbladder and CBD stones (n=NR) compared ELC versus DLC following ERCP. Patients were randomised to receive either ELC within 72 hours after ERCP or DLC 1 month after ERCP. The results found no significant differences in

terms of conversion rate to open surgery, degree of adhesion, cystic duct diameter, and intraoperative CBD injury or bleeding between both groups, whereas recurrent biliary symptoms were significantly higher in the DLC group compared to ELC group (7 versus 1 patient respectively). (52)

Intelligence gathering

NICE has produced a medtech innovation briefing; The SpyGlass direct visualisation system for diagnostic and therapeutic procedures during endoscopy of the biliary system (February 2015) MIB21. The SpyGlass system is used for diagnostic and therapeutic management of large stones of the biliary system when standard ERCP is unsuccessful or considered inappropriate.

One topic expert felt there should be a "recommendation allowing for postoperative ERCP". No evidence supporting the use of postoperative ERCP was identified.

Regarding specific subgroups of the population, a topic expert asked whether the recommendations apply to pregnant women. No evidence on management of common bile duct stones relating to this subgroup was identified.

Impact statement

Pre/post/intra operative ERCP +LC compared with bile duct exploration + LC

Evidence was identified (6 studies consisting of 2 systematic reviews, 1 meta-analysis, 3 RCT's) on single-stage laparoscopic common bile duct exploration (LCBDE) and laparoscopic cholecystectomy (LC) compared with two-

stage endoscopic retrograde cholangiopancreatography (ERCP) for endoscopic extraction of common bile duct (CBD) stones followed by surgery. The evidence indicated that single-stage management is superior compared to the two-stage management of CBD stones in terms of duration of hospital stay and cost. Several studies noted no significant differences between both strategies in terms of morbidity, mortality, overall success rate and complications. As such, it is not anticipated that this new evidence will impact current recommendations to offer both treatments for clearing the bile duct.

Timing of interventions in the management of CBD stones

Two studies (1 systematic review, 1 RCT) were identified that assessed the timing of interventions used in the management of CBD stones. Both studies reported different time intervals for early LC either within 24 or 72 hours of ERCP. There was mixed evidence on the benefit of early LC in reducing the conversion rate to open surgery compared with delayed LC. Early surgery may be associated with a reduction in recurrent biliary symptoms, based on the findings of one study. However, at present the evidence base is too small to recommend this as an area for update. We will request that Cochrane consider undertaking a review to evaluate the evidence on the timing of surgery in the management of CBD stones and consider any impact on the guideline when results are available.

New evidence is unlikely to change guideline recommendations.

1.4 Patient, family member and carer information

Recommendations in this section of the guideline

- 1.4.1 Advise people to avoid food and drink that triggers their symptoms until they have their gallbladder or gallstones removed.
- 1.4.2 Advise people that they should not need to avoid food and drink that triggered their symptoms after they have their gallbladder or gallstones removed.
- 1.4.3 Advise people to seek further advice from their GP if eating or drinking triggers existing symptoms or causes new symptoms to develop after they have recovered from having their gallbladder or gallstones removed.

Surveillance decision

This section of the guideline should not be updated.

2018 surveillance summary

Patient, family member and carer information

A Cochrane review included 4 RCT's (n=431) comparing the benefits and harms of formal preoperative patient education for patients undergoing LC. Patients were either randomised to receive formal patient education (included verbal education, multimedia DVD programme, computer-based multimedia program, and a Power Point presentation) or standard care. There was no clear evidence of effect on patient satisfaction, knowledge or anxiety between both groups.(53)

A qualitative study with a phenomenological approach involved patients (n=NR) diagnosed with acute cholecystitis and who underwent cholecystectomy to gain further insight into the experience of hospitalised patients. Face to face interviews were conducted prior to scheduled surgery. Interviews were also completed post-surgery in patients who experienced an uneventful cholecystectomy. There were 5 themes: "(a) consumed by discomfort and pain, (b) restless discomfort

interrupting sleep, (c) living in uncertainty, (d) impatience to return to normalcy, and (e) feelings of vulnerability". Patients described distressing pain both before and after cholecystectomy which affected daily activities including sleep and family responsibilities. The authors concluded that "increased awareness is needed to prevent the disruption to daily life that can result from the cholecystitis and resulting cholecystectomy surgery. Also, nurses can help ease the unpredictability of the experience by providing relevant patient education, prompt pain relief, and an attentive approach to the nursing care". (54)

Intelligence gathering

Regarding specific subgroups of the population, a topic expert asked whether the recommendations apply to pregnant women. No evidence for this group was identified.

Impact statement

Limited evidence was identified on the information and education needs of patients and carers of people with gallstone disease and the type of information people would find useful. Although one study indicated increased

awareness of gallstones and cholecystectomy is important.

The current recommendations focus on dietary advice prior and post removal of gallstones and no evidence was identified through the

surveillance review to indicate those recommendations would be impacted.

New evidence is unlikely to change guideline recommendations.

Research recommendations

2.1 Diagnosing gallstone disease

What are the long-term benefits and harms, and cost effectiveness of endoscopic ultrasound (EUS) compared with magnetic resonance cholangiopancreatography (MRCP) in adults with suspected common bile duct stones?

Summary of findings

One study relevant to the research recommendation was found (see Endoscopic ultrasound (EUS) and MRCP/ERCP).

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

2.2 Managing gallbladder stones

What are the benefits and harms, and cost effectiveness of routine intraoperative cholangiography in people with low to intermediate risk of common bile duct stones?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

2.3 Managing common bile duct stones

What models of service delivery enable intraoperative endoscopic retrograde cholangiopancreatography (ERCP) for bile duct clearance to be delivered within the NHS? What are the costs and benefits of different models of service delivery?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

2.4 Timing of laparoscopic cholecystectomy

In adults with common bile duct stones, should laparoscopic cholecystectomy be performed early (within 2 weeks of bile duct clearance), or should it be delayed (until 6 weeks after bile duct clearance)?

Summary of findings

One study was identified relevant to this research recommendation (see <u>Timing of interventions in the management of CBD stones</u>).

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

2.5 Information for patients and carers

What is the long-term effect of laparoscopic cholecystectomy on outcomes that are important to patients?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

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