

# Cystic Fibrosis: diagnosis and management

## Appendices D and E

*Main appendix document*

*Review protocols and combined search strategies*

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Gynaecologist*



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# Appendices

## Appendix D: Review protocols

### D.1 Diagnosis of cystic fibrosis

Item	Details
Key issue in the scope	The clinical manifestations of cystic fibrosis at the time of diagnosis in infants, children, young people and adults.
Review question in the scope	What are the clinical manifestations of cystic fibrosis at the time of diagnosis in infants, children, young people and adults?
Review question for the protocol	In infants, children, young people and adults (including those that have undergone newborn screening) when should cystic fibrosis be suspected?  Most children will undergo newborn screening in the UK, and most cases of CF will be picked up that way. However, for those where that did not happen it would be useful for the guideline to raise awareness to HCPs to cases where new born screening was not undertaken and where CF should be suspected.
Objective	The aim of this review was to support health care professionals in identifying cystic fibrosis even in people who have been through new-born screening.
Population and directness	Infants, children, young people and adults with suspected symptoms of CF, including those who have been through newborn screening: <ul style="list-style-type: none"> <li>• Respiratory symptoms (including recurrent pneumonia, chest x-ray evidence of chronic disease)</li> <li>• Failure to thrive</li> <li>• Symptoms of malabsorption</li> <li>• Male infertility</li> </ul> <p>Population size and directness:</p> <ul style="list-style-type: none"> <li>• No minimum sample size.</li> <li>• Indirect populations will not be considered.</li> </ul>
Subgroups and sensitivity analyses	The following groups will be assessed separately if possible: <ul style="list-style-type: none"> <li>• Infants</li> <li>• Children</li> <li>• Young people and adults</li> </ul> <p>In the presence of heterogeneity, sensitivity analysis will conducted including and excluding studies with a high risk of bias.</p>
Clinical signs and symptoms	The following clinical manifestations: <ul style="list-style-type: none"> <li>• Respiratory symptoms (including recurrent infection, chest x-ray evidence of chronic disease)</li> <li>• Faltering growth</li> <li>• Symptoms of malabsorption</li> <li>• Azoospermia</li> <li>• Acute pancreatitis</li> <li>• Meconium ileus</li> </ul> <p>Note: DIOS not included in the list, as confirmed DIOS is synonym of CF.</p>
Reference standard	<ul style="list-style-type: none"> <li>• Sweat test and genetic test for confirmation of CF</li> <li>• Faecal elastase</li> </ul>

Item	Details
Outcomes	<ul style="list-style-type: none"> <li>• Sensitivity</li> <li>• Specificity</li> <li>• Positive predictive value</li> <li>• Negative predictive values</li> <li>• Positive likelihood ratios</li> <li>• Negative likelihood ratios]</li> </ul> <p>If thresholds are established/pre-defined:</p> <ul style="list-style-type: none"> <li>• Relative risk (RR) or odds ratio (OR) (and ultimately risk difference) for patient outcomes listed above for those in higher or lower risk groups</li> </ul> <p>The expected effect of the classification strategies on clinical outcomes will be extracted if this information is reported.</p>
Importance of outcomes	<p>Critical outcomes:</p> <ul style="list-style-type: none"> <li>• Clinical diagnosis of CF</li> </ul>
Study design	<ul style="list-style-type: none"> <li>• Prospective cohort studies</li> <li>• Retrospective studies</li> </ul>
Setting	Any healthcare setting where NHS care is delivered (primary, secondary, tertiary or community).
Search strategy	<p>Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase.</p> <p>Limits (e.g. date, study design): Apply standard exclusions and English language filters.</p> <p>Supplementary search techniques: No supplementary search techniques were used.</p> <p>See appendix E.1 for full strategies</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>• The methodological quality of each study will be assessed using an appropriate checklist as per NICE guidelines manual (QUADAS-2 for diagnostic studies)</li> <li>• The quality of the evidence will be assessed by GRADE for each outcome according to the process described in the NICE guidelines manual (2014).</li> </ul> <p>Synthesis of data:</p> <ul style="list-style-type: none"> <li>• Meta-analysis will be conducted where appropriate.</li> <li>• If studies only report p-values from parametric analyses, and 95% CIs cannot be calculated from other data provided, this information will be plotted in GRADE tables, but evidence may be downgraded.</li> <li>• If studies only report p-values from non-parametric analyses, this information will be plotted in GRADE tables without downgrading the evidence, as imprecision cannot be assessed for non-parametric analyses.</li> <li>• For prognostic studies, multivariate analysis will be used.</li> </ul> <p>Review process:</p> <ul style="list-style-type: none"> <li>• A list of excluded studies will be provided following weeding.</li> <li>• Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>• Psychological and behavioural issues are more likely in people with a lower socioeconomic status</li> <li>• Gender- outcomes are worse for women although there is no evidence that</li> </ul>

Item	Details
	<p>this is a consequence of difference in care</p> <ul style="list-style-type: none"> <li>• Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	Only tools that are externally validated will be assessed

## D.2 Information and support

Item	Details
Key issue in the scope	Provision of information and support for infants, children, young people and adults, and their carers.
Review question in the scope	What information and support should be offered to people with cystic fibrosis?
Review question for the review	What information and support should be given to children, young people and adults with cystic fibrosis?
Objectives	To identify the information and support that should be provided to people with cystic fibrosis and their parents and carers.
Language	English
Study design	<p>Study designs to be considered:</p> <ul style="list-style-type: none"> <li>• Qualitative studies (for example, interviews, focus groups, observations)</li> <li>• Surveys (which include qualitative data)</li> </ul> <p>Excluded:</p> <ul style="list-style-type: none"> <li>• Purely quantitative studies (including surveys with only descriptive quantitative data)</li> </ul>
Population and directness	<p>Children, young people and adults with cystic fibrosis and their parents and carers.</p> <p>Population size and indirectness:</p> <ul style="list-style-type: none"> <li>• No sample size specification.</li> <li>• Studies with indirect population will not be considered (however we will include studies with mixed population if quotes are reported separately).</li> </ul>
Stratified and subgroup analyses	<p>Age ranges:</p> <ul style="list-style-type: none"> <li>• Children: up to 12 years</li> <li>• Young people: 12 to 18 years</li> <li>• Adults: 18 and above years</li> </ul>
Context and likely themes	<p>Context: Information content and type of support with regards to cystic fibrosis.</p> <p>Themes will be identified from the literature, but expected themes are:</p> <ul style="list-style-type: none"> <li>• Psychosocial support <ul style="list-style-type: none"> <li>○ Trained staff to provide counselling and support on the social and psychosocial issues of life limiting illness and mortality.</li> <li>○ Provision of communication and dissemination of information to families of people with CF.</li> <li>○ Input of psychologists, social workers, nutritionists</li> <li>○ Timing of when support is given (for example, diagnosis, transition).</li> <li>○ Regular formal assessments tailored to needs (for example, managing pain, when condition is directly impacting on mood, general health and wellbeing).</li> <li>○ Family centred care.</li> <li>○ Support groups/programmes and frequency of meetings.</li> <li>○ Support at home (for example, outreach services).</li> </ul> </li> </ul>

Item	Details
	<ul style="list-style-type: none"> <li>○ Support at school (nursing staff, teacher).</li> <li>● Patient/carer information:               <ul style="list-style-type: none"> <li>○ Information about named individual for point of contact.</li> <li>○ Information at the time of diagnosis.</li> <li>○ Clear and accurate information about cystic fibrosis (different formats such as written, video, online, audio, languages, age, gender, culture and stage of life of person).</li> <li>○ Social media, apps and technology.</li> <li>○ Discussion about planning management of cystic fibrosis.</li> <li>○ Checklists to remind children, young people, healthcare professionals and parents/carers about information that should be discussed during consultations.</li> <li>○ Information for access to resources for managing co-morbidities.</li> <li>○ Information on pregnancy and fertility.</li> <li>○ Education and healthcare at school.</li> <li>○ Lifestyle, leisure and social issues (for example sleep deprivation).</li> <li>○ Social security benefits and social services.</li> <li>○ Information about organisations.</li> <li>○ Support groups and charitable organisations and how to contact them.</li> </ul> </li> </ul>
Setting	Healthcare (community, primary, secondary care) ideally in UK setting, but evidence from other countries will be considered if there is insufficient direct evidence.
Search strategy	<p>Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase, PsycINFO, CINAHL, AMED, HMIC</p> <p>Limits (e.g. date, study design): Apply standard exclusions and English language filters.</p> <p>Supplementary search techniques: No supplementary search techniques will be used.</p> <p>See appendix E.2 for full strategies.</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>● The methodological quality of each study will be assessed using a qualitative study quality checklists as set out in the Developing NICE Guidelines Manual 2014 (CASP checklist for qualitative studies).</li> <li>● The quality of the evidence will be assessed by a modified GRADE approach (GRADE-CERQual) for each theme.</li> </ul> <p>Data synthesis:</p> <ul style="list-style-type: none"> <li>● Thematic analysis of the data will be conducted and findings presented.</li> </ul> <p>Review process:</p> <ul style="list-style-type: none"> <li>● A list of excluded studies will be provided following weeding.</li> <li>● Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>● Psychological and behavioural issues are more likely in people with a lower socioeconomic status</li> <li>● Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care</li> <li>● Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional	Refer to CF trust

Item	Details
information	

### D.3 Service configuration

Item	Details
Key issue in the scope	Models for delivery of care and multidisciplinary teams.
Review question in the scope	What is the most effective model for delivery of care for people with CF (including multidisciplinary teams of various compositions, shared care, centre care, community care, home care and telemedicine)?
Review question for the protocol	What is the effectiveness of different models of care (for example, specialist centre, shared care [delivered by a Network CF Clinic which is part of an agreed designated network with a Specialist CF Centre], community, telehealth and/or home care for people with CF? [This issue in the scope has been divided into 2 review questions. See protocol D.4 for multidisciplinary teams]
Objective	CF is a multi-system chronic disease that affects the respiratory tract and lungs, digestive system, sweat glands and reproductive organs. The condition is typically identified in infancy and care is required throughout an individual's lifetime through to end of life. The care aims to address the biological and psychosocial needs of the patient and their families/carers and, in the UK, is primarily provided by a specialist CF Centre. As CF is associated with poor quality of life and clinical outcomes, it is important that care adequately addresses the needs of patients by allowing flexibility for individual circumstances.
Language	English
Study design	<ul style="list-style-type: none"> <li>• SR</li> <li>• RCTs</li> <li>• Conference abstracts of RCTs (only if RCTs unavailable)</li> <li>• Comparative prospective and retrospective cohort studies</li> <li>• Registry and audit data (UK only, if no other information available)</li> </ul>
Population and directness	<p>Infants, children, young people and adults with CF, diagnosed clinically and by sweat test or genetic testing.</p> <p>No minimum sample size.</p> <p>Population size and indirectness:</p> <ul style="list-style-type: none"> <li>• No sample size specification.</li> <li>• Studies with indirect populations will not be included</li> <li>• To include RCTs and observational studies from Western countries.</li> </ul>
Stratified, subgroup and adjusted analyses	<p>The following groups will be assessed separately if possible:</p> <ul style="list-style-type: none"> <li>• Children</li> <li>• Adults</li> </ul> <p>Sensitivity analysis: Sensitivity analysis: including and excluding studies with a high risk of bias</p>
Intervention	<ul style="list-style-type: none"> <li>• Specialist centre</li> <li>• Telemedicine</li> <li>• Shared care (network cf clinic)</li> <li>• Home care (e.g. Hospital at home)</li> <li>• Outreach care</li> <li>• Community care (primary care health care professionals, i.e. Gp)</li> <li>• Any combination of the models above</li> </ul>

Item	Details
	See notes section for details on each of the below.
Comparison	<ul style="list-style-type: none"> <li>• Specialist centre</li> <li>• Shared care (network of clinic)</li> <li>• Community care</li> <li>• Telemedicine</li> <li>• Home care</li> <li>• Outreach care</li> <li>• Any combination of the models above</li> <li>• Usual care</li> </ul>
Outcomes	<ul style="list-style-type: none"> <li>• Lung function: FEV1</li> <li>• LCI</li> <li>• Time to next pulmonary exacerbation</li> <li>• Mortality</li> <li>• Nutritional status (eg BMI, Height, weight, SDS)</li> <li>• Quality of life (CF-QOL, CFQR)</li> <li>• Patient and carer satisfaction</li> <li>• Frequency of cross-infections (pseudomonas, b.cepacia)</li> <li>• Staff experience</li> <li>• Adherence to treatment</li> </ul> <p>Note: change from baseline will be prioritised over absolute values</p>
Importance of outcomes	<p>Critical outcomes for decision making:</p> <ul style="list-style-type: none"> <li>• FEV1</li> <li>• Mortality</li> <li>• Patient satisfaction</li> </ul>
Setting	All settings in which NHS-commissioned health and social care is provided.
Search strategy	<p>Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase, CINAHL</p> <p>Limits (e.g. date, study design): All study designs. Apply standard exclusions and English language filters.</p> <p>Supplementary search techniques: No supplementary search techniques will be used.</p> <p>See appendix E.3.1 for full strategies</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>• The methodological quality of each study will be assessed using an appropriate checklist as per NICE guidelines manual and the service guidance methods guide 2014 (The Cochrane Risk of Bias tool for RCTs and the Newcastle and Ottawa scale for observational studies).</li> <li>• The quality of the evidence will be assessed by GRADE for each outcome according to the process described in the NICE guidelines manual (2014).</li> </ul> <p>Synthesis of data:</p> <ul style="list-style-type: none"> <li>• Meta-analysis will be conducted where appropriate.</li> <li>• If comparative cohort studies are included, the minimum number of events per covariate to be recorded to ensure accurate multivariate analysis.</li> <li>• Final and change scores will be pooled and if any study reports both, change scores will be used in preference over final scores.</li> <li>• If studies only report p-values from parametric analyses, and 95% CIs cannot be calculated from other data provided, this information will be plotted in</li> </ul>

Item	Details
	<p>GRADE tables, but evidence may be downgraded.</p> <ul style="list-style-type: none"> <li>If studies only report p-values from non-parametric analyses, this information will be plotted in GRADE tables without downgrading the evidence, as imprecision cannot be assessed for non-parametric analyses</li> </ul> <p>MIDs:</p> <ul style="list-style-type: none"> <li>FEV1: 5 percentage points</li> <li>LCI: GRADE default</li> <li>Time to next pulmonary exacerbation: any change will be considered clinically significant</li> <li>Mortality: any change will be considered clinically significant</li> <li>Nutritional status (BMI, Height, weight, SDS): GRADE default</li> <li>Quality of life: CF-QOL = 5; CFQ-R = 8.5</li> <li>Patient and carer satisfaction: GRADE default</li> <li>Frequency of cross-infections (pseudomonas, B. cepacia): GRADE default</li> <li>Staff experience: GRADE default</li> <li>Adherence to treatment: GRADE default</li> </ul> <p>Default MIDs: 0.8 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes.</p> <p>Review process:</p> <ul style="list-style-type: none"> <li>A list of excluded studies will be provided following weeding.</li> <li>Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>Psychological and behavioural issues are more likely in people with a lower socioeconomic status</li> <li>Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care</li> <li>Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	<p>2012, Telehealth in cystic fibrosis: a systematic review (adults and children services) <a href="http://www.ncbi.nlm.nih.gov/pubmed/22198961">www.ncbi.nlm.nih.gov/pubmed/22198961</a></p> <p>Full, shared and hybrid paediatric care for cystic fibrosis in South and Mid Wales – be mindful of responses to this article: <a href="http://www.ncbi.nlm.nih.gov/pubmed/21317431">www.ncbi.nlm.nih.gov/pubmed/21317431</a></p> <p>Specialist centre:</p> <ul style="list-style-type: none"> <li>Normally with &gt;100 patients and minimum of &gt;50 patients</li> <li>Commissioned by NHS England to provide care for people with CF</li> <li>Will have the core MDT available</li> </ul> <p>Shared care/network care:</p> <ul style="list-style-type: none"> <li>Local hospital looking after a small number of people with CF</li> <li>Has input from a specialist centre at least twice a year</li> <li>May not have the core MDT and may not be full time.</li> </ul> <p>Community care:</p> <ul style="list-style-type: none"> <li>Community nurses of the region who look after people with CF and will administer treatments such as home IV antibiotics</li> <li>Normally delivered by health visitors and school nurses.</li> <li>Might include palliative services</li> </ul>

Item	Details
	<p>Home care:</p> <ul style="list-style-type: none"> <li>• Care that would normally be given at hospital which is given at home</li> <li>• Delivered by CF specialist (e.g. nurse, dietician, physiotherapist)</li> </ul> <p>Outreach:</p> <ul style="list-style-type: none"> <li>• Specialist team conduct a clinic in a local hospital</li> </ul> <p>Telemedicine:</p> <ul style="list-style-type: none"> <li>• Involves skypeing with patients and remote monitoring</li> <li>• More frequent in Scotland</li> </ul>

## D.4 Multidisciplinary teams

Item	Details
Key issue in the scope	Models for delivery of care and multidisciplinary teams.
Review question in the scope	What is the most effective model for delivery of care for people with CF (including multidisciplinary teams of various compositions, shared care, centre care, community care, home care and telemedicine)?
Review question for the protocol	What is the clinical and cost-effectiveness of multidisciplinary teams of various compositions? [This issue in the scope has been divided into 2 review questions. See protocol D.3 for service configuration]
Objective	CF is a multi-system chronic disease that affects the respiratory tract and lungs, digestive system, sweat glands and reproductive organs. The condition is typically identified in infancy and care is required throughout an individual's lifetime through to end of life. The care aims to address the biological and psychosocial needs of the patient and their families/carers and, in the UK, is primarily provided by a specialist CF Centre. As CF is associated with poor quality of life and clinical outcomes, it is important that care adequately addresses the needs of patients by allowing flexibility for individual circumstances.
Language	English
Study design	<ul style="list-style-type: none"> <li>• SRs</li> <li>• RCTs</li> <li>• Comparative prospective and retrospective cohort studies</li> <li>• Registry and audit data (UK only)</li> <li>• Conference abstracts of RCTs (Only if RCTs unavailable and the quality assessment of abstracts will be conducted based on the available information and if necessary the authors of abstracts will be contacted).</li> </ul>
Population and directness	<p>Infants, children, young people and adults with CF, diagnosed clinically and by sweat test or genetic testing.</p> <p>Population size and indirectness:</p> <ul style="list-style-type: none"> <li>• No sample size specification.</li> <li>• Studies with indirect populations will not be included</li> <li>• To include RCTs and observational studies from Western countries.</li> </ul>
Stratified, subgroup and adjusted analyses	<p>The following groups will be assessed separately if possible:</p> <ul style="list-style-type: none"> <li>• Children</li> <li>• Adults</li> </ul>

Item	Details
	<p>Sensitivity analysis:</p> <ul style="list-style-type: none"> <li>• Sensitivity analysis: including and excluding studies with a high risk of bias</li> </ul>
Intervention	<p>Studies which include any combination of the individual working together working as a MDT listed below either as a core or extended MDT.</p> <p>Core MDT</p> <ul style="list-style-type: none"> <li>• Specialist CF Clinician</li> <li>• Specialist nurse</li> <li>• Specialist dietician</li> <li>• Specialist physiotherapist</li> <li>• Specialist pharmacist</li> <li>• Specialist Psychologist</li> <li>• Specialist Social worker</li> </ul> <p>Extended MDT</p> <ul style="list-style-type: none"> <li>• Diabetologist</li> <li>• Obstetrician</li> <li>• ENT surgeon</li> <li>• General surgeon</li> <li>• Gastroenterologist/hepatologist</li> </ul>
Comparison	<ul style="list-style-type: none"> <li>• Any combination of the individuals working together working as a MDT listed above.</li> </ul>
Outcomes	<ul style="list-style-type: none"> <li>• Lung function: FEV1</li> <li>• LCI</li> <li>• Time to next pulmonary exacerbation</li> <li>• Mortality</li> <li>• Nutritional status (BMI, Height , weight, SDS)</li> <li>• Quality of life (CF-QOL, CFQR)</li> <li>• Patient and carer satisfaction</li> <li>• Frequency of cross-infections (pseudomonas, B..Cepacia)</li> <li>• Staff experience</li> <li>• Adherence to treatment</li> </ul> <p>Note: change from baseline will be prioritised over absolute values</p>
Importance of outcomes	<p>Critical outcomes for decision making:</p> <ul style="list-style-type: none"> <li>• Mortality</li> <li>• Lung function: FEV1</li> <li>• Patient satisfaction</li> </ul>
Setting	<p>Any healthcare setting where NHS care is delivered (primary, secondary, tertiary or community).</p>
Search strategy	<p>Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase, CINAHL</p> <p>Limits (e.g. date, study design): All study designs. Apply standard exclusions and English language filters.</p> <p>Supplementary search techniques: No supplementary search techniques will be used.</p> <p>See appendix E.3.2 for full strategies</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>• The methodological quality of each study will be assessed using an appropriate checklist as per NICE guidelines manual and the service guidance</li> </ul>

Item	Details
	<p>methods guide 2014 (The Cochrane Risk of Bias tool for RCTs and the Newcastle and Ottawa scale for observational studies).</p> <ul style="list-style-type: none"> <li>The quality of the evidence will be assessed by GRADE for each outcome according to the process described in the NICE guidelines manual (2014).</li> </ul> <p>Synthesis of data:</p> <ul style="list-style-type: none"> <li>Meta-analysis will be conducted where appropriate.</li> <li>If comparative cohort studies are included, the minimum number of events per covariate to be recorded to ensure accurate multivariate analysis.</li> <li>Final and change scores will be pooled and if any study reports both, change scores will be used in preference over final scores.</li> <li>If studies only report p-values from parametric analyses, and 95% CIs cannot be calculated from other data provided, this information will be plotted in GRADE tables, but evidence may be downgraded.</li> <li>If studies only report p-values from non-parametric analyses, this information will be plotted in GRADE tables without downgrading the evidence, as imprecision cannot be assessed for non-parametric analyses</li> </ul> <p>MIDs:</p> <ul style="list-style-type: none"> <li>FEV1: 5 percentage points</li> <li>LCI: GRADE default</li> <li>Time to next pulmonary exacerbation: any change will be considered clinically significant</li> <li>Mortality: any change will be considered clinically significant</li> <li>Nutritional status (BMI, Height , weight, SDS): GRADE default</li> <li>Quality of life: CF-QOL = 5; CFQ-R = 8.5</li> <li>Patient and carer satisfaction: GRADE default</li> <li>Frequency of cross-infections (pseudomonas, B. Cepacia): GRADE default</li> <li>Staff experience: GRADE default</li> <li>Adherence to treatment: GRADE default</li> </ul> <p>Default MIDs: 0.8 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes.</p> <p>Review process:</p> <ul style="list-style-type: none"> <li>A list of excluded studies will be provided following weeding.</li> <li>Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>Psychological and behavioural issues are more likely in people with a lower socioeconomic status</li> <li>Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care</li> <li>Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	<ul style="list-style-type: none"> <li>2012, Telehealth in cystic fibrosis: a systematic review (adults and children services) <a href="http://www.ncbi.nlm.nih.gov/pubmed/22198961">www.ncbi.nlm.nih.gov/pubmed/22198961</a></li> <li>Full, shared and hybrid paediatric care for cystic fibrosis in South and Mid Wales – be mindful of responses to this article: <a href="http://www.ncbi.nlm.nih.gov/pubmed/21317431">www.ncbi.nlm.nih.gov/pubmed/21317431</a></li> <li>Service guidance methods guide 2014 <a href="https://www.nice.org.uk/article/pmg8/chapter/1%20introduction">https://www.nice.org.uk/article/pmg8/chapter/1%20introduction</a></li> </ul>

## D.5 Transition from paediatric to adult services

Item	Details
Key issue in the scope	-
Review question in the scope	What parts of the transition from children's to adult services are most important for young people with cystic fibrosis and their family members and carers?
Review question for protocol	What parts of the transition from children's to adult services are most important for young people with cystic fibrosis and their family members and carers?
Objectives	To identify elements of the transition process (for example, transition planning involvement) from paediatric to adult services from perspectives of young people with cystic fibrosis and their family and carers.
Language	English
Study design	<p>Study designs to be considered:</p> <ul style="list-style-type: none"> <li>• Qualitative studies (for example, interviews, focus groups, observations)</li> <li>• Surveys (which include qualitative data)</li> </ul> <p>Excluded:</p> <ul style="list-style-type: none"> <li>• Purely quantitative studies (including surveys with only descriptive quantitative data)</li> </ul>
Population and directness	<ul style="list-style-type: none"> <li>• Children, young people and young adults with cystic fibrosis aged 12 to 25 years who are using or receiving health or social care services.</li> <li>• Family members and carers of children, young people and young adults with cystic fibrosis undergoing transition from children's to adult services.</li> </ul> <p>Population size and indirectness:</p> <ul style="list-style-type: none"> <li>• No sample size specification.</li> <li>• Studies with indirect population will not be considered (however we will include studies with mixed population if quotes are reported separately).</li> </ul>
Stratified and subgroup adjusted	<p>Age ranges:</p> <ul style="list-style-type: none"> <li>• Adolescents: 12 to 16 years</li> <li>• Young people: 16 to 18 years</li> <li>• Young people: 18 to 25 years</li> </ul> <p>Subgroups:</p> <p>People with mental health support needs and those who are looked after by parents/carers.</p>
Context and likely themes	<p>Context:</p> <p>Transition to adult services.</p> <p>Themes will be identified from the literature, but expected themes are:</p> <ul style="list-style-type: none"> <li>• Transition clinic: Transition lead (consultant/social worker) preparation of plan of transition for individual and family/carers, MDT structured approach.</li> <li>• Health care professional training in transition to improve practice.</li> <li>• Transition programme/preparation period and education programme (for young person to be able to function in the adult clinic, and able to manage illness mostly independently of parents and staff). Use of transition questionnaires.</li> <li>• Involvement of young people and family/carer in planning, implementing and reviewing transition.</li> <li>• Communication point of contact information (written, verbal, and email format), and clarity about process (eg, nurse rehabilitation specialist, community paediatrician).</li> <li>• Key transition therapist as part of paediatric and adult service.</li> </ul>

Item	Details
	<ul style="list-style-type: none"> <li>• Involvement of multiagency: health care, social care and education and passing information to adult services (e.g., admin support for records and appointments, transfer checklist, medical and MDT summaries before transfer).</li> <li>• Communication/co-ordination between paediatric and adult services.</li> <li>• Timing of transition with education and other agencies (eg social services) to make it as seamless and as flexible as possible (e.g., a joint transition clinic that consists of both paediatric and adult team members).</li> <li>• Information for young people and carers/family about health needs of cystic fibrosis as an adult, about treatment centres, available support services and resources and funding, may need to be in different format if they can't read.</li> <li>• Delivering information to the adult services- for example, booklet or passport for young people carry with them when attending hospital and other appointments.</li> <li>• Timing (age of transition) to take account of individual circumstances and problems.</li> </ul>
Setting	All health and social care settings ideally in a UK context, but evidence from other countries will be considered if there is insufficient direct evidence.
Search strategy	<p>Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase</p> <p>Limits (e.g. date, study design): Apply standard exclusions and English language filters.</p> <p>Supplementary search techniques: No supplementary search techniques will be used.</p> <p>See appendix E.4 for full strategies</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>• The methodological quality of each study will be assessed using a qualitative study quality checklists as set out in the Developing NICE Guidelines Manual 2014 (CASP checklist for qualitative studies).</li> <li>• The quality of the evidence will be assessed by a modified GRADE approach (GRADE-CERQual) for each theme.</li> </ul> <p>Data synthesis:</p> <p>Thematic analysis of the data will be conducted and findings presented.</p> <p>Review process:</p> <ul style="list-style-type: none"> <li>• A list of excluded studies will be provided following weeding.</li> <li>• Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>• Psychological and behavioural issues are more likely in people with a lower socioeconomic status.</li> <li>• Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care.</li> <li>• Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	<p>References:</p> <ul style="list-style-type: none"> <li>• Transition from children's to adult services. NICE guideline. Publication expected February 2016.</li> </ul> <p>Other notes:</p> <ul style="list-style-type: none"> <li>• Transition is considered as timely planned movement of adolescents and</li> </ul>

Item	Details
	<p>young people from child-centred to adult-orientated health care.</p> <ul style="list-style-type: none"> <li>• Models of transition: LIFEspan, Moving on well (DH)</li> <li>• Transition should be flexible and gradual, and timing of transition should depend on developmental needs, health status and readiness of the individual.</li> <li>• The number of visits to the transition clinic would be important, and dependent on individual needs.</li> <li>• An introduction to adult services (with carer/patient) may reduce anxiety about being moved to adult services, clarity of roles and expectations from MDTs.</li> <li>• Training of paediatric and adult medical teams for care and transition, disability diversity, and communication skills.</li> <li>• Understand cultural differences, dialect, sensory deprivation, environmental issues, hearing, vision, health problems.</li> <li>• Resources should be tailored to needs (eg, community services/outpatient).</li> </ul>

## D.6 Complications of cystic fibrosis

Item	Details
Key issue in the scope	The complications of cystic fibrosis.
Review question in the scope	What are the complications of cystic fibrosis?
Review question in the protocol	What are the non-lower-respiratory complications of cystic fibrosis in infants, children, young people and adults?
Objective	The objective of this review is to raise awareness of the complications of cystic fibrosis among health care professionals and inform parents and carers of infants and children and young people with cystic fibrosis.
Population and directness	<p>Infants, children, young people and adults with CF, diagnosed clinically and by sweat test or genetic testing.</p> <p>Population size and indirectness:</p> <ul style="list-style-type: none"> <li>• Only observational studies above sample size of 250 participants will be included (prevalence review).</li> <li>• Studies with indirect populations will not be considered.</li> </ul>
Subgroups and sensitivity analyses	<p>The following groups will be assessed separately:</p> <ul style="list-style-type: none"> <li>• Infants</li> <li>• Children</li> <li>• Young people and adults</li> </ul>
Clinical markers	<ul style="list-style-type: none"> <li>• Malnutrition</li> <li>• Impaired growth</li> <li>• Cystic fibrosis related renal disease</li> <li>• Delayed puberty</li> <li>• Distal intestinal obstruction syndrome (DIOS)</li> <li>• Abdominal pain</li> <li>• Cystic fibrosis related diabetes</li> <li>• Upper airways disease Cystic fibrosis related musculoskeletal disorders</li> <li>• Urinary stress incontinence</li> <li>• Reduced bone mineral density</li> <li>• Cystic fibrosis related liver disease</li> <li>• Infertility</li> <li>• Meconium ileus</li> </ul>
Outcomes	Prevalence of complications of cystic fibrosis.

Item	Details
Study design	<ul style="list-style-type: none"> <li>Registry data (UK CF Registry) will be prioritised. If no data is available from the registry, observational studies will be eligible for inclusion:</li> <li>Prospective cohort studies</li> <li>Retrospective studies</li> <li>Cross-sectional studies</li> </ul> <p>Countries/regions to prioritise:</p> <ul style="list-style-type: none"> <li>UK</li> <li>Western Europe</li> <li>Australia</li> <li>North America</li> </ul>
Setting	Any healthcare setting where NHS care is delivered (primary, secondary, tertiary or community).
Search strategy	<p>Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase</p> <p>Limits (e.g. date, study design): Apply standard exclusions and English language filters. Apply prevalence/incidence filter.</p> <p>Supplementary search techniques: No supplementary search techniques were used.</p> <p>See appendix E.5 for full strategies</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>The quality of the evidence will be assessed by using the tool developed and published by Munn et al. 2014 that assesses critical issues of internal and external validity that must be considered when addressing validity of prevalence data.</li> </ul> <p>Synthesis of data:</p> <ul style="list-style-type: none"> <li>Meta-analysis will not be conducted.</li> </ul> <p>Review process:</p> <ul style="list-style-type: none"> <li>A list of excluded studies will be provided following weeding.</li> <li>Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>Psychological and behavioural issues are more likely in people with a lower socioeconomic status</li> <li>Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care</li> <li>Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	CF registry.

## D.7 Monitoring for pulmonary disease onset in people with CF without clinical signs or symptoms of lung disease

Item	Details
Key issue in the scope	Routine monitoring of lung disease, including microbiological surveillance, radiological imaging and pulmonary function testing.
Review questions in the	<p>What is the effectiveness of the following in monitoring pulmonary disease?</p> <ul style="list-style-type: none"> <li>Microbiological investigations, including techniques such as bronchoscopy and</li> </ul>

Item	Details
scope	lavage <ul style="list-style-type: none"> <li>• Chest x-ray</li> <li>• CT scan</li> <li>• Lung function testing, including Lung Clearance Index and FEV1.</li> </ul>
Review questions for the protocol	What is the value of the following investigative strategies in monitoring the onset of pulmonary disease in people with CF without clinical signs or symptoms of lung disease? (protocol 1) <ul style="list-style-type: none"> <li>• Non-invasive microbiological investigation- induced sputum samples, cough swab, throat swab, and nasopharyngeal aspiration</li> <li>• Invasive microbiological investigation- bronchoalveolar lavage</li> <li>• Lung physiological function tests- Cardiopulmonary exercise testing, Spirometry and Lung Clearance Index</li> <li>• Imaging techniques- Chest x-ray and CT scan</li> </ul>
Objective	<p>This is the first of three reviews that aim to determine the most effective strategies for monitoring of pulmonary disease in people with cystic fibrosis, with a view to improving subsequent intervention.</p> <p>This review considers people with CF without clinical signs or symptoms of lung disease and best monitoring strategies to identify the onset of pulmonary disease.</p> <p>This most commonly would inform management in young children, but not exclusively. Young children are often prescribed antibiotics as prophylaxis against S aureus colonisation/subclinical infection, or as acute treatment. Older people are more commonly affected P. aeruginosa.</p> <p>Mucolytics and/or immunomodulatory agents may also be offered to prevent deterioration of health, lung function or tissue architecture.</p> <p>Monitoring using non-invasive microbiological techniques and lung function tests (spirometry) occurs regularly and annual assessment is currently performed. Decisions regarding the need of additional imaging tests are based on the regularly received monitoring results or may occur as part of a formal annual review.</p> <p>This review will compare monitoring strategies or combinations of monitoring strategies</p> <ul style="list-style-type: none"> <li>• to identify pulmonary disease</li> <li>• to compare their effects on clinical outcomes</li> </ul>
Language	English
Study design	<ul style="list-style-type: none"> <li>• Systematic reviews</li> <li>• Test-and-treat randomised trials (RCTs)</li> <li>• Prospective and retrospective observational studies reporting the prognostic value of monitoring assessments in terms of risk of outcome assessed by multivariate analysis will be included as a first preference.</li> <li>• Conference abstracts of RCTs (Only if RCTs unavailable and the quality assessment of abstracts will be conducted based on the available information and if necessary the authors of abstracts will be contacted).</li> </ul> <p>Exclusion:</p> <p>Observational studies will be excluded if they do not conduct multivariable adjustment for baseline differences between groups.</p>
Population and directness	<p>Children, young people and adults with defined CF, diagnosed clinically and by sweat or genetic testing.</p> <p>Population size and indirectness:</p> <ul style="list-style-type: none"> <li>• No sample size specification.</li> </ul>

Item	Details
	<ul style="list-style-type: none"> <li>• Studies with indirect populations will not be included</li> </ul>
Stratified, subgroup and adjusted analyses	<p>Groups that will be reviewed and analysed separately:</p> <ul style="list-style-type: none"> <li>• Children</li> <li>• Adults</li> </ul> <p>In the presence of heterogeneity, sensitivity analysis will be conducted including and excluding studies with high and low risk of bias.</p> <p>To be considered as important confounders if comparative cohort studies are included:</p> <ul style="list-style-type: none"> <li>• Concurrent treatment with immunomodulatory and/or mucolytic agents.</li> <li>• Age (under 5 years)</li> </ul>
Intervention	<ul style="list-style-type: none"> <li>• Non-invasive microbiological investigation- induced sputum samples, cough swab, throat swab, and nasopharyngeal aspiration</li> <li>• Invasive microbiological investigation- bronchoalveolar lavage</li> <li>• Lung physiological function tests- Lung Clearance Index and Spirometry</li> <li>• Imaging tests- Chest X-ray and CT scan</li> </ul>
Comparison	<p>Strategy A vs strategy B (a strategy could be a single or combined interventions.)</p>
Outcomes	<ul style="list-style-type: none"> <li>• Lung function <ul style="list-style-type: none"> <li>◦ Lung Clearance Index (LCI)</li> <li>◦ FEV1 (absolute values litres or % predicted or both)</li> </ul> </li> <li>• Imaging <ul style="list-style-type: none"> <li>◦ CT Scans for under 5s (in lieu of lung function test)</li> </ul> </li> <li>• Quality of life (CF-QOL, CFQR)</li> <li>• Nutritional parameters (BMI, weight/ height)</li> <li>• Time to chronic infection using any recognized definition e.g. (Lee 2003) <ul style="list-style-type: none"> <li>◦ with <i>P. aeruginosa</i></li> <li>◦ with <i>S. aureus</i></li> </ul> </li> <li>• Clearance of the organism from the cultures</li> </ul>
Importance of outcomes	<p>Critical outcomes for decision making:</p> <ul style="list-style-type: none"> <li>• Lung Clearance Index (LCI)</li> <li>• FEV1 (absolute values litres or % predicted or both)</li> <li>• CT Scans for under 5s</li> <li>• Clearance of the organism from the cultures</li> </ul>
Setting	<p>All settings in which NHS-commissioned health and social care is provided.</p>
Search strategy	<p>Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase</p> <p>Limits (e.g. date, study design): Apply standard exclusions and English language filters.</p> <p>Supplementary search techniques: No supplementary search techniques will be used.</p> <p>See appendix E.6.1 for full strategies</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>• The methodological quality of each study will be assessed using an appropriate checklist as per NICE guidelines manual (The Cochrane Risk of Bias tool for RCTs and the Newcastle and Ottawa scale for observational studies).</li> <li>• The quality of the evidence will be assessed by GRADE for each outcome</li> </ul>

Item	Details
	<p>according to the process described in the NICE guidelines manual (2014).</p> <p>Synthesis of data:</p> <ul style="list-style-type: none"> <li>• Meta-analysis will be conducted where appropriate.</li> <li>• If comparative cohort studies are included, the minimum number of events per covariate to be recorded to ensure accurate multivariate analysis</li> <li>• Final and change scores will be pooled and if any study reports both, change scores will be used in preference over final scores.</li> <li>• If studies only report p-values from parametric analyses, and 95% CIs cannot be calculated from other data provided, this information will be plotted in GRADE tables, but evidence may be downgraded.</li> <li>• If studies only report p-values from non-parametric analyses, this information will be plotted in GRADE tables without downgrading the evidence, as imprecision cannot be assessed for non-parametric analyses.</li> </ul> <p>Minimal important differences (MIDs):</p> <ul style="list-style-type: none"> <li>• LCI: GRADE default</li> <li>• FEV1: deterioration of 5 percentage points</li> <li>• CT Scans for under 5s: resolution of all inflammatory scans</li> <li>• Clearance of the organism from the cultures: any change will be considered clinically significant</li> <li>• Nutritional parameters (BMI, weight/ height): GRADE default</li> <li>• Time to chronic infection using any recognized definition (e.g. (Lee 2003) (MID TBC) (with P. aeruginosa, with S. aureus): GRADE default</li> <li>• Quality of life: CFQoL, MID = 5; CFQ-R MID = 8.5</li> </ul> <p>Default MIDs: 0.8 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes.</p> <p>Review process:</p> <ul style="list-style-type: none"> <li>• A list of excluded studies will be provided following weeding.</li> <li>• Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>• Psychological and behavioural issues are more likely in people with a lower socioeconomic status</li> <li>• Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care</li> <li>• Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	<p>Pulmonary disease: clogging of the airways due to mucus build-up, decreased mucociliary clearance, and resultant inflammation. The inflammation and infection cause injury and structural changes to the lungs, leading to a variety of symptoms.</p>

## D.8 Monitoring for evolving pulmonary disease in people with CF with established lung disease

Item	Details
Key issue in the scope	Routine monitoring of lung disease, including microbiological surveillance, radiological imaging and pulmonary function testing.
Review questions in the scope	What is the effectiveness of the following in monitoring pulmonary disease?
Review question	What is the value of the following investigative strategies in monitoring evolving

Item	Details
for the protocol	<p>pulmonary disease in people with established lung disease? (protocol 2)</p> <ul style="list-style-type: none"> <li>• Non-invasive microbiological investigation- induced sputum samples, cough swab, throat swab, and nasopharyngeal aspiration</li> <li>• Invasive microbiological investigation- bronchoalveolar lavage</li> <li>• Lung physiological function tests- Cardiopulmonary exercise testing, Spirometry and Lung Clearance Index</li> <li>• Imaging techniques- Chest x-ray and CT scan</li> </ul> <p>Evolving pulmonary disease defined as decline in lung function (based on FEV1), increased exacerbations and/or infections, (symptom based?) and CT changes.</p>
Objective	<p>This is the second of three reviews that aim to determine the most effective strategies for monitoring of pulmonary disease in people with cystic fibrosis, with a view to improving subsequent intervention.</p> <p>This review considers people with CF with established lung disease and the added value of monitoring strategies to monitor evolving pulmonary disease. People are likely to be receiving a mucolytic, and/or an immunomodulatory agent and/or a prophylactic antibiotic.</p> <p>Monitoring helps inform initiation of or changes to treatment (e.g. if there are issues of adherence to treatment).</p> <p>Monitoring using non-invasive microbiological techniques and lung function tests occurs regularly and annual assessment is currently performed. Decisions regarding the need of additional imaging tests are based on the regularly received monitoring results or may occur as part of a formal annual review.</p> <p>This review will assess the added value of imaging in addition to the above listed monitoring strategies or combinations of monitoring tests:</p> <ul style="list-style-type: none"> <li>• to identify evolving pulmonary disease</li> <li>• to compare their effects on prioritised outcomes</li> </ul>
Language	English
Study design	<ul style="list-style-type: none"> <li>• Systematic reviews</li> <li>• Test-and-treat randomised trials (RCTs)</li> <li>• Conference abstracts of RCTs (only if fully published RCTs are not available)</li> <li>• Observational (prospective and retrospective) studies reporting the prognostic value of monitoring assessments in terms of risk of outcome assessed by multivariate analysis will be included as a first preference.</li> </ul> <p>To exclude studies if they do not conduct multivariable adjustment for baseline differences between groups.</p>
Population and directness	<p>Children, young people and adults with defined cystic fibrosis, diagnosed clinically and by sweat test or genetic testing.</p> <p>Population size and indirectness:</p> <ul style="list-style-type: none"> <li>• No sample size specification.</li> <li>• Studies with indirect populations will not be included</li> </ul>
Stratified, subgroup and adjusted analyses	<p>Stratified analysis: groups that will be reviewed and analysed separately:</p> <ul style="list-style-type: none"> <li>• Children</li> <li>• Adults</li> </ul> <p>In the presence of heterogeneity sensitivity analysis will be conducted including and excluding studies with a high risk of bias.</p> <p>To be considered as important confounders if comparative cohort studies are</p>

Item	Details
	<p>included:</p> <ul style="list-style-type: none"> <li>• Concurrent treatment with immunomodulatory and/or mucolytic agents.</li> <li>• Age (under 5 years)</li> </ul>
Monitoring techniques	<ul style="list-style-type: none"> <li>• Non-invasive microbiological investigation- induced sputum samples, cough swab, throat swab, and nasopharyngeal aspiration</li> <li>• Invasive microbiological investigation- bronchoalveolar lavage</li> <li>• Lung physiological function tests- Lung Clearance Index and Spirometry</li> <li>• Imaging tests- Chest X-ray and CT scan</li> <li>• Imaging tests in addition to any of the other strategies.</li> </ul>
Comparison	<ul style="list-style-type: none"> <li>• Any of techniques above</li> </ul>
Outcomes	<ul style="list-style-type: none"> <li>• Lung function <ul style="list-style-type: none"> <li>○ Lung Clearance Index (LCI)</li> <li>○ FEV1 (absolute values litres or % predicted or both)</li> <li>○ VO2 max (CPEX testing)</li> <li>○ CT Scans for under 5s (in lieu of lung function test)</li> </ul> </li> <li>• Time to next exacerbation</li> <li>• Time to chronic infection using any recognized definition e.g. (Lee 2003) <ul style="list-style-type: none"> <li>○ with <i>P. aeruginosa</i></li> <li>○ with <i>S. aureus</i></li> </ul> </li> <li>• Mortality</li> <li>• Nutritional parameters (BMI, weight/ height)</li> <li>• Quality of life (CF-QOL, CFQR)</li> </ul>
Importance of outcomes	<p>Critical outcomes for decision making:</p> <ul style="list-style-type: none"> <li>• Lung function <ul style="list-style-type: none"> <li>○ Lung Clearance Index (LCI)</li> <li>○ FEV1 (absolute values litres or % predicted or both)</li> <li>○ VO2 max (CPEX testing)</li> <li>○ High-resolution computed tomography (CT) appearances using a recognised scoring system (e.g. Brody 2004; Loeve 2009)</li> </ul> </li> <li>• Time to next exacerbation</li> </ul>
Setting	<p>All settings in which NHS-commissioned health and social care is provided.</p>
Search strategy	<p>Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase</p> <p>Limits (e.g. date, study design): Apply standard exclusions and English language filters.</p> <p>Supplementary search techniques: No supplementary search techniques will be used.</p> <p>See appendix E.6.2 for full strategies</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>• The methodological quality of each study will be assessed using an appropriate checklist as per NICE guidelines manual (The Cochrane Risk of Bias tool for RCTs and the Newcastle and Ottawa scale for observational studies).</li> <li>• The quality of the evidence will be assessed by GRADE for each outcome according to the process described in the NICE guidelines manual (2014).</li> </ul> <p>Synthesis of data:</p> <ul style="list-style-type: none"> <li>• Meta-analysis will be conducted where appropriate.</li> <li>• If comparative cohort studies are included, the minimum number of events per</li> </ul>

Item	Details
	<p>covariate to be recorded to ensure accurate multivariate analysis</p> <ul style="list-style-type: none"> <li>Final and change scores will be pooled and if any study reports both, the method used in the majority of studies will be analysed.</li> <li>If studies only report p-values, this information will be plotted in GRADE tables without an assessment of imprecision possible to be made.</li> </ul> <p>MIDs:</p> <ul style="list-style-type: none"> <li>Lung function <ul style="list-style-type: none"> <li>Lung Clearance Index (LCI): GRADE default</li> <li>FEV1: deterioration of 5 percentage points</li> <li>VO2 max: GRADE default</li> <li>High-resolution computed tomography (CT) appearances using a recognised scoring system (e.g. Brody 2004; Loeve 2009): resolution of all inflammatory scans</li> </ul> </li> <li>Time to next exacerbation: any difference will be considered clinically significant</li> <li>Quality of life: CFQoL MID = 5; CFQ-R MID = 8.5</li> <li>Mortality: any difference will be considered clinically significant</li> <li></li> <li>Nutritional parameters (BMI, weight/ height): GRADE default</li> <li>Time to chronic infection using any recognized definition e.g. (Lee 2003) <ul style="list-style-type: none"> <li>with <i>P. aeruginosa</i>: GRADE default</li> <li>with <i>S. aureus</i>: GRADE default</li> </ul> </li> </ul> <p>Default MIDs: 0.8 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes.</p> <p>Review process:</p> <ul style="list-style-type: none"> <li>A list of excluded studies will be provided following weeding.</li> <li>Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>Psychological and behavioural issues are more likely in people with a lower socioeconomic status</li> <li>Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care</li> <li>Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	None.

## D.9 Monitoring for pulmonary disease

Item	Details
Key issue in the scope	Routine monitoring of lung disease, including microbiological surveillance, radiological imaging and pulmonary function testing.
Review questions in the scope	What is the effectiveness of the following in monitoring pulmonary disease?
Review question for the protocol	<p>What is the added value of imaging and invasive microbiological testing in addition to non-invasive microbiological testing and lung function tests in monitoring the response to treatment following an acute exacerbation? (protocol 3)</p> <p>Definition of established lung disease: clinical signs and symptoms and/or</p>

Item	Details
	radiological signs of lung disease.
Objective	<p>This is the last of three reviews that aim to determine the most effective strategies for monitoring of pulmonary disease in people with cystic fibrosis, with a view to improving subsequent intervention.</p> <p>This review considers people with CF who have had an acute pulmonary exacerbation and the value of adding invasive microbiological investigations and/or imaging techniques to non-invasive microbiological testing and lung function tests to evaluate treatment response.</p> <p>Monitoring using non-invasive microbiological techniques and lung function tests (spirometry) occurs regularly and annual assessment is currently performed. Decisions regarding the need of additional imaging tests are based on the regularly received monitoring results or may occur as part of a formal annual review.</p> <p>This review will compare monitoring strategies or combinations of monitoring tests</p> <ul style="list-style-type: none"> <li>• to identify response to treatment following an acute pulmonary exacerbation</li> <li>• to compare their effects on prioritised outcomes</li> </ul>
Language	English
Study design	<ul style="list-style-type: none"> <li>• Systematic reviews</li> <li>• Test-and-treat randomised trials (RCTs)</li> <li>• Conference abstracts of RCTs (only if fully published RCTs are not available)</li> <li>• Observational (prospective and retrospective) studies reporting the prognostic value of monitoring assessments in terms of risk of outcome assessed by multivariate analysis will be included as a first preference.</li> </ul> <p>To exclude studies if they do not conduct multivariable adjustment for baseline differences between groups.</p> <p>Derivation and validation studies of the accuracy of these measures to predict outcomes will not be included as they cannot control for the effect of confounders on outcomes.</p>
Population and directness	<p>Children, young people and adults with defined cystic fibrosis, diagnosed clinically and by sweat test or genetic testing.</p> <p>Population size and indirectness:</p> <ul style="list-style-type: none"> <li>• No sample size specification.</li> <li>• Studies with indirect populations will not be included</li> </ul>
Stratified, subgroup and adjusted analyses	<p>Stratified analysis: groups that will be reviewed and analysed separately:</p> <ul style="list-style-type: none"> <li>• Children</li> <li>• Adults</li> </ul> <p>In the presence of heterogeneity sensitivity analysis will be conducted including and excluding studies with a high risk of bias.</p> <p>To be considered as important confounders if comparative cohort studies are included:</p> <ul style="list-style-type: none"> <li>• Concurrent treatment with immunomodulatory and/or mucolytic agents.</li> <li>• Age (under 5 years)</li> </ul>
Monitoring strategies	<p>Invasive microbiological investigations (such as bronchoalveolar lavage) <i>and/or</i></p> <p>Imaging techniques (such as Chest X-rays or CT scans)</p> <p>+</p> <p>Non-invasive microbiological investigation (such as induced sputum samples,</p>

Item	Details
	<p>cough swab, and throat swab, nasopharyngeal aspiration) <i>and/or</i> Lung physiological function tests (such as Spirometry, Lung Clearance Index)</p>
Comparison	<p>Non-invasive microbiological investigation (such as induced sputum samples, cough swab, throat swab, and nasopharyngeal aspiration) <i>and/or</i> Lung physiological function tests (such as Spirometry, and Lung Clearance Index)</p>
Outcomes	<ul style="list-style-type: none"> <li>• Lung function <ul style="list-style-type: none"> <li>○ Lung Clearance Index (LCI)</li> <li>○ FEV1 (absolute values litres or % predicted or both)</li> <li>○ Oxygen saturation</li> </ul> </li> <li>• High-resolution computed tomography (CT) appearances using a recognised scoring system (e.g. Brody 2004; Loeve 2009) or Chest X-ray appearances</li> <li>• Time to next exacerbation</li> <li>• Clearance of the organism from the cultures</li> <li>• Inflammatory markers (White cell count , CRP, ESR)</li> <li>• Quality of life (CF-QOL, CFQR)</li> <li>• Nutritional parameters (weight, height, body mass index (BMI))</li> </ul>
Importance of outcomes	<p>Critical outcomes for decision making:</p> <ul style="list-style-type: none"> <li>• Lung function <ul style="list-style-type: none"> <li>○ LCI</li> <li>○ (FEV1) (absolute values or change from start of treatment (post hoc change) (litres or per cent (%) predicted or both))</li> <li>○ Oxygen saturation</li> </ul> </li> <li>• Time to next exacerbation</li> <li>• Clearance of the organism from the cultures</li> </ul>
Setting	<p>All settings in which NHS-commissioned health and social care is provided.</p>
Search strategy	<p>Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase</p> <p>Limits (e.g. date, study design): Apply standard exclusions and English language filters.</p> <p>Supplementary search techniques: No supplementary search techniques will be used.</p> <p>See appendix E.6.3 for full strategies</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>• The methodological quality of each study will be assessed using an appropriate checklist as per NICE guidelines manual (The Cochrane Risk of Bias tool for RCTs and the Newcastle and Ottawa scale for observational studies).</li> <li>• The quality of the evidence will be assessed by GRADE for each outcome according to the process described in the NICE guidelines manual (2014).</li> </ul> <p>Synthesis of data:</p> <ul style="list-style-type: none"> <li>• Meta-analysis will be conducted where appropriate.</li> <li>• If comparative cohort studies are included, the minimum number of events per covariate to be recorded to ensure accurate multivariate analysis</li> <li>• Final and change scores will be pooled and if any study reports both, the method used in the majority of studies will be analysed.</li> <li>• If studies only report p-values, this information will be plotted in GRADE tables</li> </ul>

Item	Details
	<p>without an assessment of imprecision possible to be made.</p> <p>MIDs</p> <ul style="list-style-type: none"> <li>• Lung function <ul style="list-style-type: none"> <li>○ Lung Clearance Index (LCI): GRADE default</li> <li>○ FEV1 (absolute values litres or % predicted or both): 2 percentage points</li> <li>○ Oxygen saturation: 2 percentage points</li> </ul> </li> <li>• High-resolution computed tomography (CT) appearances using a recognised scoring system (e.g. Brody 2004; Loeve 2009) or Chest X-ray appearances = resolution of all inflammatory scans</li> <li>• Time to next exacerbation: any change will be considered clinically significant</li> <li>• Inflammatory markers = normalisation</li> <li>• Quality of life: CFQoL = 5; CFQ-R = 8.5</li> <li>• Nutritional parameters (BMI, weight/ height): GRADE default</li> <li>• Clearance of the organism from the cultures: any change will be considered clinically significant</li> </ul> <p>Default MIDs: 0.8 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes.</p> <p>Review process:</p> <ul style="list-style-type: none"> <li>• A list of excluded studies will be provided following weeding.</li> <li>• Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>• Psychological and behavioural issues are more likely in people with a lower socioeconomic status</li> <li>• Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care</li> <li>• Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	None.

## D.10 Airway clearance techniques

Item	Details
Key issue in the scope	Airway clearance techniques.
Review question in the scope	What is the effectiveness of airway clearance techniques in people with cystic fibrosis?
Review question for the protocol	What is the effectiveness of airway clearance techniques in people with cystic fibrosis?
Objective	To examine the effectiveness of airway clearance techniques in people with cystic fibrosis.
Language	English
Study design	<ul style="list-style-type: none"> <li>• Systematic reviews of RCTs</li> <li>• RCTs (Only RCTs with N &gt;10 will be included. RCTs with N ≤ 10 and analysed in an included Cochrane systematic review will be included).</li> <li>• Conference abstracts of RCTs (Only if RCTs unavailable and the quality assessment of abstracts will conducted based on the available information and if necessary the authors of abstracts will be contacted. Conference abstracts included in the Cochrane reviews will be included).</li> <li>• Comparative cohort studies (only if RCTs unavailable or limited data to inform</li> </ul>

Item	Details
	decision making)
Population and directness	<p>Children and adults with defined CF (diagnosed clinically and by sweat test or genetic testing).</p> <p>Population size and indirectness:</p> <ul style="list-style-type: none"> <li>• Studies with &lt;10 participants will not be included.</li> <li>• Studies with indirect population will not be included.</li> </ul>
Stratified, subgroup and adjusted analyses	<p>If possible the following groups will be analysed separately:</p> <ul style="list-style-type: none"> <li>• Children (particularly under 2 for hospitalisations)</li> <li>• Adults</li> <li>• Symptomatic CF</li> <li>• Asymptomatic CF</li> </ul> <p>In the presence of heterogeneity, sensitivity analysis will be conducted including and excluding studies with a high risk of bias.</p>
Intervention	<ul style="list-style-type: none"> <li>• Manual physiotherapy techniques including: chest shaking / vibrations, chest percussion</li> <li>• Positive expiratory pressure (PEP) mask therapy</li> <li>• Active cycle of breathing techniques (ACBT)</li> <li>• relaxation or breathing control forced expiration technique (FET) which includes huffing and breathing control</li> <li>• thoracic expansion exercises</li> <li>• Autogenic Drainage (AD)</li> <li>• Oscillating devices (acapella and flutter, cornet)</li> <li>• High Frequency Chest Wall Oscillation (e.g. The Vest)</li> <li>• Non-invasive ventilation</li> </ul>
Comparison	<p>The comparisons prioritised in this review are:</p> <ul style="list-style-type: none"> <li>• Intervention A compared with no intervention/control.</li> <li>• Intervention A compared with intervention B (as advised by the committee).</li> </ul>
Outcomes	<ul style="list-style-type: none"> <li>• Expecterated secretions (mucus, sputum, phlegm)</li> <li>• Sputum volume</li> <li>• Patient preference</li> <li>• Pulmonary exacerbations, change in frequency</li> <li>• Pulmonary function tests (change from baseline would be prioritised over final scores) <ul style="list-style-type: none"> <li>○ forced expiratory volume in one second (FEV1)</li> <li>○ forced vital capacity (FVC)</li> </ul> </li> <li>• Oxygen saturation measured by pulse or transcutaneous oximetry</li> <li>• Quality of life (CF-QOL, CFQR)</li> <li>• Hospitalisations, change in frequency</li> </ul> <p>Note: change from baseline will be prioritised over absolute values</p>
Importance of outcomes	<p>Critical outcomes for decision making:</p> <ul style="list-style-type: none"> <li>• Sputum volume</li> <li>• Exacerbations</li> <li>• Patient preference</li> </ul>
Setting	Any healthcare setting where NHS care is delivered (primary, secondary, tertiary or community).
Search strategy	Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Databases of Abstracts of Reviews of Effectiveness, Health

Item	Details
	<p>Technology Assessment Database, Embase, AMED, CINAHL, PEDro Limits (e.g. date, study design): Limit to English-language only where possible (Medline and Embase); apply standard exclusions filter Supplementary search techniques: No supplementary search techniques were used. See appendix E.7 for full strategies</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>• The methodological quality of each study will be assessed using an appropriate checklist as per NICE guidelines manual (The Cochrane Risk of Bias tool for RCTs and the Newcastle and Ottawa scale for observational studies).</li> <li>• The quality of the evidence will be assessed by GRADE for each outcome according to the process described in the NICE guidelines manual (2014).</li> </ul> <p>Synthesis of data:</p> <ul style="list-style-type: none"> <li>• Meta-analysis will be conducted where appropriate.</li> <li>• Final and change scores will be pooled and if any study reports both, change scores will be used in preference over final scores.</li> <li>• If studies only report p-values from parametric analyses, and 95% CIs cannot be calculated from other data provided, this information will be plotted in GRADE tables, but evidence may be downgraded.</li> <li>• If studies only report p-values from non-parametric analyses, this information will be plotted in GRADE tables without downgrading the evidence, as imprecision cannot be assessed for non-parametric analyses</li> </ul> <p>Minimal important differences (MIDs):</p> <ul style="list-style-type: none"> <li>• Expecterated secretions (mucus, sputum, phlegm): GRADE default</li> <li>• Sputum volume: GRADE default</li> <li>• Patient preference: GRADE default</li> <li>• Pulmonary exacerbations, change in frequency: any change will be considered clinically significant</li> <li>• Pulmonary function tests (change from baseline would be prioritised over final scores) <ul style="list-style-type: none"> <li>○ forced expiratory volume in one second (FEV1): 5 percentage points</li> <li>○ forced vital capacity (FVC): GRADE default</li> </ul> </li> <li>• Oxygen saturation measured by pulse or transcutaneous oximetry: GRADE defaults</li> <li>• Quality of life: CF-QOL = 5; CFQ-R = 8.5</li> <li>• Hospitalisations, change in frequency = GRADE default</li> </ul> <p>Default MIDs: 0.8 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes.</p> <p>Review process:</p> <ul style="list-style-type: none"> <li>• This question will be prioritised for dual weeding.</li> <li>• A list of excluded studies will be provided following weeding.</li> <li>• Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>• Psychological and behavioural issues are more likely in people with a lower socioeconomic status</li> <li>• Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care</li> <li>• Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>

Item	Details
Notes/additional information	

## D.11 Mucoactive agents

Item	Details
Key issue in the scope	Management with mucoactive or mucolytic agents.
Review question in the scope	What is the effectiveness of mucoactive or mucolytic agents, including rhDNase, nebulised saline (isotonic and hypertonic) and mannitol?
Review question in the protocol	What is the effectiveness of mucoactive or mucolytic agents, including dornase alpha, nebulised sodium chloride (isotonic and hypertonic) and mannitol?
Objective	<p>Mucolytics are prescribed to facilitate expectoration by reducing sputum viscosity. In some patients with a chronic productive cough, mucolytics can reduce exacerbations; mucolytic therapy should be stopped if there is no benefit after a 5-week trial.</p> <p>The aim of this review is to establish the clinical and cost effectiveness of mucoactive or mucolytic agents in improving airway clearance in children, young people and adults with cystic fibrosis.</p>
Language	English
Study design	<ul style="list-style-type: none"> <li>• Systematic reviews of RCTs</li> <li>• RCTs (including cross over RCTs)</li> <li>• Conference abstracts of RCTs (Only if RCTs unavailable and the quality assessment of abstracts will be conducted based on the available information and if necessary the authors of abstracts will be contacted).</li> <li>• Comparative cohort studies (only if RCTs unavailable or limited data to inform decision making)</li> </ul>
Population and directness	<p>Children, young people and adults with CF, diagnosed clinically and by sweat test or genetic testing.</p> <p>Population size and indirectness:</p> <ul style="list-style-type: none"> <li>• Studies with N &lt; 10 will not be included.</li> <li>• Studies with indirect population will not be considered.</li> </ul>
Stratified, subgroup and adjusted analyses	<p>Groups that will be reviewed and analysed separately:</p> <ul style="list-style-type: none"> <li>• Children</li> <li>• Young people and adults</li> </ul> <p>Sensitivity analysis:</p> <p>In the presence of heterogeneity, sensitivity analysis will be conducted including and excluding studies with a high risk of bias.</p> <p>In the presence of heterogeneity, the following subgroups will be considered for subgroup analysis:</p> <ul style="list-style-type: none"> <li>• Disease severity</li> </ul>
Intervention	<p>Nebulised and Inhaled Mucolytics</p> <ul style="list-style-type: none"> <li>• Dornase alfa</li> <li>• Acetylcysteine</li> <li>• Nebulised sodium chloride (saline) (hypertonic and isotonic)</li> <li>• Mannitol (only in children and young people up to the age of 18 years as TA in adults will be included).</li> </ul>
Comparison	<ul style="list-style-type: none"> <li>• Mucoactive agents vs placebo</li> <li>• Mucoactive agent A versus mucoactive agent B</li> </ul>

Item	Details
Outcomes	<ul style="list-style-type: none"> <li>• Lung function: FEV1</li> <li>• Inflammatory markers (change from baseline)               <ul style="list-style-type: none"> <li>○ Serum (white blood cell (WBC), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR))</li> <li>○ Sputum (IL-8)</li> </ul> </li> <li>• Quality of life (CF-QOL, CFQR)</li> <li>• Time to pulmonary exacerbations</li> <li>• Need for intravenous antibiotics for pulmonary exacerbation               <ul style="list-style-type: none"> <li>○ Number of days of treatment</li> <li>○ Number of courses</li> </ul> </li> <li>• Adverse events               <ul style="list-style-type: none"> <li>○ alteration in voice</li> <li>○ haemoptysis</li> <li>○ bronchospasm</li> </ul> </li> </ul> <p>Note: change from baseline will be prioritised over absolute values</p>
Importance of outcomes	<p>Critical outcomes for decision making:</p> <ul style="list-style-type: none"> <li>• Lung function: FEV1</li> <li>• Time to pulmonary exacerbations</li> <li>• Need for intravenous antibiotics for pulmonary exacerbation</li> </ul>
Setting	<p>All settings in which NHS-commissioned health and social care is provided.</p>
Search strategy	<p>Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase</p> <p>Limits (e.g. date, study design): Apply standard exclusions and English language filters. Limit to RCTs and systematic reviews unless overall return is small</p> <p>Supplementary search techniques: No supplementary search techniques will be used.</p> <p>See appendix E.8 for full strategies</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>• The methodological quality of each study will be assessed using an appropriate checklist as per NICE guidelines manual (The Cochrane Risk of Bias tool for RCTs and the Newcastle and Ottawa scale for observational studies).</li> <li>• The quality of the evidence will be assessed by GRADE for each outcome according to the process described in the NICE guidelines manual (2014).</li> </ul> <p>Synthesis of data:</p> <ul style="list-style-type: none"> <li>• Meta-analysis will be conducted where appropriate.</li> <li>• Final and change scores will be pooled and if any study reports both, change scores will be used in preference over final scores.</li> <li>• If studies only report p-values from parametric analyses, and 95% CIs cannot be calculated from other data provided, this information will be plotted in GRADE tables, but evidence may be downgraded.</li> <li>• If studies only report p-values from non-parametric analyses, this information will be plotted in GRADE tables without downgrading the evidence, as imprecision cannot be assessed for non-parametric analyses</li> </ul> <p>Minimal important differences (MIDs):</p> <ul style="list-style-type: none"> <li>• FEV1: 5 percentage points</li> <li>• Inflammatory markers (change from baseline): GRADE default</li> <li>• Quality of life: CF-QOL = 5; CFQ-R = 4</li> </ul>

Item	Details
	<ul style="list-style-type: none"> <li>• Time to pulmonary exacerbations: any change will be considered clinically significant</li> <li>• Need for intravenous antibiotics for pulmonary exacerbation               <ul style="list-style-type: none"> <li>◦ Number of days of treatment: GRADE default</li> <li>◦ Number of courses: GRADE default</li> </ul> </li> <li>• Adverse events (alteration in voice, haemoptysis): GRADE default</li> <li>• Serious adverse events leading to discontinuation of treatment: any change will be considered clinically significant</li> </ul> <p>Default MIDs: 0.8 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes.</p> <p>Review process:</p> <ul style="list-style-type: none"> <li>• This question will be prioritised for dual weeding.</li> <li>• A list of excluded studies will be provided following weeding.</li> <li>• Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>• Psychological and behavioural issues are more likely in people with a lower socioeconomic status</li> <li>• Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care</li> <li>• Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	<p>Relevant Cochrane reviews include:</p> <ul style="list-style-type: none"> <li>• Dornase alfa for cystic fibrosis</li> <li>• Nebulised hypertonic saline for cystic fibrosis</li> <li>• Nebulized and oral thiol derivatives for pulmonary disease in cystic fibrosis</li> </ul>

## D.12 Pulmonary Infection prophylaxis

Item	Details
Key issue in the scope	<p>Antimicrobial management in CF to:</p> <ul style="list-style-type: none"> <li>• Prevent bacterial colonisation</li> <li>• Treat acute pulmonary infection</li> <li>• Treat chronic pulmonary infection, including clinical exacerbations and colonisation</li> </ul>
Review question in the scope	<p>What is the effectiveness of antimicrobial treatment to:</p> <ul style="list-style-type: none"> <li>• Prevent bacterial colonisation</li> <li>• Treat acute pulmonary infection</li> <li>• Treat chronic pulmonary infection, including clinical exacerbations and colonisation</li> </ul>
Review question for the protocol	<p>What is the effectiveness of long-term antimicrobial prophylaxis to prevent pulmonary bacterial colonisation with <i>Staphylococcus aureus</i> in people with CF? (protocol 1)</p>
Objective	<p>The aim of this review is to compare the clinical and cost effectiveness of different antimicrobials given as long-term (more than 3 months) prophylaxis against bacterial colonisation to people with Cystic Fibrosis.</p>
Language	English
Study design	<ul style="list-style-type: none"> <li>• Systematic reviews</li> <li>• RCTs</li> <li>• Conference abstracts of RCTs (Only if RCTs unavailable and the quality assessment of abstracts will conducted based on the available information and if necessary the authors of abstracts will be contacted).</li> </ul>

Item	Details
	<p>Exclusions: Cross-over studies, as this study design will not allow evaluation of the effects of prophylaxis on long-term outcomes measures.</p>
Population and directness	<p>Infants, children, young people and adults with defined CF, diagnosed clinically and by sweat test or genetic testing. Population size and indirectness:</p> <ul style="list-style-type: none"> <li>• Studies where N&lt;10 will not be included.</li> <li>• Studies with indirect populations will not be considered.</li> </ul>
Stratified, subgroup and adjusted analyses	<p>Groups that will be reviewed and analysed separately:</p> <ul style="list-style-type: none"> <li>• Infants and young children &lt;3 years</li> <li>• Children 3-12 years</li> <li>• Young people and adults &gt;12 years</li> </ul> <p>Sensitivity analysis: In the presence of heterogeneity, sensitivity analysis will be conducted including and excluding studies with a high risk of bias.</p> <p>Sub-group analysis: In the presence of heterogeneity, the following subgroups will be analysed separately:</p> <ul style="list-style-type: none"> <li>• Duration of treatment</li> </ul>
Intervention	<p>Oral Antibiotics administration with any of the following, alone or in combination for long-term (more than 3 months) prophylaxis of infection, including:</p> <ul style="list-style-type: none"> <li>• Combination antibiotics <ul style="list-style-type: none"> <li>○ Co-amoxiclav</li> <li>○ Co-trimoxazole</li> </ul> </li> <li>• Penicillins <ul style="list-style-type: none"> <li>○ Flucloxacillin</li> </ul> </li> <li>• Beta-lactam antibiotics <ul style="list-style-type: none"> <li>○ Cephalosporins</li> <li>○ Cefalexin</li> <li>○ Cefradine/cephradine</li> </ul> </li> <li>• Tetracycline (only for over 12 years)</li> <li>• Macrolides <ul style="list-style-type: none"> <li>○ Azithromycin</li> </ul> </li> </ul>
Comparison	<ul style="list-style-type: none"> <li>• Placebo</li> <li>• No treatment</li> <li>• Antibiotic A vs antibiotic B</li> </ul>
Outcomes	<ul style="list-style-type: none"> <li>• Time to identification of the pathogen (<i>S aureus</i>) in sputum culture</li> <li>• Number of positive pathogen cultures (<i>S aureus</i>) identified during study period</li> <li>• Lung function, measured by: <ul style="list-style-type: none"> <li>○ Lung clearance index (&gt; 5 yrs)</li> <li>○ FEV1 (absolute values litres or % predicted or both) (&gt; 7 yrs)</li> <li>○ Evidence of inflammation in CT scan (only for &lt; 5 yrs)</li> </ul> </li> <li>• Time to next pulmonary exacerbation</li> <li>• Quality of life (CF-QOL, CFQR)</li> <li>• Adherence to treatment</li> <li>• Adverse events <ul style="list-style-type: none"> <li>○ Minor events:</li> </ul> </li> </ul>

Item	Details
	<ul style="list-style-type: none"> <li>○ Major events which leads to discontinuation</li> <li>○ emergence of resistant organisms</li> </ul> <p>Note: change from baseline will be prioritised over absolute values</p>
Importance of outcomes	<p>Critical outcomes for decision making:</p> <ul style="list-style-type: none"> <li>● Time to identification of the pathogen (<i>S aureus</i>) in sputum culture</li> <li>● Time to next pulmonary exacerbation</li> </ul>
Setting	<p>All settings in which NHS-commissioned health and social care is provided.</p>
Search strategy	<p>Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase</p> <p>Limits (e.g. date, study design): Apply standard exclusions and English language filters. Limit to RCTs and systematic reviews in the first instance but download all study designs.</p> <p>See appendix E.9.1 for a full search strategy</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>● The methodological quality of each study will be assessed using an appropriate checklist as per NICE guidelines manual (The Cochrane Risk of Bias tool for RCTs).</li> <li>● The quality of the evidence will be assessed by GRADE for each outcome according to the process described in the NICE guidelines manual (2014).</li> </ul> <p>Synthesis of data:</p> <ul style="list-style-type: none"> <li>● Meta-analysis will be conducted where appropriate.</li> <li>● Final and change scores will be pooled and if any study reports both, change scores will be used in preference over final scores.</li> <li>● If studies only report p-values from parametric analyses, and 95% CIs cannot be calculated from other data provided, this information will be plotted in GRADE tables, but evidence may be downgraded.</li> <li>● If studies only report p-values from non-parametric analyses, this information will be plotted in GRADE tables without downgrading the evidence, as imprecision cannot be assessed for non-parametric analyses.</li> </ul> <p>Minimal important differences (MIDs):</p> <ul style="list-style-type: none"> <li>● Time to identification of the pathogen (<i>S aureus</i>) in sputum culture = GRADE default</li> <li>● Number of positive pathogen cultures (<i>S aureus</i>) identified during study period = GRADE default</li> <li>● Lung clearance index (&gt; 5 yrs) = GRADE default</li> <li>● FEV1 = 5 percentage points</li> <li>● Evidence of inflammation in CT scan (only for &lt; 5 yrs) = GRADE default</li> <li>● MIDTime to next pulmonary exacerbation = any difference</li> <li>● Quality of life: CF-QOL = 5; CFQ-R = 8.5</li> <li>● Adherence to treatment = GRADE default</li> <li>● Minor adverse events = GRADE default</li> <li>● Major events which leads to discontinuation = any difference</li> <li>● Emergence of resistant organisms = GRADE default</li> </ul> <p>Default MIDs: 0.8 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes.</p> <p>Review process:</p> <ul style="list-style-type: none"> <li>● This question will be prioritised for dual weeding</li> </ul>

Item	Details
	<ul style="list-style-type: none"> <li>• A list of excluded studies will be provided following weeding.</li> <li>• Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>• Psychological and behavioural issues are more likely in people with a lower socioeconomic status</li> <li>• Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care</li> <li>• Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	None.

## D.13 Pulmonary Infection - Antimicrobials for the treatment of acute pulmonary infection or those with an exacerbation

Item	Details
Key issue in the scope	<p>Antimicrobial management in CF to:</p> <ul style="list-style-type: none"> <li>• Prevent bacterial colonisation</li> <li>• Treat acute pulmonary infection</li> <li>• Treat chronic pulmonary infection, including clinical exacerbations and colonisation</li> </ul>
Review question in the scope	<p>What is the effectiveness of antimicrobial treatment to:</p> <ul style="list-style-type: none"> <li>• Prevent bacterial colonisation</li> <li>• Treat acute pulmonary infection</li> <li>• Treat chronic pulmonary infection, including clinical exacerbations and colonisation</li> </ul>
Review question for the protocol	<p>What is the effectiveness of antimicrobial treatment for acute pulmonary infection or those with an exacerbation in children and adults with cystic fibrosis? (protocol 2)</p>
Objective	<p>The aim of this review is to compare the clinical and cost effectiveness of different antimicrobial regimens in achieving clinical resolution of acute pulmonary infection or exacerbation in children and adults with cystic fibrosis. In this evidence review, pulmonary exacerbation was defined in accordance with:</p> <ul style="list-style-type: none"> <li>• Fuchs definition (original form (4/16 symptoms leading to IV antibiotic treatment) or modified form (4/16 symptoms leading to any change in antibiotic therapy))</li> <li>• or</li> <li>• European CF Society Consensus definition: “need for additional antibiotic treatment as indicated by a recent change in at least 2 of 6 defined symptoms”.</li> </ul> <p>Additionally, acute infection a person with cystic fibrosis who is found on routine microbiological investigation to have a significant respiratory pathogen (newly identified infection).</p>
Language	English
Study design	<ul style="list-style-type: none"> <li>• Systematic reviews</li> <li>• RCTs</li> <li>• Cross-over trials: only the first period of intervention prior to cross-over trials will be included.</li> <li>• Conference abstracts of RCTs (Only if RCTs unavailable and the quality assessment of abstracts will conducted based on the available information and if necessary the authors of abstracts will be contacted).</li> </ul>

Item	Details
Population and directness	<p>Children and adults with CF (diagnosed clinically and by sweat test or genetic testing) who present with clinical manifestations suggesting development of an acute pulmonary infection or those with an exacerbation and who are already known to have a positive sputum/airway culture for one of the following pathogens at entry to the trial:</p> <ul style="list-style-type: none"> <li>• <i>Staphylococcus aureus</i></li> <li>• <i>Pseudomonas aeruginosa</i></li> <li>• <i>Burkholderia cepacia complex</i></li> <li>• <i>Haemophilus influenza</i></li> <li>• <i>Nontuberculous mycobacteria (Mycobacterium avium complex and Mycobacterium abscessus)</i></li> <li>• Children and adults with CF who present with clinical manifestations suggesting development of an acute pulmonary infection or those with an exacerbation without an identified pathogen at trial entry</li> </ul> <p>Population size and indirectness:</p> <ul style="list-style-type: none"> <li>• Studies where N &lt; 20 will not be included.</li> <li>• Studies with indirect populations will not be considered.</li> </ul>
Stratified, subgroup and adjusted analyses	<p>Stratified analyses:</p> <ul style="list-style-type: none"> <li>• Type of pathogen</li> </ul> <p>Sensitivity analysis:</p> <p>In the presence of heterogeneity, sensitivity analysis will be conducted including and excluding studies with a high risk of bias.</p> <p>In the presence of heterogeneity, the following subgroups will be considered for subgroup analysis:</p> <ul style="list-style-type: none"> <li>• Route of administration</li> <li>• Duration of treatment</li> <li>• Dose</li> </ul>
Intervention	<p><b>For <i>Staphylococcus aureus</i></b></p> <ul style="list-style-type: none"> <li>• Flucloxacillin (oral or IV)</li> <li>• Cotrimoxazole (oral or IV)</li> <li>• Doxycycline (oral) (not for under 12's)</li> <li>• Cefradine (oral)</li> </ul> <p><b>For <i>Pseudomonas Aeruginosa</i> (inhaled, IV, oral)</b></p> <ul style="list-style-type: none"> <li>• Ciprofloxacin (Cipro) (oral)</li> <li>• Aztreonam (inhaled or IV)</li> <li>• Ceftazidime IV</li> <li>• Meropenem IV</li> <li>• Piperacillin-Tazobactam IV</li> <li>• Fosfomycin IV</li> <li>• Ticarcillin-Clavulanate IV</li> <li>• Aztreonam (inhaled or IV)</li> <li>• Chloramphenicol (oral)</li> <li>• Sequencing antibiotics- Ciprofloxacin (oral) then either Colistin or Tobramycin (inhaled) (<b>first infection only</b>)</li> </ul> <p><b>For <i>Burkholderia Cepacia complex</i> (oral or IV)</b></p> <ul style="list-style-type: none"> <li>• Cotrimoxazole</li> </ul>

Item	Details
	<ul style="list-style-type: none"> <li>• Meropenem (IV or inhaled)</li> <li>• Ceftazidime (IV or inhaled)</li> <li>• Temocillicin</li> <li>• Imipenem</li> <li>• Trimethoprim</li> <li>• Tobramycin</li> </ul> <p><b>For <i>Haemophilus influenzae</i> ( IV)</b></p> <ul style="list-style-type: none"> <li>• Co-amoxiclav (oral or IV)</li> <li>• Cefuroxime (IV)</li> <li>• Cefaclor</li> <li>• Cefixime</li> <li>• Doxycycline (&gt;12 years)</li> <li>• Macrolide (clarithromycin/azithromycin)</li> </ul> <p><b>Nontuberculous mycobacteria (<i>Mycobacterium avium complex</i>)</b></p> <ul style="list-style-type: none"> <li>• Clarithromycin (oral)</li> <li>• Azithromycin (oral)</li> <li>• Rifampicin (oral)</li> <li>• Ethambutol (oral)</li> <li>• Amikacin (inhaled and potentially IV)</li> </ul> <p><b>Nontuberculous mycobacteria (<i>Mycobacterium abscessus</i>)</b></p> <ul style="list-style-type: none"> <li>• Cefoxitin (IV)</li> <li>• Clarithromycin (IV)</li> <li>• Amikacin (IV and inhaled)</li> <li>• Meropenem (IV and inhaled)</li> <li>• Tigecycline</li> <li>• Co-trimoxazole (oral)</li> <li>• Moxifloxacin (oral)</li> <li>• Ciprofloxain (oral)</li> <li>• Doxycycline/minocycline (tetracyclines) (oral)</li> <li>• Linezolid (oral)</li> <li>• Clofazimine (oral)</li> </ul> <p>No identified pathogen at entry level</p> <ul style="list-style-type: none"> <li>• Any of the antibiotics listed above</li> </ul>
Comparison	<ul style="list-style-type: none"> <li>• Antibiotic A vs. antibiotic B</li> <li>• Combinations of antibiotics</li> <li>• Single vs combination</li> </ul>
Outcomes	<p><b>Pulmonary exacerbation:</b></p> <ul style="list-style-type: none"> <li>• Lung function: <ul style="list-style-type: none"> <li>○ Lung Clearance Index (LCI)</li> <li>○ FEV1</li> <li>○ CT Scans for under 5s</li> </ul> </li> <li>• Eradication of specific pathogen</li> <li>• Resolution of infection/exacerbation or measure of treatment failure (e.g. need for additional antibiotics)</li> <li>• Duration of the acute episode</li> </ul>

Item	Details
	<ul style="list-style-type: none"> <li>• Quality of life (CF-QOL, CFQR)</li> <li>• Mortality</li> <li>• Adverse events               <ul style="list-style-type: none"> <li>○ mild, that require transient discontinuation of treatment</li> <li>○ severe, that require discontinuation of treatment</li> </ul> </li> </ul> <p><b>For acute infection:</b></p> <ul style="list-style-type: none"> <li>• Lung function:               <ul style="list-style-type: none"> <li>○ Lung Clearance Index (LCI)</li> <li>○ FEV1</li> <li>○ CT Scans for under 5s</li> </ul> </li> <li>• Eradication of specific pathogen</li> <li>• Time to next pulmonary exacerbation</li> <li>• Resolution of infection/exacerbation or measure of treatment failure (e.g. need for additional antibiotics)</li> <li>• Quality of life (CF-QOL, CFQR)</li> <li>• Adverse events               <ul style="list-style-type: none"> <li>○ mild, that require transient discontinuation of treatment</li> <li>○ severe, that require discontinuation of treatment</li> </ul> </li> </ul> <p>Note: change from baseline will be prioritised over absolute values</p>
Importance of outcomes	<p>Critical outcomes for decision making:</p> <ul style="list-style-type: none"> <li>• Eradication of specific pathogen</li> <li>• Lung function:               <ul style="list-style-type: none"> <li>○ Lung Clearance Index (LCI)</li> <li>○ FEV1</li> <li>○ CT Scans for under 5s</li> </ul> </li> </ul>
Setting	All settings in which NHS-commissioned health and social care is provided.
Search strategy	<p>Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase.</p> <p>Limits (e.g. date, study design): Apply standard exclusions and English language filters. Limit to RCTs and systematic reviews in the first instance but download all study designs.</p> <p>Supplementary search techniques: No supplementary search techniques will be used.</p> <p>See appendix E.9.2 for full search strategy</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>• The methodological quality of each study will be assessed using an appropriate checklist as per NICE guidelines manual (The Cochrane Risk of Bias tool for RCTs).</li> <li>• The quality of the evidence will be assessed by GRADE for each outcome according to the process described in the NICE guidelines manual (2014).</li> </ul> <p>Synthesis of data:</p> <ul style="list-style-type: none"> <li>• Meta-analysis will be conducted where appropriate.</li> <li>• Final and change scores will be pooled and if any study reports both, change scores will be used in preference over final scores.</li> <li>• If studies only report p-values from parametric analyses, and 95% CIs cannot be calculated from other data provided, this information will be plotted in GRADE tables, but evidence may be downgraded.</li> <li>• If studies only report p-values from non-parametric analyses, this information</li> </ul>

Item	Details
	<p>will be plotted in GRADE tables without downgrading the evidence, as imprecision cannot be assessed for non-parametric analyses.</p> <p>Minimal important differences (MIDs):</p> <ul style="list-style-type: none"> <li>• Eradication of the pathogen: any change will be considered clinically significant</li> <li>• Lung function: <ul style="list-style-type: none"> <li>○ LCI = GRADE default</li> <li>○ FEV1 = deterioration of 3 percentage points</li> <li>○ CT Scans for under 5s = resolution of all inflammatory scans</li> </ul> </li> <li>• Resolution of acute infection or measure of treatment failure (e.g. need for additional antibiotics) = any change</li> <li>• Quality of life: CF-QOL = 5; CFQ-R = 8.5</li> <li>• Adverse events: GRADE default</li> <li>• Serious adverse events leading to discontinuation of treatment: any change will be considered clinically significant</li> </ul> <p>Default MIDs: 0.8 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes.</p> <p>Review process:</p> <ul style="list-style-type: none"> <li>• This question will be prioritised for dual weeding.</li> <li>• A list of excluded studies will be provided following weeding.</li> <li>• Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>• Psychological and behavioural issues are more likely in people with a lower socioeconomic status</li> <li>• Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care</li> <li>• Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	<p><a href="http://www.cff.org/UploadedFiles/treatments/CFCareGuidelines/Respiratory/CF-Care-Guidelines-Pulmonary-Exacerbations.pdf">http://www.cff.org/UploadedFiles/treatments/CFCareGuidelines/Respiratory/CF-Care-Guidelines-Pulmonary-Exacerbations.pdf</a></p> <p>Topic group agree that if the definition of infection given in the paper is not relevant evidence will be downgraded for indirectness</p> <p>TG agreed that we will use the definition of an acute exacerbation given in the paper and downgrade by 1 or 2 if it does not match accepted definitions (see EMA 2002)</p> <p>1) Fuchs definition (original form (4/16 symptoms leading to IV antibiotic treatment) or modified form (4/16 symptoms leading to any change in antibiotic therapy))</p> <p>or</p> <p>2) European CF Society Consensus definition: “need for additional antibiotic treatment as indicated by a recent change in at least 2 of six defined symptoms”.</p>

## D.14 Pulmonary Infection - Antimicrobial agents for chronic pulmonary infection

Item	Details
Key issue in the scope	<p>Antimicrobial management in CF to:</p> <ul style="list-style-type: none"> <li>• Prevent bacterial colonisation</li> <li>• Treat acute pulmonary infection</li> </ul>

Item	Details
	<ul style="list-style-type: none"> <li>• Treat chronic pulmonary infection, including clinical exacerbations and colonisation</li> </ul>
Review question in the scope	<p>What is the effectiveness of antimicrobial treatment to:</p> <ul style="list-style-type: none"> <li>• Prevent bacterial colonisation</li> <li>• Treat acute pulmonary infection</li> <li>• Treat chronic pulmonary infection, including clinical exacerbations and colonisation</li> </ul>
Review question for the protocol	<p>What is the effectiveness of antimicrobial regimens in suppressing chronic pulmonary infection in children and adults with CF with any of the following pathogens:</p> <ul style="list-style-type: none"> <li>• <i>Pseudomonas aeruginosa</i></li> <li>• <i>Burkholderia cepacia complex</i></li> <li>• <i>Staphylococcus aureus</i></li> <li>• <i>Aspergillus fumigatus</i></li> </ul>
Objective	<p>The aim of this review is to determine the clinical and cost-effectiveness of treatment with antimicrobial regimens to suppress chronic pulmonary infection in people with cystic fibrosis.</p> <p>Regimens aimed at bacterial suppression can be continuous or intermittent For example, options for suppressive treatments for P aeruginosa include colistimethate sodium which is given continuously and tobramycin or aztreonam which are given month on, month off with or without a second antibiotic in the intercurrent months. Inhaled and intravenous antibiotics are used to suppress pulmonary infection.</p> <p>In some parts of the UK it is practice to schedule additional intermittent 2 week IV antimicrobial therapy (e.g. every 3 months) to ensure cover where there may have been non-adherence to suppressive antimicrobial treatment at home. Although this practice may be protective for lung disease when young, there is a concern that long term side effects can develop by adulthood e.g. hearing loss or renal failure associated with tobramycin. This review also aims to examine the clinical and cost-effectiveness of scheduled intermittent IV antimicrobial therapy in addition to oral/nebulised chronic suppressive therapy.</p>
Language	English
Study design	<ul style="list-style-type: none"> <li>• Systematic reviews of RCTs</li> <li>• RCTs</li> <li>• Conference abstracts of RCTs (Only if RCTs unavailable and the quality assessment of abstracts will conducted based on the available information and if necessary the authors of abstracts will be contacted).</li> </ul>
Population and directness	<p>Children and adults with cystic fibrosis (diagnosed clinically and by sweat test or genetic testing) and chronic pulmonary infection without an exacerbation of their pulmonary disease with one of the following specific pathogens identified in sputum/airway cultures:</p> <ul style="list-style-type: none"> <li>• <i>Pseudomonas aeruginosa</i></li> <li>• <i>Burkholderia cepacia complex</i></li> <li>• <i>Staphylococcus aureus</i></li> <li>• <i>Aspergillus fumigatus</i></li> </ul> <p>Population size and indirectness:</p> <ul style="list-style-type: none"> <li>• Studies where N&lt;30 (N&lt;15 for crossover trials) will not be included.</li> <li>• Studies with indirect populations will not be considered.</li> </ul>
Stratified, subgroup and adjusted analyses	<p>Stratified analyses:</p> <ul style="list-style-type: none"> <li>• Type of pathogen</li> <li>• Route of administration</li> <li>• Duration of treatment</li> </ul>

Item	Details
	<p>Sensitivity analysis: In the presence of heterogeneity, sensitivity analysis will be conducted including and excluding studies with a high risk of bias.</p> <p>In the presence of heterogeneity, the following subgroups will be considered for subgroup analysis:</p> <ul style="list-style-type: none"> <li>• Patients known to be receiving treatment with immunomodulatory agents and/or mucolytic agents</li> <li>• Patients with prior exposure to the treatment (prior vs naïve)</li> </ul> <p>Important confounders to be considered if comparative observational studies are included:</p> <ul style="list-style-type: none"> <li>• Concurrent treatment with immunomodulatory and/or mucolytic agents</li> <li>• Any other confounders noted in studies</li> <li>• Age is not considered to be an important confounder</li> </ul>
Intervention	<p><b>For <i>Burkholderia cepacia</i> complex</b></p> <ul style="list-style-type: none"> <li>• Ceftazidime* (inhaled)</li> <li>• Cotrimoxazole (oral)</li> <li>• Meropenem* (inhaled)</li> <li>• Imipenem (oral)</li> <li>• Trimethoprim (oral)</li> </ul> <p><b>For <i>Staphylococcus aureus</i></b></p> <ul style="list-style-type: none"> <li>• Flucloxacillin (oral)</li> <li>• Cotrimoxazole (oral)</li> <li>• Doxycycline (oral)</li> <li>• Cefradine (oral)</li> </ul> <p><b>For <i>Pseudomonas aeruginosa</i></b></p> <ul style="list-style-type: none"> <li>• Colistimethate sodium* (dry powder, inhaled)</li> <li>• Tobramycin (dry powder, inhaled)</li> <li>• Aztreonam lysine* (inhaled)</li> <li>• Azithromycin (oral, antibiotic-dose only)</li> <li>• Ciprofloxacin (oral)</li> <li>• Fosfomycin (inhaled)</li> </ul> <p><b>For <i>Aspergillus fumigatus</i></b></p> <ul style="list-style-type: none"> <li>• Itraconazole (oral)</li> <li>• Voriconazole (oral)</li> <li>• Amphotericin (inhaled)</li> <li>• Posaconazole (oral)</li> </ul>
Comparison	<ul style="list-style-type: none"> <li>• Placebo</li> <li>• No treatment</li> <li>• The antibiotics listed in the interventions group (other than the one tested as intervention)</li> <li>• Different combinations of drugs</li> </ul>
Outcomes	<ul style="list-style-type: none"> <li>• Lung function: <ul style="list-style-type: none"> <li>◦ FEV1</li> </ul> </li> </ul>

Item	Details
	<ul style="list-style-type: none"> <li>○ CT Scans for under 5s</li> <li>● Time to next pulmonary exacerbation</li> <li>● Number of patients with at least 1 pulmonary exacerbation</li> <li>● Eradication of the specified organism from sputum/airway cultures</li> <li>● Nutritional status (BMI, weight/ height)</li> <li>● Quality of life (CF-QOL, CFQR)</li> <li>● Adverse events:               <ul style="list-style-type: none"> <li>○ mild, that require transient discontinuation of treatment</li> <li>○ severe, that require discontinuation of treatment</li> </ul> </li> <li>● Emergence of resistant organisms/ antibiotic resistance</li> </ul> <p>Note: change from baseline will be prioritised over absolute values</p>
Importance of outcomes	<p>Critical outcomes for decision making:</p> <ul style="list-style-type: none"> <li>● FEV1</li> <li>● Time to next pulmonary exacerbation</li> </ul>
Setting	<p>All settings in which NHS-commissioned health and social care is provided.</p>
Search strategy	<p>Sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA, Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase</p> <p>Limits (e.g. date, study design): Apply standard exclusions and English language filters. Limit to RCTs and systematic reviews in the first instance but download all study designs.</p> <p>Supplementary search techniques: No supplementary search techniques were used.</p> <p>See appendix E.9.3 for full strategies</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>● The methodological quality of each study will be assessed using an appropriate checklist as per NICE guidelines manual (The Cochrane Risk of Bias tool for RCTs).</li> <li>● The quality of the evidence will be assessed by GRADE for each outcome according to the process described in the NICE guidelines manual (2014).</li> </ul> <p>Synthesis of data:</p> <ul style="list-style-type: none"> <li>● Meta-analysis will be conducted where appropriate</li> <li>● Network meta-analysis will be conducted for chronic infection with each organism where there is sufficient evidence for an outcome (see separate protocol).</li> <li>● Final and change scores will be pooled and if any study reports both, change scores will be used in preference over final scores.</li> <li>● If studies only report p-values from parametric analyses, and 95% CIs cannot be calculated from other data provided, this information will be plotted in GRADE tables, but evidence may be downgraded.</li> <li>● If studies only report p-values from non-parametric analyses, this information will be plotted in GRADE tables without downgrading the evidence, as imprecision cannot be assessed for non-parametric analyses.</li> </ul> <p>Minimal important differences (MIDs):</p> <ul style="list-style-type: none"> <li>● Eradication of the specified organism from sputum/airway cultures (complete eradication): any difference will be considered clinically significant</li> <li>● FEV1: 3 percentage points</li> <li>● CT Scans for under 5s: resolution of all inflammatory scans</li> </ul>

Item	Details
	<ul style="list-style-type: none"> <li>• Time to next exacerbation: any difference will be considered clinically significant</li> <li>• Nutritional status (BMI, weight/ height): GRADE default</li> <li>• Quality of life: CF-QOL = 5; CFQ-R = 4</li> <li>• Adverse events: GRADE default</li> <li>• Serious adverse events leading to discontinuation of treatment: any difference will be considered clinically significant</li> <li>• Emergence of resistant organisms/ antibiotic resistance: GRADE default</li> </ul> <p>Default MIDs: 0.8 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes.</p> <p>Review process:</p> <ul style="list-style-type: none"> <li>• This question will be prioritised for dual weeding.</li> <li>• This question will be prioritised for data extraction.</li> <li>• A list of excluded studies will be provided following weeding.</li> <li>• Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>• Psychological and behavioural issues are more likely in people with a lower socioeconomic status</li> <li>• Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care</li> <li>• Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	<p>Cystic fibrosis Trust, “ANTIBIOTIC TREATMENT FOR CYSTIC FIBROSIS”. Retrieved from: <a href="https://www.cysticfibrosis.org.uk/media/82010/CD_Antibiotic_treatment_for_CF_May_09.pdf">https://www.cysticfibrosis.org.uk/media/82010/CD_Antibiotic_treatment_for_CF_May_09.pdf</a></p> <p>Note in evidence tables (see corresponding NMA protocol):</p> <ul style="list-style-type: none"> <li>• Prior exposure to study drug</li> <li>• Baseline values (for FEV1)</li> <li>• Current treatment with mucolytic agents</li> <li>• Current treatment with immunomodulatory agents</li> <li>• Age</li> </ul>

## D.15 Immunomodulatory agents

Item	Details
Key issue in the scope	Immunomodulatory management in chest disease.
Review question in the scope	What is the effectiveness of immunomodulatory agents in the management of lung disease (for example corticosteroids, azithromycin)?
Review question	What is the effectiveness of immunomodulatory agents in the management of lung disease?
Objective	The aim of this review is to determine the clinical and cost effectiveness of immunomodulatory agents in reducing pulmonary inflammation in children and young people and adults with cystic fibrosis.
Language	English
Study design	<ul style="list-style-type: none"> <li>• Systematic reviews of RCTs</li> <li>• RCTs</li> <li>• Conference abstracts of RCTs (Only if RCTs unavailable and the quality assessment of abstracts will be conducted based on the available information and</li> </ul>

Item	Details
	<p>if necessary the authors of abstracts will be contacted).</p> <ul style="list-style-type: none"> <li>• Comparative cohort studies (only if RCTs unavailable or limited data to inform decision making)</li> </ul>
Population and directness	<p>Children and young people with cystic fibrosis (diagnosed clinically and by sweat test or genetic testing) with lung disease.</p> <p>Population size and indirectness:</p> <ul style="list-style-type: none"> <li>• Studies where N&lt;20 will not be included.</li> <li>• Studies with indirect populations will not be considered.</li> </ul>
Stratified, subgroup and adjusted analyses	<p>Groups that will be reviewed and analysed separately, if possible:</p> <ul style="list-style-type: none"> <li>• Children</li> <li>• Young people and adults</li> <li>• People with chronic lung disease</li> <li>• People with acute exacerbations</li> <li>• People with allergic bronchopulmonary aspergillosis (ABPA)</li> </ul> <p>In the event of heterogeneity, analysis will be conducted excluding studies with high-risk of bias.</p> <p>In the presence of heterogeneity, the following subgroups will be considered for sensitivity analysis:</p> <ul style="list-style-type: none"> <li>• Chronic Pseudomonas</li> <li>• Duration of treatment</li> </ul>
Intervention	<ul style="list-style-type: none"> <li>• Inhaled corticosteroids <ul style="list-style-type: none"> <li>◦ Beclamethozone</li> <li>◦ Budesimide</li> <li>◦ Fluticazone</li> </ul> </li> <li>• Oral and IV Corticosteroids <ul style="list-style-type: none"> <li>◦ IV Methylprednisolone</li> <li>◦ Oral Prednisolone</li> </ul> </li> <li>• Macrolide antibiotics <ul style="list-style-type: none"> <li>◦ Azithromycin</li> </ul> </li> <li>• NSAIDs <ul style="list-style-type: none"> <li>◦ Ibuprofen</li> </ul> </li> <li>• Monoclonal antibody <ul style="list-style-type: none"> <li>◦ Omalizumab</li> </ul> </li> </ul>
Comparison	<ul style="list-style-type: none"> <li>• Placebo</li> <li>• Treatment A vs treatment B</li> </ul>
Outcomes	<ul style="list-style-type: none"> <li>• Lung function: <ul style="list-style-type: none"> <li>◦ forced expiratory volume in one second (FEV1)</li> </ul> </li> <li>• Quality of life measures (CF-QOL, CF-QR)</li> <li>• Nutritional status as noted by weight gain, body mass index, z score or other indices of nutritional state</li> <li>• Time to next pulmonary exacerbation</li> <li>• Adverse effects: <ul style="list-style-type: none"> <li>◦ Growth retardation</li> <li>◦ Reduction in bone mineral density</li> <li>◦ Cataracts</li> <li>◦ Renal failure</li> <li>◦ Diabetes</li> </ul> </li> </ul>

Item	Details
	<ul style="list-style-type: none"> <li>○ Deafness</li> <li>○ Cardiac arrhythmia</li> <li>○ Abdominal pain (for ibuprofen use)</li> <li>● Mortality</li> </ul> <p>Note: change from baseline will be prioritised over absolute values</p>
Importance of outcomes	<p>Critical outcomes for decision making:</p> <ul style="list-style-type: none"> <li>● Forced expiratory volume in one second (FEV1)</li> <li>● Time to next exacerbation</li> <li>● Adverse events (particularly growth retardation in children)</li> </ul>
Setting	All settings in which NHS-commissioned health and social care is provided.
Search strategy	<p>Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase</p> <p>Limits (e.g. date, study design): Apply standard exclusions and English language filters. Limit to RCTs and systematic reviews unless overall return is small</p> <p>Supplementary search techniques: No supplementary search techniques will be used.</p> <p>See appendix E.10 for full strategies</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>● The methodological quality of each study will be assessed using an appropriate checklist as per NICE guidelines manual (The Cochrane Risk of Bias tool for RCTs and the Newcastle and Ottawa scale for observational studies).</li> <li>● The quality of the evidence will be assessed by GRADE for each outcome according to the process described in the NICE guidelines manual (2014).</li> </ul> <p>Synthesis of data:</p> <ul style="list-style-type: none"> <li>● Meta-analysis will be conducted where appropriate.</li> <li>● If comparative cohort studies are included, the minimum number of events per covariate to be recorded to ensure accurate multivariate analysis.</li> <li>● Final and change scores will be pooled and if any study reports both, change scores will be used in preference over final scores.</li> <li>● If studies only report p-values from parametric analyses, and 95% CIs cannot be calculated from other data provided, this information will be plotted in GRADE tables, but evidence may be downgraded.</li> <li>● If studies only report p-values from non-parametric analyses, this information will be plotted in GRADE tables without downgrading the evidence, as imprecision cannot be assessed for non-parametric analyses.</li> </ul> <p>Minimal important differences (MIDs):</p> <ul style="list-style-type: none"> <li>● FEV1: 2 percentage points</li> <li>● Change in number of respiratory exacerbations: any difference will be considered clinically significant</li> <li>● Quality of life measures: CF-QOL = 5; CFQ-R = 8.5</li> <li>● Nutritional status as noted by weight gain, body mass index, z score or other indices of nutritional state = GRADE default</li> <li>● Time to next pulmonary exacerbation: any difference will be considered clinically significant</li> <li>● Adverse effects: GRADE default</li> <li>● Adverse events that lead to discontinuation of treatment: any difference will be considered clinically significant</li> <li>● Mortality: any difference will be considered clinically significant</li> </ul>

Item	Details
	<p>Default MIDs: 0.8 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes.</p> <p>Review process:</p> <ul style="list-style-type: none"> <li>• This question will be prioritised for dual weeding.</li> <li>• This question will be prioritised for data extraction.</li> <li>• A list of excluded studies will be provided following weeding.</li> <li>• Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>• Psychological and behavioural issues are more likely in people with a lower socioeconomic status</li> <li>• Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care</li> <li>• Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	<p>Relevant Cochrane reviews include:</p> <ul style="list-style-type: none"> <li>• Oral steroids for long-term use in cystic fibrosis</li> <li>• Oral non-steroidal anti-inflammatory drug therapy for lung disease in cystic fibrosis</li> <li>• Macrolide antibiotics for cystic fibrosis</li> </ul> <p>Anti-IgE therapy for allergic bronchopulmonary aspergillosis in people with cystic fibrosis. Cochrane Database of Systematic Reviews 2013, Issue 9. Art. No.: CD010288.) but it includes only one unpublished trial.</p>

## D.16 Nutritional interventions

Item	Details
Key issue in the scope	Management of nutrition.
Review question in the scope	What is the effectiveness of nutritional interventions in cystic fibrosis?
Review question for the protocol	What is the clinical and cost effectiveness of nutritional interventions in people with cystic fibrosis?
Objective	<p>Nutritional status is a strong predictor of morbidity and mortality in people with CF and malnutrition is a common problem due to faecal fat loss, increased energy requirements due to chronic infections and because people with CF often suffer from pancreatic insufficiency, resulting in malabsorption.</p> <p>While guideline recommends that people with CF should intake up to twice the recommended daily caloric intake, this can be difficult to achieve because they may have reduced appetite, infection-related anorexia, gastro-oesophageal reflux or abdominal pain.</p> <p>This review aims to determine which nutritional intervention achieves the best outcomes for people with cystic fibrosis.</p>
Language	English
Study design	<ul style="list-style-type: none"> <li>• Systematic review of RCTs</li> <li>• RCTs</li> <li>• Conference abstracts of RCTs (Only if RCTs unavailable and the quality assessment of abstracts will conducted based on the available information and if necessary the authors of abstracts will be contacted).</li> <li>• Observational studies (only if RCTs unavailable or limited data to inform decision making)</li> </ul>

Item	Details
	<p>Exclusions:</p> <ul style="list-style-type: none"> <li>• Cross-over RCTs are not an appropriate design for this review.</li> <li>• Only articles published after 1997 will be considered. Woestenenk (2013) states that “as CF treatment, and thus the nutritional status of patients has changed during the last 15 years, effectiveness of nutritional interventions might have changed too”</li> </ul>
Population and directness	<p>Infants, children, young people and adults with defined CF, diagnosed clinically and by sweat test or genetic testing</p> <p>Population size and indirectness:</p> <ul style="list-style-type: none"> <li>• No sample size specification.</li> <li>• Studies with indirect populations will not be included</li> </ul>
Stratified, subgroup and adjusted analyses	<p>Groups that will be reviewed and analysed separately if data are available:</p> <ul style="list-style-type: none"> <li>• Infants (&lt;12 months)</li> <li>• Children (less than 12 years)</li> <li>• Young people (12-17 years)</li> <li>• Adults (≥18 years)</li> <li>• gender (male vs female)</li> </ul> <p>Sensitivity analysis:</p> <p>In the presence of heterogeneity, sensitivity analysis will be conducted including and excluding studies with a high risk of bias.</p> <p>In the presence of heterogeneity, the following subgroups will be considered for subgroup analysis:</p> <ul style="list-style-type: none"> <li>• duration of the study</li> </ul>
Intervention	<ul style="list-style-type: none"> <li>• Dietary advice including increase in conventional food {snacks}, high energy foods.</li> <li>• Oral supplementary prescribed feeds</li> <li>• enteral tube feeding</li> <li>• psychological and behavioural interventions (Such as managing meal times {children} and disturbed eating behaviour and body image disorders {adults})</li> <li>• appetite stimulants (cyproheptadine, megestrol)</li> </ul>
Comparison	<ul style="list-style-type: none"> <li>• Usual care</li> <li>• Placebo</li> <li>• Other intervention</li> </ul> <p>(There may be more specific comparisons for certain groups within CF, Committee to advise on relevant comparisons)</p>
Outcomes	<ul style="list-style-type: none"> <li>• Change in weight or height or body mass index (BMI) or z score or other indices of nutrition or growth</li> <li>• Lung function: FEV1</li> <li>• Pulmonary exacerbations</li> <li>• Changes to body composition detected by anthropometric measure (weight or height or body mass index (BMI) or z score or other indices of nutrition or growth)</li> <li>• Adverse effects including diarrhoea, reduced appetite, abdominal bloating, episodes of distal intestinal obstruction syndrome; for appetite stimulants the following adverse effects will also be considered: high blood glucose and adrenal insufficiency (decreased cortisol levels)</li> <li>• Quality of life (CF-QOL, CFQR)</li> <li>• Patient and parent or carer satisfaction</li> <li>• Note: change from baseline will be prioritised over absolute values</li> </ul>
Importance of	Critical outcomes for decision making:

Item	Details
outcomes	<ul style="list-style-type: none"> <li>• Lung function: FEV1</li> <li>• Quality of life (CF-QOL, CFQR)</li> <li>• Changes to body composition detected by anthropometric measure (weight or height or body mass index (BMI) or z score or other indices of nutrition or growth)</li> </ul>
Setting	All settings in which NHS-commissioned health and social care is provided.
Search strategy	<p>Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase</p> <p>Limits (e.g. date, study design): Apply standard exclusions and English language filters. Limit to RCTs, systematic reviews and observational studies.</p> <p>Supplementary search techniques: No supplementary search techniques will be used.</p> <p>See appendix E.11 for full strategies</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>• The methodological quality of each study will be assessed using an appropriate checklist as per NICE guidelines manual (The Cochrane Risk of Bias tool for RCTs and the Newcastle and Ottawa scale for observational studies).</li> <li>• The quality of the evidence will be assessed by GRADE for each outcome according to the process described in the NICE guidelines manual (2014).</li> </ul> <p>Synthesis of data:</p> <ul style="list-style-type: none"> <li>• Meta-analysis will be conducted where appropriate.</li> <li>• Final and change scores will be pooled and if any study reports both, change scores will be used in preference over final scores.</li> <li>• If studies only report p-values from parametric analyses, and 95% CIs cannot be calculated from other data provided, this information will be plotted in GRADE tables, but evidence may be downgraded.</li> <li>• If studies only report p-values from non-parametric analyses, this information will be plotted in GRADE tables without downgrading the evidence, as imprecision cannot be assessed for non-parametric analyses</li> </ul> <p>Minimal important differences (MIDs):</p> <ul style="list-style-type: none"> <li>• Change in weight or height or body mass index (BMI) or z score or other indices of nutrition or growth = GRADE default</li> <li>• FEV1 = 5 percentage points</li> <li>• Pulmonary exacerbations = any change will be considered clinically significant</li> <li>• Adverse effects including diarrhoea, reduced appetite, abdominal bloating, episodes of distal intestinal obstruction syndrome; for appetite stimulants the following adverse effects will also be considered: high blood glucose and adrenal insufficiency (decreased cortisol levels) = GRADE default</li> <li>• Quality of life: CF-QOL = 5; CFQ-R = 8.5</li> <li>• Patient and parent or carer satisfaction = GRADE default</li> </ul> <p>Default MIDs: 0.8 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes.</p> <ul style="list-style-type: none"> <li>• Review process:</li> <li>• A list of excluded studies will be provided following weeding.</li> <li>• Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>• Psychological and behavioural issues are more likely in people with a lower socioeconomic status</li> <li>• Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care</li> </ul>

Item	Details
	<ul style="list-style-type: none"> <li>Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	<p>Key papers:</p> <p>Nutritional intervention in patients with Cystic Fibrosis: A systematic review, Woestenenk 2013</p> <p>Use of oral supplements to increase calorie intake in people with cystic fibrosis (Cochrane Review), Smyth 2014</p>

## D.17 Exocrine pancreatic insufficiency

Item	Details
Key issue in the scope	Management of exocrine pancreatic insufficiency.
Review question in the scope	Gastrointestinal manifestations: What is the effectiveness of enzyme replacement in the treatment of exocrine pancreatic insufficiency?
Review question for the protocol	In people with cystic fibrosis, what is the most effective regimen of enzyme replacement therapy in the treatment of exocrine pancreatic insufficiency?
Objective	<p>Cystic fibrosis is the most common cause of pancreatic insufficiency in children and the reported prevalence within this group is 80% to 90%.</p> <p>The CF gene defect results in a thickening of the pancreatic secretions and accumulation of these causes obstruction eventually leading to pancreatic damage. Pancreatic enzyme insufficiency prevents digestion and absorption of nutrients, resulting in nutrient malabsorption and other symptoms such as diarrhoea. These in turn can affect quality of life and eventually result in malnutrition.</p> <p>Pancreatic enzyme supplementation is the standard of care for fat malabsorption among patients with exocrine pancreatic insufficiency. Treatment is started when clinically significant malabsorption occurs resulting in steatorrhea and weight loss. Treatment failure is addressed in a sequential fashion.</p> <p>Effective therapy has been limited by the ability to replicate the physiologic process of enzyme delivery to the duodenum, at the appropriate time. The challenges include enzyme destruction in the stomach, lack of adequate mixing with the chyme in the duodenum, and failing to deliver and activate at the appropriate time.</p> <p>The aim of this evidence review is to establish the most effective regimen enzyme replacement therapy in the treatment of exocrine pancreatic insufficiency.</p>
Language	English
Study design	<ul style="list-style-type: none"> <li>Systematic reviews of RCTs</li> <li>RCTs</li> <li>Conference abstracts of RCTs (Only if RCTs unavailable and the quality assessment of abstracts will conducted based on the available information and if necessary the authors of abstracts will be contacted).</li> <li>Comparative cohort studies (only if RCTs unavailable or limited data to inform decision making)</li> </ul> <p>Exclusions:</p> <ul style="list-style-type: none"> <li>Exclude studies which examine PERT for very short duration and do not reflect clinical situation e.g. 1 dose</li> <li>Exclude studies examining Panzytrat , Pancrease HL and Nutrizym 22 in paediatric populations.</li> <li>Exclude studies with less than 10 participants (parallel RCT) or 10 observations (crossover RCT).</li> </ul>
Population and	Children and adults with defined CF (diagnosed clinically and by sweat test or

Item	Details
directness	genetic testing) with exocrine pancreatic insufficiency requiring management. Population size and indirectness: <ul style="list-style-type: none"> <li>• No sample size specification.</li> <li>• Studies with indirect populations will not be included</li> </ul> Exclusions: <ul style="list-style-type: none"> <li>• People with tube feeding excluded</li> </ul>
Stratified, subgroup and adjusted analyses	Groups that will be reviewed and analysed separately: <ul style="list-style-type: none"> <li>• Children</li> <li>• Young people and adults</li> </ul> Sensitivity analysis: <ul style="list-style-type: none"> <li>• In the presence of heterogeneity, sensitivity analysis will conducted including and excluding studies with a high risk of bias.</li> </ul>
Intervention	Enteric coated pancreatic enzyme supplementation/replacement therapy. (PERT).
Comparison	<ul style="list-style-type: none"> <li>• ECT PERT 1 vs ECT PERT 1 + Acid suppression</li> <li>• ECT PERT high dose (Creon® 25 000, Creon® 40 000, Nutrizym 22®, Pancrease HL® or similar)</li> <li>• ECT PERT low dose (for example Creon® 10 000, Creon® Micro, Pancrex®, Pancrex V® or similar)</li> </ul>
Outcomes	<ul style="list-style-type: none"> <li>• Quality of life (CF-QOL, CFQR)</li> <li>• Weight and/or BMI (also %weight for height if available)</li> <li>• Satisfaction</li> <li>• Reduction of steatorrhoea and faecal fat (CFA and FFE specific outcomes and others)</li> <li>• Resolution of symptoms of malabsorption</li> <li>• Drug related side effects/adverse events</li> </ul> Time period for outcome measurement: <ul style="list-style-type: none"> <li>• Quality of Life and symptoms – days</li> <li>• Weight – 1-2 weeks</li> <li>• Nutrition – days</li> <li>• Note: change from baseline will be prioritised over absolute values</li> </ul>
Importance of outcomes	Critical outcomes for decision making: <ul style="list-style-type: none"> <li>• Reduction of steatorrhoea and faecal fat (CFA and FFE specific outcomes and others)</li> <li>• Weight and/or BMI (also %weight for height if available)</li> <li>• Resolution of symptoms of malabsorption</li> </ul>
Setting	All settings in which NHS-commissioned health and social care is provided.
Search strategy	Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase Limits (e.g. date, study design): Limit to English language only where possible (Medline and Embase). Limit to RCTs and systematic reviews unless overall return is small Supplementary search techniques: No supplementary search techniques will be used. See appendix E.12 for full strategies
Review strategy	Appraisal of methodological quality: <ul style="list-style-type: none"> <li>• The methodological quality of each study will be assessed using an appropriate checklist as per NICE guidelines manual (The Cochrane Risk of Bias tool for RCTs and the Newcastle and Ottawa scale for observational</li> </ul>

Item	Details
	<p>studies).</p> <ul style="list-style-type: none"> <li>The quality of the evidence will be assessed by GRADE for each outcome according to the process described in the NICE guidelines manual (2014).</li> </ul> <p>Synthesis of data:</p> <ul style="list-style-type: none"> <li>Meta-analysis will be conducted where appropriate.</li> <li>Final and change scores will be pooled and if any study reports both, change scores will be used in preference over final scores.</li> <li>If studies only report p-values from parametric analyses, and 95% CIs cannot be calculated from other data provided, this information will be plotted in GRADE tables, but evidence may be downgraded.</li> <li>If studies only report p-values from non-parametric analyses, this information will be plotted in GRADE tables without downgrading the evidence, as imprecision cannot be assessed for non-parametric analyses</li> </ul> <p>Minimal important differences (MIDs):</p> <ul style="list-style-type: none"> <li>Health related Quality of Life: CF-QOL = 5; CFQ-R = 4</li> <li>Weight and/or BMI (also %weight for height if available): GRADE default</li> <li>Satisfaction: GRADE default</li> <li>Reduction of steatorrhoea and faecal fat (CFA and FFE specific outcomes and others): GRADE default</li> <li>Resolution of symptoms of malabsorption: GRADE default</li> <li>Drug related side effects/adverse events: GRADE default</li> </ul> <p>Default MIDs: 0.8 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes.</p> <p>Review process:</p> <ul style="list-style-type: none"> <li>A list of excluded studies will be provided following weeding.</li> <li>Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>Psychological and behavioural issues are more likely in people with a lower socioeconomic status</li> <li>Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care</li> <li>Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	<p>Cochrane reviews:</p> <p>PERT  <a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008227.pub2/pdf">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008227.pub2/pdf</a>  Gastric Acid suppression  <a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003424.pub3/pdf">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003424.pub3/pdf</a>  Systematic review: efficacy and safety of pancreatic enzyme supplements for exocrine pancreatic insufficiency (Taylor 2010)  <a href="http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2036.2009.04157.x/pdf">http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2036.2009.04157.x/pdf</a>  Guidelines also exist eg  Evidence-based practice recommendations for nutrition-related management of children and adults with cystic fibrosis and pancreatic insufficiency: results of a systematic review  <a href="http://www.ncbi.nlm.nih.gov/pubmed/18442507">http://www.ncbi.nlm.nih.gov/pubmed/18442507</a>  Pancreatic enzyme replacement therapy in cystic fibrosis: Australian guidelines. Pediatric Gastroenterological Society and the Dietitians Association of Australia. J Paediatr Child Health. 1999 Apr;35(2):125-9.  <a href="http://www.ncbi.nlm.nih.gov/pubmed/10365346">http://www.ncbi.nlm.nih.gov/pubmed/10365346</a></p>

## D.18 Treatment and secondary prevention for distal ileal obstruction syndrome

Item	Details
Issue in the scope	Management of distal ileal obstruction syndrome.
Review question in the scope	What are the effective strategies for treatment and secondary prevention of distal ileal obstruction syndrome?
Review question for the protocol	What are the effective strategies for treatment and secondary prevention of distal ileal obstruction syndrome?
Objective	This review aims to identify the effective strategies of primary treatment (acute treatment) in those with a diagnosis of CF and DIOS. Additionally, this review aims to identify the effective strategies for the secondary prevention of DIOS.
Language	English
Study design	<ul style="list-style-type: none"> <li>• Systematic reviews of RCTs</li> <li>• RCTs</li> <li>• Conference abstracts of RCTs (Only if RCTs unavailable and the quality assessment of abstracts will be conducted based on the available information and if necessary the authors of abstracts will be contacted).</li> <li>• Comparative cohort studies (only if RCTs unavailable or limited data to inform decision making)</li> </ul>
Population and directness	<p>Primary prevention</p> <p>Infants, children, young people and adults with CF, diagnosed clinically and by sweat test or genetic testing and DIOS based on clinical diagnosis with or without imaging studies.</p> <p>Secondary prevention</p> <p>Infants, children, young people and adults with CF, diagnosed clinically and by sweat test or genetic testing and one or more previous episodes of DIOS.</p> <p>Population size and indirectness:</p> <ul style="list-style-type: none"> <li>• No sample size specification.</li> <li>• Studies with indirect populations will not be included</li> </ul>
Stratified, subgroup and adjusted analyses	<p>Stratified analysis:</p> <ul style="list-style-type: none"> <li>• primary treatment</li> <li>• secondary prevention</li> </ul> <p>Sensitivity analysis: including and excluding studies with a high risk of bias.</p> <p>Subgroup analysis:</p> <ul style="list-style-type: none"> <li>• None identified</li> </ul>
Intervention	<p>Primary (acute) interventions</p> <ul style="list-style-type: none"> <li>• osmotic laxative containing polyethylene glycol (macrogol)(movicol)</li> <li>• sodium meglumine diatrizoate (Gastrografin)</li> <li>• N-acetyl cysteine</li> <li>• Lactulose</li> <li>• Stimulant laxative e.g. senna/ sennosides, sodium picosulfate</li> <li>• Enemas (phosphate, gastrografin)</li> <li>• Surgery for example distal ileal resection</li> </ul> <p>Secondary prevention interventions</p> <ul style="list-style-type: none"> <li>• Osmotic laxative containing polyethylene glycol (macrogol)</li> <li>• Lactulose</li> <li>• Pancreatic enzyme replacement therapy (PERT)</li> <li>• N-acetyl cysteine</li> <li>• Sodium meglumine diatrizoate (Gastrografin)</li> </ul> <p>Administration of oral treatments may also be via nasogastric tube and this is</p>

Item	Details
	included within the protocol.
Comparison	<ul style="list-style-type: none"> <li>• Treatment 1 vs Treatment 2</li> <li>• Placebo</li> <li>• No treatment</li> </ul>
Outcomes	<p>Primary treatment</p> <p>1) Reduction in clinical manifestations including:</p> <ul style="list-style-type: none"> <li>○ Abdominal pain</li> <li>○ Vomiting</li> <li>○ Distention</li> <li>○ Abdominal mass (also by radiological imaging X-ray/ultrasound)</li> <li>○ Stool frequency</li> </ul> <p>2) Adverse events from treatment</p> <ul style="list-style-type: none"> <li>○ abdominal pain</li> <li>○ flatulence</li> <li>○ nausea or vomiting</li> <li>○ diarrhoea</li> <li>○ fluid overload</li> <li>○ bowel perforation</li> <li>○ bowel ischemia</li> <li>○ hypotension</li> </ul> <p>3) Patient satisfaction (including adherence to treatment)</p> <p>4) Duration of hospital stay (days)</p> <p>5) Treatment failure (need for surgery)</p> <p>6) Adverse events from surgery</p> <ul style="list-style-type: none"> <li>○ Mortality</li> <li>○ Perforation/Infection</li> </ul> <p>Secondary prevention</p> <p>Outcomes 1, 2, 3 above and</p> <p>4) Recurrence of DIOS</p> <p>5) Admission to hospital</p> <p>Note: change from baseline will be prioritised over absolute values</p>
Importance of outcomes	<p>Critical outcomes for decision making:</p> <p>Primary treatment</p> <ul style="list-style-type: none"> <li>• Reduction in clinical manifestations</li> <li>• Adverse events for treatment/ surgery</li> <li>• Treatment failure</li> </ul> <p>Secondary treatment</p> <ul style="list-style-type: none"> <li>• Reduction in clinical manifestations</li> <li>• Adverse events for treatment</li> <li>• Recurrence of DIOS</li> </ul>
Setting	Any healthcare setting where NHS care is delivered (primary, secondary, tertiary or community).
Search strategy	<p>Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase</p> <p>Limits (e.g. date, study design): Limit to RCTs and systematic reviews in the first instance but download all study designs. Apply standard exclusions and English language filters.</p> <p>Supplementary search techniques: No supplementary search techniques will be used.</p>

Item	Details
	See appendix E.13 for full strategies
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>The methodological quality of each study will be assessed using an appropriate checklist as per NICE guidelines manual (The Cochrane Risk of Bias tool for RCTs and the Newcastle and Ottawa scale for observational studies).</li> <li>The quality of the evidence will be assessed by GRADE for each outcome according to the process described in the NICE guidelines manual (2014).</li> </ul> <p>Synthesis of data:</p> <ul style="list-style-type: none"> <li>Meta-analysis will be conducted where appropriate. If comparative cohort studies are included, the minimum number of events per covariate to be recorded to ensure accurate multivariate analysis.</li> <li>Final and change scores will be pooled and if any study reports both, change scores will be used in preference over final scores.</li> <li>If studies only report p-values from parametric analyses, and 95% CIs cannot be calculated from other data provided, this information will be plotted in GRADE tables, but evidence may be downgraded.</li> <li>If studies only report p-values from non-parametric analyses, this information will be plotted in GRADE tables without downgrading the evidence, as imprecision cannot be assessed for non-parametric analyses.</li> </ul> <p>Minimal important differences (MIDs):</p> <p>Primary treatment</p> <ul style="list-style-type: none"> <li>Reduction in clinical manifestations: any change will be considered clinically significant</li> <li>Treatment failure: GRADE default</li> <li>Adverse events for treatment/ surgery: GRADE default</li> </ul> <p>Secondary treatment</p> <ul style="list-style-type: none"> <li>Reduction in clinical manifestations: any change will be considered clinically significant</li> <li>Recurrence of DIOS: GRADE default</li> <li>Adverse events for treatment/ surgery: GRADE default</li> </ul> <p>Default MIDs: 0.8 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes.</p> <ul style="list-style-type: none"> <li>Review process:</li> <li>A list of excluded studies will be provided following weeding.</li> </ul> <p>Evidence tables and an evidence profile will be used to summarise the evidence.</p>
Equalities	<ul style="list-style-type: none"> <li>Psychological and behavioural issues are more likely in people with a lower socioeconomic status</li> <li>Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care</li> <li>Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	None.

## D.19 Monitoring for liver disease

Item	Details
Issue in the scope	Surveillance for cystic-fibrosis related liver disease and prevention of progression.
Review questions in the scope	What is the effectiveness of ultrasound scanning to detect clinically important cystic-fibrosis-related liver disease?

Item	Details
Review questions in the protocol	<ul style="list-style-type: none"> <li>1. What is the diagnostic accuracy of tests to detect/ strategies to detect early and late CF liver disease?</li> <li>2. What is the diagnostic and prognostic value of different strategies to detect CF liver disease and predict progression (including progression to cirrhosis and portal hypertension with (out) oesophageal varices)?</li> </ul>
Objective	<p>Diagnosis of CF liver disease is based on radiological methods (e.g. ultrasound scanning), biochemical tests, clinical methods (presence or absence of hepatosplenomegaly) and histological assessment. More recently liver stiffness testing using transient elastography has been developed although its use in CF patients is not well established. The estimated prevalence of hepatic fibrosis and liver disease is proposed to be between 26%-45% in patients with CF. Clinical presentation with hepatomegaly and/or splenomegaly is usually around 10 years of age.</p> <p>Progression of disease is from focal hepatic biliary fibrosis to development of cirrhosis and then portal hypertension with or without oesophageal varices. Early detection of hepatic injury and fibrosis allows treatment to be started (e.g. URSO).</p> <p>The gold standard test is a liver biopsy but in practice this is rarely performed (it is invasive, may miss focal lesions and has associated risks e.g. with respect to general anaesthesia or infection). Other gold standard tests are CT scanning and MRI scanning, however, although these investigations are not invasive, they are expensive and not routinely performed. More recently, definitions of liver disease have come into practice using recommendations based on the tests performed at clinical review e.g. CF liver disease is diagnosed if on at least 2 consecutive examinations spanning a one year period, two of the following conditions are met:</p> <ul style="list-style-type: none"> <li>Hepatomegaly (liver span &gt; 2cm below the costal margin on the medioclavicular line) confirmed by ultrasound</li> <li>Two abnormal (&gt; upper limit of normal) serum liver enzyme levels (ALT, AST, gammaGT)</li> <li>Ultrasound abnormalities other than hepatomegaly (increased heterogeneous echogenicity, nodularity, irregular margins)</li> </ul> <p>Current recommended practice is to offer an ultrasound test at annual review to determine a baseline value (from 5 years of age) and to monitor progression of disease thereafter. Clinical examination and biochemical liver tests may also be performed at this review and in interim periods as necessary.</p> <p>This review aims to assess the diagnostic accuracy of different diagnostic strategies to detect CF liver disease (including cirrhosis, portal hypertension and oesophageal varices) defined by gold standard tests and to identify whether any tests are useful in predicting the progression of CF liver disease.</p>
Language	English
Population and directness	<p>Infants, children, young people and adults with defined CF, diagnosed clinically and by sweat test or genetic testing.</p> <p>Population size and indirectness:</p> <ul style="list-style-type: none"> <li>Studies with indirect populations will not be considered.</li> <li>No restrictions to sample size.</li> </ul>
Subgroups and sensitivity analyses	<p>The following groups will be assessed separately if possible:</p> <ul style="list-style-type: none"> <li>Children</li> <li>Adults</li> </ul> <p>Sensitivity analysis:</p> <p>In the presence of heterogeneity sensitivity analysis will be conducted including and excluding studies with a high risk of bias.</p> <p>Important confounders:</p> <p>None identified</p>
Index tests	<ul style="list-style-type: none"> <li>Clinical examination (hepatomegaly, splenomegaly)</li> </ul>

Item	Details
	<ul style="list-style-type: none"> <li>• Liver function blood tests (AST, ALT, GGT, Alkaline phosphatase, bilirubin, albumin, platelets and clotting) and indices based on these tests (eg APRI, Forns score, INR ratio)</li> <li>• Imaging techniques – US</li> <li>• Liver stiffness measurement - transient elastography (Fibroscan)</li> <li>• Any of 1, 2, 3 or 4 alone or in combination</li> </ul>
Reference standard	<ul style="list-style-type: none"> <li>• Any of clinical examination, LFTs (AST, ALT, GGT) or ultrasound alone or in combination</li> <li>• Abdominal computed tomography (CT)</li> <li>• Magnetic resonance imaging (MRI)</li> <li>• Biopsy</li> </ul>
Outcomes	<p>For the diagnostic accuracy question:</p> <ul style="list-style-type: none"> <li>• Positive likelihood ratios/ Negative likelihood ratios (LR+/ LR-)</li> <li>• Sensitivity/ Specificity</li> <li>• Area under the curve (AUC)</li> </ul> <p>For the following target conditions:</p> <ul style="list-style-type: none"> <li>• Liver disease</li> <li>• Cirrhosis</li> <li>• Portal hypertension</li> <li>• Oesophageal varices</li> </ul> <p>For the prognostic question:</p> <ul style="list-style-type: none"> <li>• adjORs</li> <li>• adjHRs</li> </ul> <p>For the identification of:</p> <ul style="list-style-type: none"> <li>• Liver disease</li> <li>• Cirrhosis</li> <li>• Portal hypertension</li> </ul>
Importance of outcomes	<p>Critical outcomes for the diagnostic accuracy question:</p> <ul style="list-style-type: none"> <li>• Sensitivity/Specificity</li> <li>• Likelihood ratios</li> </ul> <p>Critical outcomes for the prognostic question:</p> <ul style="list-style-type: none"> <li>• Liver disease</li> <li>• Cirrhosis</li> <li>• Portal hypertension</li> </ul>
Study design	<ul style="list-style-type: none"> <li>• Test and treat studies</li> <li>• If test and treat studies not available we will aim to use both diagnostic accuracy and prognostic studies.</li> </ul> <p>For the diagnostic accuracy question:</p> <ul style="list-style-type: none"> <li>• Systematic reviews</li> <li>• Cross sectional diagnostic accuracy studies</li> <li>• Cohort studies (where cross-sectional data were reported therefore 2 x 2 table could be tabulated)</li> <li>• Case control studies will only be considered for inclusion where there is no evidence from cohort studies available</li> </ul> <p>For the prognostic question:</p> <ul style="list-style-type: none"> <li>• Systematic reviews</li> <li>• Prognostic cohort studies</li> </ul>
Setting	Any healthcare setting where NHS care is delivered (primary, secondary, tertiary or community).
Search strategy	Sources to be searched: Medline, Medline In-Process, Cochrane Central

Item	Details
	<p>Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase</p> <p>Limits (e.g. date, study design): Limit to English language only where possible (Medline and Embase). Apply standard exclusions filter.</p> <p>Supplementary search techniques: No supplementary search techniques will be used.</p> <p>See appendix E.14 for full strategies</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>• The methodological quality of each diagnostic study will be assessed using a quality checklist for diagnostic studies (QUADAS-2) as set out in the Developing NICE Guidelines Manual 2014.</li> <li>• For prognostic studies, the quality was assessed using the checklist created by Hayden et al. (2013) as set out in the Developing NICE Guidelines Manual 2014.</li> <li>• The quality of the evidence for an outcome (i.e. across studies) will be assessed using adapted GRADE approach.</li> </ul> <p>Synthesis of data: Meta-analysis will be conducted when appropriate. The cut-offs for diagnostic accuracy measures:</p> <ul style="list-style-type: none"> <li>• Sensitivity and specificity: <ul style="list-style-type: none"> <li>○ High &gt;90%</li> <li>○ Moderate 75-90%</li> <li>○ Low &lt;75%</li> </ul> </li> <li>• Positive likelihood ratio: <ul style="list-style-type: none"> <li>○ Very useful test &gt;10</li> <li>○ Moderately useful test 5-10</li> <li>○ Not a useful test &lt;5</li> </ul> </li> <li>• Negative likelihood ratio: <ul style="list-style-type: none"> <li>○ Very useful test &lt;0.1</li> <li>○ Moderately useful test 0.1 to 0.2</li> <li>○ Not a useful test &gt;0.2</li> </ul> </li> </ul> <p>Imprecision of results: The sensitivity and specificity of each diagnostic test will be considered. The judgement of precision for sensitivity and specificity separately will be based on visual inspection of the confidence interval of the sensitivity value (decided that a CI with a width of &lt;0.2 was deemed to be precise, ≥0.2 – 0.3 was downgraded to serious imprecision and ≥0.3 downgraded to very serious imprecision).</p> <ul style="list-style-type: none"> <li>• Review process:</li> <li>• A list of excluded studies will be provided following weeding.</li> <li>• Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>• Psychological and behavioural issues are more likely in people with a lower socioeconomic status.</li> <li>• Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care.</li> <li>• Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	<p>Not all people with CF will develop liver disease or progressively worsening liver disease. Therefore the Committee also queried the value of using ultrasound at annual review in addition to clinical examination and biochemical liver function tests when there was no indication of liver disease from these 2 tests in adults.</p>

## D.20 Ursodeoxycholic acid for cystic fibrosis-related liver disease

Item	Details
Key issue in the scope	Surveillance for cystic-fibrosis-related liver disease and prevention of progression.
Review question in scope	Liver disease: What is the effectiveness of ursodeoxycholic acid for preventing liver disease progression in people with cystic fibrosis?
Review question for the protocol	What is the effectiveness of ursodeoxycholic acid for preventing the development or progression of liver disease in people with cystic fibrosis?
Objective	To assess the clinical and cost effectiveness of ursodeoxycholic acid for the development or prevention of liver disease progression in people with cystic fibrosis.
Language	English
Study design	<ul style="list-style-type: none"> <li>• Systematic reviews of RCTs</li> <li>• RCTs</li> <li>• Conference abstracts of RCTs (Only if RCTs unavailable and the quality assessment of abstracts will be conducted based on the available information and if necessary the authors of abstracts will be contacted).</li> <li>• Comparative cohort studies (only if RCTs unavailable or limited data to inform decision making)</li> </ul>
Population and directness	<p>Infants, children, young people and adults with defined CF, diagnosed clinically and by sweat test or genetic testing.</p> <p>Population size and indirectness:</p> <ul style="list-style-type: none"> <li>• Studies where N&lt;10 will not be included.</li> <li>• Studies with indirect populations will not be considered.</li> </ul>
Stratified, subgroup and adjusted analyses	<p>Sensitivity analysis:</p> <p>In the presence of heterogeneity, sensitivity analysis will be conducted including and excluding studies with a high risk of bias.</p> <p>In the presence of heterogeneity, subgroup analyses will be conducted examining patients with evidence of liver disease at randomisation separately from those without liver disease.</p>
Intervention	UDCA administered orally, at any dose, given for a period of at least three months.
Comparison	<ul style="list-style-type: none"> <li>• Placebo</li> <li>• No additional therapy (i.e. both groups receiving usual CF therapy)</li> </ul>
Outcomes	<ul style="list-style-type: none"> <li>• Quality of life (CF-QOL, CFQR)</li> <li>• Hepatocellular enzymes or bilirubin level</li> <li>• Liver failure</li> <li>• Liver transplantation</li> <li>• Liver related mortality</li> <li>• Development of portal hypertension indicated by an: <ul style="list-style-type: none"> <li>○ Enlarged spleen (increased by at least 15%)</li> <li>○ Development of varices</li> <li>○ Ultrasound evidence of portal hypertension</li> </ul> </li> <li>• No development of liver disease</li> <li>• Note: change from baseline will be prioritised over absolute values</li> </ul>
Importance of outcomes	<p>Critical outcomes for decision making:</p> <ul style="list-style-type: none"> <li>• Change of hepatocellular enzymes</li> <li>• Liver failure</li> <li>• Development of portal hypertension indicated by an:</li> </ul>

Item	Details
	<ul style="list-style-type: none"> <li>○ Enlarged spleen (increased by at least 15%)</li> <li>○ Development of varices</li> <li>○ Ultrasound evidence of portal hypertension</li> </ul> <p>Outcomes to be measured at 6 months and 12 months</p>
Setting	All settings in which NHS-commissioned health and social care is provided.
Search strategy	<p>Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase</p> <p>Limits (e.g. date, study design): Limit to English language only where possible (Medline and Embase). Limit to RCTs and systematic reviews unless overall return is small</p> <p>Supplementary search techniques: No supplementary search techniques were used.</p> <p>See appendix E.15 for full strategies</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>• The methodological quality of each study will be assessed using an appropriate checklist as per NICE guidelines manual (The Cochrane Risk of Bias tool for RCTs and the Newcastle and Ottawa scale for observational studies).</li> <li>• The quality of the evidence will be assessed by GRADE for each outcome according to the process described in the NICE guidelines manual (2014).</li> </ul> <p>Synthesis of data:</p> <ul style="list-style-type: none"> <li>• Meta-analysis will be conducted where appropriate.</li> <li>• If comparative cohort studies are included, the minimum number of events per covariate to be recorded to ensure accurate multivariate analysis.</li> <li>• Final and change scores will be pooled and if any study reports both, change scores will be used in preference over final scores.</li> <li>• If studies only report p-values from parametric analyses, and 95% CIs cannot be calculated from other data provided, this information will be plotted in GRADE tables, but evidence may be downgraded.</li> <li>• If studies only report p-values from non-parametric analyses, this information will be plotted in GRADE tables without downgrading the evidence, as imprecision cannot be assessed for non-parametric analyses.</li> </ul> <p>Minimal important differences (MIDs):</p> <ul style="list-style-type: none"> <li>• Health related quality of life: CF-QOL = 5; CFQ-R = 8.5</li> <li>• Change of hepatocellular enzymes or bilirubin level: GRADE default</li> <li>• Liver failure: any change will be considered clinically significant</li> <li>• Liver transplantation: any change will be considered clinically significant</li> <li>• Liver related mortality: any change will be considered clinically significant</li> <li>• Development of portal hypertension: any change will be considered clinically significant</li> <li>• No development of liver disease: any change will be considered clinically significant</li> </ul> <p>Default MIDs: 0.8 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes.</p> <p>Review process:</p> <ul style="list-style-type: none"> <li>• A list of excluded studies will be provided following weeding.</li> <li>• Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>• Psychological and behavioural issues are more likely in people with a lower socioeconomic status</li> <li>• Gender- outcomes are worse for women although there is no evidence that</li> </ul>

Item	Details
	<p>this is a consequence of difference in care</p> <ul style="list-style-type: none"> <li>Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	<p>Based on a Cochrane Review <a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000222.pub3/full">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000222.pub3/full</a></p> <p>There have been no RCTs investigating UDCA for preventing the development of liver disease in people with CF. This review has shown the absence of any significant effects of UDCA treatment on people with CF, apart from a slight effect on the surrogate endpoint of reduction of raised liver enzymes to normal.</p>

## D.21 Monitoring for CFRD

Item	Details
Issue in the scope	Surveillance for CF-related diabetes.
Review question in the scope	How should people with CF be monitored for the onset of CF-related diabetes (CFRD)?
Review question	<ol style="list-style-type: none"> <li>What criteria should be used to determine the need for insulin therapy to achieve optimal patient outcomes?</li> <li>What thresholds of glucose dysregulation are associated with more rapid progression of lung disease?</li> </ol>
Objective	<p>CFRD is a common comorbidity that leads to an increase in morbidity and mortality in people with cystic fibrosis. It is distinct from Type 1 and 2 diabetes and is due to a slowly progressive loss of the insulin-producing <math>\beta</math>-cells in the pancreas. Early identification of this condition allows for the introduction of insulin therapy which typically leads to an improvement in lung function and reduces the number of acute respiratory infections.</p> <p>There is questionable value of using WHO diagnostic criteria to interpret the results of a 75g 2 hour OGTT as diabetes because of the difference in pathology in those with CF and because a diabetes diagnosis may not be stable. However, the WHO criteria for glucose intolerance are higher than those suggested for the onset of lung pathology in a CF population.</p> <p>The aim of this review is to determine the prognostic information from thresholds of glucose dysregulation that are associated with more rapid progression of lung disease and criteria that should be used to instigate treatment with insulin) in a population of adults and children with CF.</p>
Language	English
Study design	<p>For review question 1:</p> <ul style="list-style-type: none"> <li>Systematic reviews</li> <li>RCTs (test and treat)</li> <li>Conference abstracts of RCTs (Only if RCTs unavailable and the quality assessment of abstracts will be conducted based on the available information and if necessary the authors of abstracts will be contacted).</li> <li>Prospective or retrospective comparative cohort studies (only if RCTs unavailable or limited data to inform decision making)</li> </ul> <p>For review question 2:</p> <ul style="list-style-type: none"> <li>Prospective or retrospective cohort studies</li> </ul>
Population and directness	<p>Infants, children, young people and adults with defined CF, diagnosed clinically and by sweat test or genetic testing.</p> <p>Population size and indirectness:</p> <ul style="list-style-type: none"> <li>No sample size specification.</li> <li>Studies with indirect populations will not be included</li> </ul>
Stratified, subgroup and	<p>Groups that will be reviewed and analysed separately:</p> <ul style="list-style-type: none"> <li>age (young people vs adults)</li> </ul>

Item	Details
adjusted analyses	<ul style="list-style-type: none"> <li>clinical signs or risk factor (incidental indication of blood glucose dysregulation)</li> </ul> <p>Sensitivity analysis: In the presence of heterogeneity, sensitivity analysis will be conducted including and excluding studies with a high risk of bias. State important confounders (when comparative observational studies are included for interventional reviews)</p> <ul style="list-style-type: none"> <li>Steroid use</li> <li>Azole (anti fungal)</li> <li>Age</li> <li>Lung disease severity</li> <li>Exocrine pancreatic insufficiency</li> <li>Enteral tube feeding?</li> <li>Transplant</li> </ul>
Screening strategy	<p>For review question 1: Any OGTT vs serial/continuous glucose monitoring diagnosis followed up with treatment</p> <p>For review question 2: Continuous glucose monitoring (different groups according to thresholds)</p>
Outcomes	<p>For review question 1: Ideally specify a time to event outcome</p> <ul style="list-style-type: none"> <li>Change in lung function (FEV1, FVC, LCI)</li> <li>Pulmonary exacerbation</li> <li>BMI (z-scores for children)</li> <li>Adverse events: <ul style="list-style-type: none"> <li>hypoglycaemic episodes (with insulin therapy)</li> </ul> </li> <li>Patient acceptability/ satisfaction (with insulin therapy)</li> </ul> <p>For review question 2: Ideally specify a time to event outcome</p> <ul style="list-style-type: none"> <li>Change in lung function (FEV1, FVC, LCI)</li> <li>Pulmonary exacerbation</li> <li>BMI (z-scores for children)</li> <li>Adverse events: <ul style="list-style-type: none"> <li>hypoglycaemic episodes (with insulin therapy)</li> </ul> </li> <li>Patient acceptability/ satisfaction (with insulin therapy)</li> </ul>
Importance of outcomes	<p>Critical outcomes for decision making:</p> <ul style="list-style-type: none"> <li>Change in lung function (FEV1, FVC, LCI)</li> <li>BMI (z scores)</li> <li>Pulmonary exacerbations</li> </ul>
Setting	All settings in which NHS-commissioned health and social care is provided.
Search strategy	<p>Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase</p> <p>Limits (e.g. date, study design): Apply standard exclusions and English language filters.</p> <p>Supplementary search techniques: No supplementary search techniques were used.</p> <p>See appendix E.16 for full strategies</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>The methodological quality of each study will be assessed using the checklist created by Hayden et al. (2013), as set out in the Developing NICE Guidelines</li> </ul>

Item	Details
	<p>Manual 2014.</p> <ul style="list-style-type: none"> <li>The quality of the evidence for an outcome (i.e. across studies) will be assessed using adapted GRADE approach.</li> </ul> <p>Synthesis of data:</p> <ul style="list-style-type: none"> <li>Meta-analysis will be conducted where appropriate.</li> <li>If comparative cohort studies are included, the minimum number of events per covariate to be recorded to ensure accurate multivariate analysis.</li> <li>Final and change scores will be pooled and if any study reports both, change scores will be used in preference over final scores.</li> <li>If studies only report p-values from parametric analyses, and 95% CIs cannot be calculated from other data provided, this information will be plotted in GRADE tables, but evidence may be downgraded.</li> <li>If studies only report p-values from non-parametric analyses, this information will be plotted in GRADE tables without downgrading the evidence, as imprecision cannot be assessed for non-parametric analyses.</li> </ul> <p>Review process:</p> <ul style="list-style-type: none"> <li>A list of excluded studies will be provided following weeding.</li> <li>Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>Psychological and behavioural issues are more likely in people with a lower socioeconomic status</li> <li>Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care</li> <li>Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	None.

## D.22 Monitoring for low BMD

Item	Details
Issue in the scope	Surveillance for reduced bone mineral density.
Review question in the scope	How should monitoring be carried out to identify reduced bone mineral density?
Review question for the protocol	What is the most effective strategy to monitor for the identification of reduced bone mineral density in people with CF?
Objective	<p>The increase in life expectancy of cystic fibrosis (CF) patients has brought about a rise in new clinical problems in these patients, such as a decrease in bone mineral density (BMD). The cause of diminished BMD in CF is multi-factorial and can lead to osteoporosis. It is of clinical importance to identify bone disease related to CF early in its course to allow therapeutic interventions that optimize bone health.</p> <p>BMD is usually normal in well-nourished children with CF who have good lung function. Even so many patients fail to gain bone normally, or experience premature bone loss, in adolescence. About one third of adults with CF have low bone mineral density, which may predispose them to bone fractures.</p> <p>CF-related low BMD probably has many causes:</p> <ol style="list-style-type: none"> <li>Bone health is strongly linked to the severity of lung disease and body weight. Severely ill patients are more likely to have low BMD. Conversely patients with normal weight and height, and good lung function, have near normal bone density. Lung infection in CF is associated with more intense inflammation and raised levels of chemicals called cytokines in blood and sputum. These cytokines increase the activity of cells which break down bone.</li> </ol>

Item	Details
	<p>2. Apart from the general malnutrition associated with more severe disease, many aspects of nutrition affect bone status, including vitamins (e.g., vitamins D and K), minerals (e.g., calcium), and protein intake.</p> <p>3. Oral corticosteroids cause rapid bone loss, especially during the first year of therapy. They reduce calcium absorption from the gut, increase calcium loss in the urine, decrease the number of bone-forming cells and increase bone resorption. Most of the larger studies in individuals with CF have shown an association between oral steroid use and low BMD.</p> <p>4. A number of studies in people who do not have CF have found an association between greater physical activity and higher BMD levels. However, it is not known if weight-bearing exercise in people with CF can increase peak bone mass, preserve BMD or increase BMD in those with low BMD.</p> <p>5. Despite most children with CF achieving normal or near normal growth, puberty is often delayed. Bone mineral deficiencies resulting from late onset of puberty may not be corrected when puberty eventually starts. Low sex hormone levels, oestrogen and testosterone, are associated with low BMD in adults with cystic fibrosis.</p> <p>6. Low bone mineral density has been associated with CF-related diabetes.</p> <p>7. There may be a direct link between CF-related low BMD and the abnormal protein produced by the CF gene.</p> <p>Lung infection damages bone health. Therefore treatments that prevent the progression of lung disease should be optimised.</p>
Language	English
Study design	<ul style="list-style-type: none"> <li>• Systematic reviews</li> <li>• RCTs (test and treat)</li> <li>• Conference abstracts of RCTs (Only if RCTs unavailable and the quality assessment of abstracts will be conducted based on the available information and if necessary the authors of abstracts will be contacted).</li> <li>• Prospective or retrospective cohort studies (only if RCTs unavailable or limited data to inform decision making)</li> </ul>
Population and directness	<p>Infants, children, young people and adults with defined CF, diagnosed clinically and by sweat test or genetic testing.</p> <p>Population size and indirectness:</p> <ul style="list-style-type: none"> <li>• No sample size specification.</li> <li>• Studies with indirect populations will not be included</li> </ul>
Stratified, subgroup and adjusted analyses	<p>Groups that will be reviewed and analysed separately:</p> <ul style="list-style-type: none"> <li>• Gender (male versus female)</li> <li>• Age (<math>\leq 10</math> years versus 11 to 17 years versus <math>\geq 18</math> years)</li> <li>• Puberty staging</li> <li>• Patients with osteoporosis and osteopenia</li> </ul> <p>Sensitivity analysis:</p> <p>In the presence of heterogeneity, sensitivity analysis will be conducted including and excluding studies with a high risk of bias.</p>
Prognostic test	<ul style="list-style-type: none"> <li>• Regular DXA scans</li> <li>• Peripheral quantitative computed tomography (pQCT)</li> </ul> <p>Notes:</p> <ul style="list-style-type: none"> <li>• Challenges for interpretation of bone densitometry data: good reproducibility is dependent on the quality of the scanning procedure, which itself is dependent on the correct positioning of the patient, the protocol used for analysis and the systematic use of a calibration phantom. Precision can be further enhanced for longitudinal BMD measurements through using the same densitometer/analysis software and the same operator as for the original measurement.</li> <li>• BMD measured by dual energy X-ray absorptiometry (DXA) – gold standard.</li> <li>• DXA scans should be performed in centres experienced in interpreting BMD</li> </ul>

Item	Details
	<p>data from people with CF.</p> <ul style="list-style-type: none"> <li>• Normative data should be age, gender and geographically matched to the patients measured.</li> <li>• BMD should be measured at the total body and the lumbar spine in patients younger than 20 years of age, and at the lumbar spine and proximal hip in patients of 20 years of age or older.</li> <li>• With DXA, BMD deficits may be overestimated in patients with short stature, because they display a more severe decrease in bone area than in bone mineral content</li> <li>• For patients younger than 20 years of age whose height is at least 1 SD below age and sex matched healthy controls, BMD Z-scores should be adjusted for height or statural age to avoid overestimating deficits in BMD in people with short stature.</li> </ul>
Outcomes	<ul style="list-style-type: none"> <li>• Change in body bone mineral density (BMD) (adjusted for children)</li> <li>• Number of fractures</li> <li>• Quality of life (measured with CF-QOL or CFQR)</li> </ul> <p>Notes:</p> <ul style="list-style-type: none"> <li>• When reporting results, it is important to specify the machine make, model, and software version used, to enable comparison with other published data.</li> <li>• Z-scores are usually the most appropriate method in people with cystic fibrosis. The Z-score compares a measured BMD value to the average value obtained from a healthy population of the same sex and age as the patient. BMD is considered low in people with CF when the BMD Z-score in the spine or hip is lower than -2. However there are limitations to this approach, as all the BMD work is based on normal ranged in postmenopausal women, and we extrapolate this to CF patients, who of course are a much younger population.</li> </ul>
Importance of outcomes	<p>Critical outcome for decision making:</p> <ul style="list-style-type: none"> <li>• Change in body bone mineral density (BMD) (adjusted for children)</li> </ul>
Setting	<p>All settings in which NHS-commissioned health and social care is provided.</p>
Search strategy	<p>Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase.</p> <p>Limits (e.g. date, study design): Apply standard exclusions and English language filters.</p> <p>Supplementary search techniques: No supplementary search techniques were used.</p> <p>See appendix E.17 for full strategies</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>• The methodological quality of each prognostic study will be assessed using the checklist created by Hayden et al. (2013), as set out in the Developing NICE Guidelines Manual 2014.</li> <li>• The quality of the evidence for an outcome (i.e. across studies) will be assessed using adapted GRADE approach.</li> </ul> <p>Synthesis of data:</p> <ul style="list-style-type: none"> <li>• If comparative cohort studies are included, the minimum number of events per covariate to be recorded to ensure accurate multivariate analysis where possible.</li> <li>• Final and change scores will be pooled and if any study reports both, change scores will be used in preference over final scores.</li> <li>• If studies only report p-values from parametric analyses, and 95% CIs cannot be calculated from other data provided, this information will be plotted in GRADE tables, but evidence may be downgraded.</li> <li>• If studies only report p-values from non-parametric analyses, this information</li> </ul>

Item	Details
	<p>will be plotted in GRADE tables without downgrading the evidence, as imprecision cannot be assessed for non-parametric analyses</p> <ul style="list-style-type: none"> <li>Review process:</li> <li>A list of excluded studies will be provided following weeding.</li> <li>Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>Psychological and behavioural issues are more likely in people with a lower socioeconomic status.</li> <li>Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care.</li> <li>Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	<p>Bone mineral density in cystic fibrosis patients under the age of 18 years, 2008: <a href="http://www.ncbi.nlm.nih.gov/pubmed/18449130">http://www.ncbi.nlm.nih.gov/pubmed/18449130</a></p> <p>2011 European cystic fibrosis bone mineralisation guidelines recommendation:</p> <ul style="list-style-type: none"> <li>“In children, routine bone density scans should first be performed from around the age of eight to 10 years, and should be repeated approximately: every five years if the BMD Z-score is &gt; -1; every two years if the Z-score is between -1 and -2; and every year if the Z-score is &lt; -2 or if the child has experienced low trauma fractures. Bone density measurements can be first done at an earlier age and/or yearly in children with significant risk factors for low BMD and in children before prescribing specific treatments for low BMD.”</li> <li>In adults with CF less than 50 years of age, routine bone density scans are recommended approximately: every five years if the BMD Z-score is &gt; -1; every two years if the Z-score is between -1 and -2; every year if the Z-score is &lt; -2. BMD measurements can be done yearly in adults with significant risk factors for low BMD. BMD measurements must be done before prescribing bone protective therapy.</li> <li>In adults after 50 years of age, routine bone density scans are recommended approximately: every five years if the T-score is &gt; -1; every two years if the T-score is between -1 and -2.5; every year if the T-score is &lt; -2.5. BMD measurements can be done yearly in adults with significant risk factors for low BMD. BMD measurements must be done before prescribing bone protective therapy”</li> </ul> <p>Bone densitometry in children assessed by dual x ray absorptiometry: uses and pitfalls: <a href="http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1719622/pdf/v088p00795.pdf">http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1719622/pdf/v088p00795.pdf</a> “It is suggested that performance of a DXA scan should be considered if a child has one of these conditions in conjunction with one of the following symptoms: low trauma or recurrent fractures, back pain, spinal deformity or loss of height, change in mobility status (for example, difficulty walking), or malnutrition” “given the difficulties discussed, a child may most appropriately act as his or her own control, with serial scans to monitor progress. Scan intervals of less than six months should only be considered in special situations such as monitoring the response to a pharmacological intervention, and for most patients annual scans should suffice”.</p> <p>Relevant references:</p> <ul style="list-style-type: none"> <li>Henderson RC, Madsen CD. Bone mineral content and body composition in children and young adults with cystic fibrosis. <i>Pediatr Pulmonol</i> 1999;27:80 – 4.</li> <li>Cystic fibrosis-related bone disease in children: Examination of peripheral quantitative computed tomography (pQCT) data. <a href="http://www.ncbi.nlm.nih.gov/pubmed/25957706">http://www.ncbi.nlm.nih.gov/pubmed/25957706</a></li> <li>Bone mineral and body composition alterations in paediatric cystic fibrosis patients: <a href="http://link.springer.com/article/10.1007%2Fs00247-009-1446-8">http://link.springer.com/article/10.1007%2Fs00247-009-1446-8</a></li> <li>The prevalence of osteoporosis, osteopenia, and fractures among adults with</li> </ul>

Item	Details
	<p>cystic fibrosis: a systematic literature review with meta-analysis <a href="http://www.ncbi.nlm.nih.gov/pubmed/19949942">http://www.ncbi.nlm.nih.gov/pubmed/19949942</a></p> <ul style="list-style-type: none"> <li>• A cross-sectional study of bone mineral density in children and adolescents attending a Cystic Fibrosis Centre.</li> <li>• Buntain 2004 Bone mineral density in Australian children, adolescents and adults with cystic fibrosis: a controlled cross sectional study.</li> <li>• Sermet-Gaudelus 2008 Low Bone Mineral Density in Young Children with Cystic Fibrosis.</li> </ul>

## D.23 Exercise

Item	Details
Key issue in the scope	The role of exercise in maintaining health.
Review question in the scope	What is the effectiveness of programmes of exercise in the management of cystic fibrosis?
Review question for the protocol	What is the effectiveness of programmes of exercise in the management of cystic fibrosis?
Objective	<p>Exercise has been identified as potential therapeutic and prognostic tool which has been linked to many improved outcomes in people with CF. While physical training is part of the typical care offered to a person with CF, many people are thought to refrain from physical activity due to fatigue and shortness of breath. Further, a 2012 Cochrane review suggested that the benefits of exercise may be influenced by the “type of training programme and the inclusion of aerobic and anaerobic training”.</p> <p>The aim of this review is to evaluate whether specific programmes of physical exercise lead to improved outcomes and benefits for people with CF.</p>
Language	English
Study design	<ul style="list-style-type: none"> <li>• Systematic reviews of RCTs</li> <li>• RCTs (Only RCTs with N&gt;10 will be included. RCTs with n = 10 or n &lt; 10 and analysed in an included Cochrane systematic review will be included).</li> <li>• Conference abstracts of RCTs (Only if RCTs unavailable and the quality assessment of abstracts will conducted based on the available information and if necessary the authors of abstracts will be contacted).</li> <li>• Comparative cohort studies (only if RCTs unavailable or limited data to inform decision making)</li> </ul>
Population and directness	<p>Children, young people and adults with CF, diagnosed clinically and by sweat test or genetic testing.</p> <p>Population size and indirectness:</p> <ul style="list-style-type: none"> <li>• Studies with N &lt; 10 will not be included.</li> <li>• Studies with indirect population will not be considered.</li> </ul>
Stratified, subgroup and adjusted analyses	<p>Stratified analysis:</p> <ul style="list-style-type: none"> <li>• Supervised vs unsupervised training</li> </ul> <p>In the event of heterogeneity, the following subgroups that will be analysed separately:</p> <ul style="list-style-type: none"> <li>• Severity</li> <li>• Gender (male versus female)</li> <li>• Age (<math>\leq 17</math> years versus <math>\geq 18</math> years)</li> <li>• Duration of exercise programme (short versus long)</li> </ul> <p>In the presence of heterogeneity, sensitivity analysis will conducted including and excluding studies with a high risk of bias.</p>
Intervention	Any clearly defined (supervised and unsupervised) physical exercise programme:

Item	Details
	<ul style="list-style-type: none"> <li>• Aerobic exercise programmes</li> <li>• Strength resistance training (anaerobic exercise programmes)</li> <li>• High intensity interval training</li> <li>• Habitual physical activity</li> <li>• Inspiratory muscle training (&gt; 80%)</li> <li>• Any combination of the above</li> </ul>
Comparison	<ul style="list-style-type: none"> <li>• No defined exercise programme</li> <li>• A different defined exercise programme – for example different activities or different duration or intensity of the same activity</li> </ul>
Outcomes	<ul style="list-style-type: none"> <li>• Lung function tests - forced expiratory volume in one second (FEV1) per cent predicted (change from baseline will be favoured over absolute data)</li> <li>• Forced vital capacity (FVC) per cent predicted (change from baseline will be favoured over absolute data)</li> <li>• VO2 (change from baseline will be favoured over absolute data)</li> <li>• Time to next exacerbation</li> <li>• Preference for training programme</li> <li>• Quality of life (CFQ-R, CF-QOL)</li> <li>• Body composition (change in BMI or weight) (≥ 3 months follow-up)</li> <li>• Adverse events, i.e. fractures</li> <li>• Note: change from baseline will be prioritised over absolute values</li> </ul>
Importance of outcomes	<p>Critical outcomes for decision making:</p> <ul style="list-style-type: none"> <li>• Lung function (FEV1)</li> <li>• Quality of life (CFQ-R, CF-QOL)</li> <li>• Time to next exacerbation</li> </ul>
Setting	Any healthcare setting where NHS care is delivered (primary, secondary, tertiary or community).
Search strategy	<p>Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase</p> <p>Limits (e.g. date, study design): Apply standard exclusions and English language filters. Limit to RCTs and systematic reviews in the first instance but download all study designs.</p> <p>Supplementary search techniques: No supplementary search techniques will be used.</p> <p>See appendix E.18 for full search strategies</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>• The methodological quality of each study will be assessed using an appropriate checklist as per NICE guidelines manual (The Cochrane Risk of Bias tool for RCTs and the Newcastle and Ottawa scale for observational studies).</li> <li>• The quality of the evidence will be assessed by GRADE for each outcome according to the process described in the NICE guidelines manual (2014).</li> </ul> <p>Synthesis of data:</p> <ul style="list-style-type: none"> <li>• Meta-analysis will be conducted where appropriate.</li> <li>• Final and change scores will be pooled and if any study reports both, change scores will be used in preference over final scores.</li> <li>• If studies only report p-values from parametric analyses, and 95% CIs cannot be calculated from other data provided, this information will be plotted in GRADE tables, but evidence may be downgraded.</li> <li>• If studies only report p-values from non-parametric analyses, this information will be plotted in GRADE tables without downgrading the evidence, as</li> </ul>

Item	Details
	<p>imprecision cannot be assessed for non-parametric analyses.</p> <p>Minimal important differences (MIDs):</p> <ul style="list-style-type: none"> <li>• FEV1: 5 percentage points</li> <li>• FVC: GRADE default</li> <li>• VO2 max: GRADE default</li> <li>• Time to next exacerbation: any change will be considered clinically significant</li> <li>• BMI or weight: GRADE default</li> <li>• Quality of life: CF-QOL = 5; CFQ-R = 8.5</li> <li>• Preference: GRADE default</li> <li>• Adverse events = GRADE default</li> <li>• Major adverse events leading to discontinuation of treatment: any change will be considered clinically significant</li> </ul> <p>Default MIDs: 0.8 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes.</p> <ul style="list-style-type: none"> <li>• Review process:</li> <li>• A list of excluded studies will be provided following weeding.</li> <li>• Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>• Psychological and behavioural issues are more likely in people with a lower socioeconomic status</li> <li>• Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care</li> <li>• Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	<p>Physical training for cystic fibrosis (Cochrane Review), Bradley 2012 <a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002768.pub2/pdf">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002768.pub2/pdf</a></p> <p>A randomized controlled trial of a 3-year home exercise program in cystic fibrosis: <a href="http://www.jpeds.com/article/S0022-3476(00)12109-2/pdf">http://www.jpeds.com/article/S0022-3476(00)12109-2/pdf</a></p> <p>Individualised unsupervised exercise training in adults with cystic fibrosis: a 1 year randomised controlled trial: <a href="http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1746905/pdf/v059p01074.pdf">http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1746905/pdf/v059p01074.pdf</a></p> <p>Exercise programs for children with cystic fibrosis: A systematic review of randomized controlled trials: <a href="http://informahealthcare.com/doi/abs/10.3109/09638280902991842">http://informahealthcare.com/doi/abs/10.3109/09638280902991842</a></p> <p>The evidence regarding exercise training in the management of cystic fibrosis: a systematic review <a href="http://europepmc.org/articles/PMC2845226?jsessionid=RQBvQg74VEBAkBCbVUMH.11">http://europepmc.org/articles/PMC2845226?jsessionid=RQBvQg74VEBAkBCbVUMH.11</a></p>

## D.24 Psychosocial assessment

Item	Details
Key issue in the scope	Recognising psychological and behavioural problems.
Review question in the scope	How should people with cystic fibrosis be monitored for psychological or behavioural problems?
Review question for the protocol	What strategies are effective at identifying people with cystic fibrosis for the presence of a psychological and/or behavioural problem?
Objectives	Cystic fibrosis is a life-threatening disease and poses cognitive, emotional and behavioral challenges for many children and adults with CF as well as their families and/or carers. Areas of concern might include anxiety and depression, disordered eating disorders and adherence to treatments. These psychological and/or behavioural problems are also not well recognised by health care

Item	Details
	<p>professionals, vary across the country and require a multi-disciplinary assessment.</p> <p>The aim of this review is to determine which assessment strategies are effective at identifying mental health problems in children and adults with cystic fibrosis. It is hoped that this information will lead to improvements in quality of life outcomes and, in turn, inform service requirements. A recent survey by the Cystic Fibrosis Organisation UK suggests that access to psychosocial input in the UK is not currently equitable.</p>
Language	English
Study design	<ul style="list-style-type: none"> <li>• Systematic review of diagnostic studies</li> <li>• Cross-sectional studies</li> <li>• Prospective or retrospective cohort studies where cross-sectional data is reported</li> </ul>
Population and directness	<p>Infants, children, young people and adults with defined CF, diagnosed clinically and by sweat test or genetic testing.</p> <p>Population size and indirectness:</p> <ul style="list-style-type: none"> <li>• Studies with indirect populations will not be considered.</li> <li>• No restrictions to sample size.</li> </ul>
Stratified, subgroup and adjusted analyses	<p>The following groups will be assessed separately if possible:</p> <ul style="list-style-type: none"> <li>• Children under 6 years</li> <li>• Children and young people aged 7 to 16 years</li> <li>• Young people and adults over 16 years</li> </ul> <p>Sensitivity analysis:</p> <ul style="list-style-type: none"> <li>• Sensitivity analysis: including and excluding studies with a high risk of bias</li> </ul>
Index test: recognition or assessment tool	<p>Clinical assessment:</p> <ul style="list-style-type: none"> <li>• Generalised Anxiety Disorder 7-item scale (GAD-7)</li> <li>• Patient Health Questionnaire 2-item scale (PHQ-2)</li> <li>• Patient Health Questionnaire 9-item primary care scale (PHQ-9)</li> <li>• Hospital Anxiety and Depression Scale (HADS)</li> <li>• Paediatric Index of Emotional Distress (PI-ED)</li> <li>• Centre for Epidemiologic Studies Depression Scale (CES-D)</li> <li>• Eating Disorders Examination (EDE)</li> <li>• Child Eating Disorders Examination (CEDE)</li> <li>• Eating Attitu</li> <li>• des Test (EAT)</li> <li>• Child Eating Attitude Test (ChEAT)</li> </ul>
Reference standard	<ul style="list-style-type: none"> <li>• Diagnosis statistical manual (DSM) or International Classification of diseases (ICD) diagnosis for anxiety, depression, mood disorders, emotional distress and eating disorders</li> <li>• Electronic monitoring of adherence or pharmacy records for adherence to drug treatment</li> <li>• As reported by study for other psychological and behavioural problems stated in the protocol</li> </ul>
Outcomes	<ul style="list-style-type: none"> <li>• Sensitivity</li> <li>• Specificity</li> <li>• Positive likelihood ratio</li> <li>• Negative likelihood ratio</li> <li>• AUROC</li> <li>• Reliability and validity</li> </ul>
Importance of outcomes	Critical outcomes for decision making:

Item	Details
	<ul style="list-style-type: none"> <li>• Sensitivity</li> <li>• Specificity</li> </ul>
Setting	Any healthcare setting where NHS care is delivered (primary, secondary, tertiary or community)
Search strategy	<p>Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase, PsycINFO.</p> <p>Limits (e.g. date, study design): All study designs. Apply standard exclusions and English language filters.</p> <p>Supplementary search techniques: No supplementary search techniques will be used.</p> <p>See appendix E.18 for full search strategy</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>• The methodological quality of each study will be assessed using a quality checklists for diagnostic studies (QUADAS-2) or a critical appraisal of outcome measures checklist (Jerosch-Herold,2005) as set out in the Developing NICE Guidelines Manual 2014.</li> <li>• The quality of the evidence for an outcome (i.e. across studies) will be assessed using adapted GRADE for diagnostic studies.</li> </ul> <p>Data analysis:</p> <ul style="list-style-type: none"> <li>• Meta-analysis will be conducted if appropriate for diagnostic studies.</li> <li>• The cut-offs for diagnostic accuracy measures: <ul style="list-style-type: none"> <li>○ Sensitivity and specificity: <ul style="list-style-type: none"> <li>- High &gt;90%</li> <li>- Moderate 75 to 90%</li> <li>- Low &lt;75%</li> </ul> </li> <li>○ Positive likelihood ratio: <ul style="list-style-type: none"> <li>- Very useful test &gt;10</li> <li>- Moderately useful test 5 to 10</li> <li>- Not a useful test &lt;5</li> </ul> </li> <li>○ Negative likelihood ratio: <ul style="list-style-type: none"> <li>- Very useful test &lt;0.1</li> <li>- Moderately useful test 0.1 to 0.2</li> <li>- Not a useful test &gt;0.2</li> </ul> </li> </ul> </li> </ul> <p>Review process:</p> <ul style="list-style-type: none"> <li>• A list of excluded studies will be provided following weeding.</li> <li>• Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>• Psychological and behavioural issues are more likely in people with a lower socioeconomic status.</li> <li>• Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care.</li> <li>• Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	<p>Most common problems in people with CF:</p> <ul style="list-style-type: none"> <li>• Depression</li> <li>• Anxiety</li> <li>• Non adherence to treatment</li> <li>• Needle phobias</li> <li>• Feeding issues (i.e. anorexia, bulimia but also avoidant and restrictive food intake disorder and body dysmorphia)</li> </ul>

Item	Details
	<ul style="list-style-type: none"> <li>• Low mood</li> <li>• School refusal</li> </ul> <p>Relevant documents:</p> <ul style="list-style-type: none"> <li>• ECFS consensus guidelines</li> <li>• CF Org UK psychosocial report: <a href="https://www.cysticfibrosis.org.uk/media/281430/psychosocial%20report%20v3.pdf">https://www.cysticfibrosis.org.uk/media/281430/psychosocial%20report%20v3.pdf</a></li> <li>• Psychological interventions for Cystic Fibrosis: <a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003148/pdf">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003148/pdf</a></li> <li>• M. Bryon, Summary to date of eating disorders in children and adults with cystic fibrosis. Presented at the 20th Annual North American Cystic Fibrosis Conference, Denver, CD (2006)</li> </ul>

## D.25 Cross infection control

Item	Details
Key issue in the scope	Models for delivery of care and multidisciplinary teams.
Review question in the scope	<p>Delivery of care:</p> <p>How can services be organised to minimise the risk of cross-infection?</p>
Review questions for the protocol	<ul style="list-style-type: none"> <li>• What is the effectiveness of cohorting on the basis of pathogen status versus not cohorting on the basis of pathogen status in reducing transmission of CF pathogens?</li> <li>• What is the effectiveness of different models of segregating patient's in reducing transmission of CF pathogens?</li> <li>• What is the effectiveness of individual protective equipment in reducing transmission of CF pathogens?</li> <li>• What is the effectiveness of the combination of cohorting, segregating and protective equipment in reducing transmission of CF pathogens?</li> </ul>
Objective	<p>The majority of CF-related deaths are due to respiratory failure caused by chronic lung infection. Pathogen transmission can occur via three main routes:</p> <ul style="list-style-type: none"> <li>• direct (person-to-person) contact</li> <li>• indirect contact (a contaminated object infects another person)</li> <li>• aerosol/droplet created in exhalates.</li> </ul> <p>The configuration of a healthcare service can influence the cross-contamination of pathogens and specific infection control practices are needed for inpatient, ambulatory, and non-healthcare settings, based on the types of activities and risks associated with each.</p>
Population and directness	<p>Infants, children, young people and adults with defined CF, diagnosed clinically and by sweat test or genetic testing.</p> <p>Population size and indirectness:</p> <ul style="list-style-type: none"> <li>• No sample size specification.</li> <li>• Studies with indirect populations will not be included</li> </ul>
Intervention	<ul style="list-style-type: none"> <li>• Cohorts by pathogen (separation by location or by clinic time)</li> <li>• Individual patient segregation/separation by clinic room (Separation by location) including: <ul style="list-style-type: none"> <li>• Inpatient room with ensuite facilities</li> <li>• Inpatient Recreational facilities for example day rooms</li> </ul> </li> <li>• Individual patient and health care professional protective equipment: <ul style="list-style-type: none"> <li>○ Masks</li> </ul> </li> </ul>

Item	Details
	<ul style="list-style-type: none"> <li>○ Gloves</li> <li>○ Gowns/aprons</li> <li>● Combinations of the interventions listed above</li> </ul>
Comparison	<ul style="list-style-type: none"> <li>● Configurations other than those listed above</li> <li>● No segregation/ cohorting/ equipment</li> </ul>
Outcomes	<ul style="list-style-type: none"> <li>● Incidence of patients infected with transmissible pathogens</li> <li>● Prevalence of patients infected with transmissible pathogens</li> <li>● Quality of life (CF-QOL, CFQR)</li> <li>● Emotional function including anxiety and depression (scale not specified)</li> <li>● Carer satisfaction</li> <li>● Patient satisfaction</li> <li>● Staff experience</li> <li>● Staff and patient compliance</li> </ul>
Importance of outcomes	<p>Critical outcomes for decision making:</p> <ul style="list-style-type: none"> <li>● Incidence of patients infected with transmissible pathogens</li> <li>● Prevalence of patients infected with transmissible pathogens</li> </ul>
Setting	All settings in which NHS-commissioned health and social care is provided
Stratified, subgroup and adjusted analyses	<p>No subgroups or stratified analyses identified.</p> <p>Sensitivity analysis: including and excluding studies with a high risk of bias and duration of study if necessary.</p>
Language	English
Study design	<ul style="list-style-type: none"> <li>● Systematic reviews</li> <li>● RCTs</li> <li>● Prospective and retrospective comparative cohort studies</li> <li>● Before and after studies</li> <li>● Conference abstracts of RCTs (Only if RCTs unavailable and the quality assessment of abstracts will be conducted based on the available information and if necessary the authors of abstracts will be contacted).</li> <li>● Registry and audit data (UK only)</li> <li>● Surveys (for patient satisfaction and compliance and staff experience only)</li> </ul> <p>To include RCTs and observational studies from Western countries.</p>
Search strategy	<p>Sources to be searched: Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase</p> <p>Limits (e.g. date, study design): Apply standard exclusions filter only.</p> <p>Supplementary search techniques: No supplementary search techniques will be used.</p> <p>See appendix E.11 for full strategies</p>
Review strategy	<p>Appraisal of methodological quality:</p> <ul style="list-style-type: none"> <li>● The methodological quality of each study will be assessed using an appropriate checklist as per NICE guidelines manual and the service guidance methods guide 2014 (The Cochrane Risk of Bias tool for RCTs and the Newcastle and Ottawa scale for observational studies).</li> <li>● The quality of the evidence will be assessed by GRADE for each outcome according to the process described in the NICE guidelines manual (2014).</li> </ul> <p>Synthesis of data:</p>

Item	Details
	<ul style="list-style-type: none"> <li>• Meta-analysis will be conducted where appropriate.</li> <li>• If comparative cohort studies are included, the minimum number of events per covariate to be recorded to ensure accurate multivariate analysis.</li> <li>• Final and change scores will be pooled and if any study reports both, change scores will be used in preference over final scores.</li> <li>• If studies only report p-values from parametric analyses, and 95% CIs cannot be calculated from other data provided, this information will be plotted in GRADE tables, but evidence may be downgraded.</li> <li>• If studies only report p-values from non-parametric analyses, this information will be plotted in GRADE tables without downgrading the evidence, as imprecision cannot be assessed for non-parametric analyses</li> </ul> <p>MIDs:</p> <ul style="list-style-type: none"> <li>• Incidence of patients infected with transmissible pathogens: GRADE default</li> <li>• Prevalence of patients infected with transmissible pathogens: GRADE default</li> <li>• Quality of life: CF-QOL = 5; CFQ-R = 8.5</li> <li>• Emotional function including anxiety and depression (scale not specified): GRADE default</li> <li>• Carer satisfaction: GRADE default</li> <li>• Patient satisfaction: GRADE default</li> <li>• Staff experience: GRADE default</li> <li>• Staff and patient compliance: GRADE default</li> </ul> <p>Default MIDs: 0.8 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes.</p> <p>Review process:</p> <ul style="list-style-type: none"> <li>• A list of excluded studies will be provided following weeding.</li> <li>• Evidence tables and an evidence profile will be used to summarise the evidence.</li> </ul>
Equalities	<ul style="list-style-type: none"> <li>• Psychological and behavioural issues are more likely in people with a lower socioeconomic status</li> <li>• Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care</li> <li>• Geographical issues – care is given through specialist centres and this may be a problem if a person with CF is living in an isolated location.</li> </ul>
Notes/additional information	<p>2015, <a href="http://linkinghub.elsevier.com/retrieve/pii/S0195-6701(15)00074-2">http://linkinghub.elsevier.com/retrieve/pii/S0195-6701(15)00074-2</a></p> <p>Review of medical evidence by an expert committee convened by the Cystic Fibrosis Foundation (U.S.A): Infection Control and Hospital Epidemiology <a href="http://www.jstor.org/stable/10.1086/676882">www.jstor.org/stable/10.1086/676882</a></p> <p>2003, Infection control recommendations for patients with cystic fibrosis: microbiology, important pathogens, and infection control practices to prevent patient to patient transmission: <a href="http://www.shea-online.org/Assets/files/position_papers/cf_ic.pdf">http://www.shea-online.org/Assets/files/position_papers/cf_ic.pdf</a></p> <p>Section 4.1 infection control: <a href="http://www.cysticfibrosis.org.uk/media/448939/cd-standards-of-care-dec-2011.pdf">www.cysticfibrosis.org.uk/media/448939/cd-standards-of-care-dec-2011.pdf</a></p> <p>Audit: What arrangements are in place to minimise the risk of cross-infection in clinics and inpatient facilities?</p> <p>Is there evidence of cross-infection in the unit?</p> <p>What proportion of patients is infected with Burkholderia cepacia complex and MRSA, and what is the annual rate of new acquisition of these organisms?</p>

Item	Details
	<p>Infection Control in Cystic Fibrosis: Cohorting, Cross-Contamination, and the Respiratory Therapist <a href="http://www.rcjournal.com/contents/05.09/05.09.0641.pdf">www.rcjournal.com/contents/05.09/05.09.0641.pdf</a></p> <p>Infection: Prevention and control of healthcare-associated infections in primary and community care: <a href="https://www.nice.org.uk/guidance/cg139">https://www.nice.org.uk/guidance/cg139</a> Note: does not cover secondary care settings</p> <p>Healthcare infection society: <a href="http://www.his.org.uk/">www.his.org.uk/</a></p> <p>Standard infection control procedures NHS: <a href="http://www.nhsprofessionals.nhs.uk/download/comms/cg1_nhsp_standard_infection_control_precautions_v3.pdf">www.nhsprofessionals.nhs.uk/download/comms/cg1_nhsp_standard_infection_control_precautions_v3.pdf</a></p>

## Appendix E: Search strategies

### E.1 In infants, children, young people and adults (including those that have undergone newborn screening) when should cystic fibrosis be suspected?

#### E.1.1 Database: Medline

Last searched on Ovid MEDLINE(R) 1946 to December Week 1 2016 on 5th January 2017.

#	Searches
1	*CYSTIC FIBROSIS/ and exp *DIAGNOSIS/
2	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj7 diag\$).ti,ab.
3	*CYSTIC FIBROSIS/di [Diagnosis]
4	or/1-3
5	exp *"SIGNS AND SYMPTOMS, RESPIRATORY"/
6	(symptom\$ adj3 respirat\$).ti,ab.
7	((Chronic\$ or recur\$) adj5 (lung adj3 infection?)).ti,ab.
8	exp PNEUMONIA/
9	pneumoni\$.ti,ab.
10	(inflamm\$ adj3 (lung? or pulmonary)).ti,ab.
11	exp *RESPIRATORY TRACT DISEASES/ and CHRONIC DISEASE/
12	(chronic\$ adj3 respirat\$).ti,ab.
13	((Recurr\$ or chronic\$) adj2 cough\$).ti,ab.
14	FAILURE TO THRIVE/
15	GROWTH DISORDERS/
16	MALNUTRITION/
17	((fail\$ or falter\$) adj3 (thriv\$ or weight or grow\$)).ti,ab.
18	((grow\$ or weight or height or length) adj3 (disorder? or deficien\$ or poor\$ or retard\$ or restrict\$)).ti,ab.
19	(malnutrition\$ or underweight? or under weight? or wasting or stunting or stunted).ti,ab.

#	Searches
20	exp "SIGNS AND SYMPTOMS, DIGESTIVE"/
21	exp MALABSORPTION SYNDROMES/
22	INTESTINAL ABSORPTION/
23	malabsorption.ti,ab.
24	(Blind Loop Syndrome or C?eliac Disease or Sprue or Lactose Intoleran\$ or Short Bowel Syndrome or Steatorrhea or Whipple Disease).ti,ab.
25	INFERTILITY, MALE/
26	((Infertil\$ or Steril\$ or sub-fertil\$ or subfertil\$) adj10 (male? or men)).ti,ab.
27	(Aspermia or Asthenozoospermia or Azoospermia or Oligospermia or Sertoli Cell-Only Syndrome).ti,ab.
28	exp PANCREATITIS/
29	pancreatitis.ti,ab.
30	MECONIUM/
31	Meconium ileus.ti,ab.
32	or/5-31
33	4 and 32
34	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 (Diagnos\$ adj5 (doubt\$ or problem?))).ti,ab.
35	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 (Diagnos\$ adj5 symptom?)).ti,ab.
36	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 (sign? adj3 symptom?)).ti,ab.
37	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 (Symptom? adj3 progress\$)).ti,ab.
38	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj7 (Clinical adj2 (characteristic\$ or manifest\$))).ti,ab.
39	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 Atypical presentation?).ti,ab.
40	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj5 suspect\$).ti,ab.
41	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 ("no screen\$" or "not screen\$" or unscreen\$ or "no test\$" or "not test\$")).ti,ab.
42	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 ((miss\$ or never) adj3 (screen\$ or test\$))).ti,ab.
43	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj5 (present\$ or manifest\$)).ti,ab.
44	diagnos\$.ab. /freq=2
45	43 and 44
46	CYSTIC FIBROSIS/
47	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
48	mucov\$.ti,ab.
49	or/46-48
50	DELAYED DIAGNOSIS/
51	*DIAGNOSTIC ERRORS/
52	or/50-51
53	49 and 52
54	33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 45 or 53
55	limit 54 to english language
56	LETTER/

#	Searches
57	EDITORIAL/
58	NEWS/
59	exp HISTORICAL ARTICLE/
60	ANECDOTES AS TOPIC/
61	COMMENT/
62	CASE REPORT/
63	(letter or comment*).ti.
64	or/56-63
65	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
66	64 not 65
67	ANIMALS/ not HUMANS/
68	exp ANIMALS, LABORATORY/
69	exp ANIMAL EXPERIMENTATION/
70	exp MODELS, ANIMAL/
71	exp RODENTIA/
72	(rat or rats or mouse or mice).ti.
73	or/66-72
74	55 not 73

### E.1.2 Database: Medline In-Process & Other Non-Indexed Citations

Last searched on Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations January 04, 2017 on 5th January 2017.

#	Searches
1	((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj7 diag\$).ti,ab.
2	(symptom\$ adj3 respirat\$).ti,ab.
3	((Chronic\$ or recur\$) adj5 (lung adj3 infection?)).ti,ab.
4	pneumoni\$.ti,ab.
5	(inflamm\$ adj3 (lung? or pulmonary)).ti,ab.
6	(chronic\$ adj3 respirat\$).ti,ab.
7	((Recurr\$ or chronic\$) adj2 cough\$).ti,ab.
8	((fail\$ or falter\$) adj3 (thriv\$ or weight or grow\$)).ti,ab.
9	((grow\$ or weight or height or length) adj3 (disorder? or deficien\$ or poor\$ or retard\$ or restrict\$)).ti,ab.
10	(malnutrition\$ or underweight? or under weight? or wasting or stunting or stunted).ti,ab.
11	malabsorption.ti,ab.
12	(Blind Loop Syndrome or C?eliac Disease or Sprue or Lactose Intoleran\$ or Short Bowel Syndrome or Steatorrhea or Whipple Disease).ti,ab.
13	((Infertil\$ or Steril\$ or sub-fertil\$ or subfertil\$) adj10 (male? or men)).ti,ab.
14	(Aspermia or Asthenozoospermia or Azoospermia or Oligospermia or Sertoli Cell-Only Syndrome).ti,ab.
15	pancreatitis.ti,ab.
16	Meconium ileus.ti,ab.
17	or/2-16
18	1 and 17
19	((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 (Diagnos\$ adj5 (doubt\$ or problem?))).ti,ab.

#	Searches
20	(((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 (Diagnos\$ adj5 symptom?).ti,ab.
21	(((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 (sign? adj3 symptom?).ti,ab.
22	(((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 (Symptom? adj3 progress\$).ti,ab.
23	(((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj7 (Clinical adj2 (characteristic\$ or manifest\$)).ti,ab.
24	(((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 Atypical presentation?).ti,ab.
25	(((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj5 suspect\$).ti,ab.
26	(((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 ("no screen\$" or "not screen\$" or unscreen\$ or "no test\$" or "not test\$").ti,ab.
27	(((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 ((miss\$ or never) adj3 (screen\$ or test\$)).ti,ab.
28	(((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj5 (present\$ or manifest\$).ti,ab.
29	diagnos\$.ab. /freq=2
30	28 and 29
31	18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 30

### E.1.3 Database: Cochrane Central Register of Controlled Trials

Last searched on EBM Reviews - Cochrane Central Register of Controlled Trials November 2016 on 10th January 2017.

#	Searches
1	*CYSTIC FIBROSIS/ and exp *DIAGNOSIS/
2	(((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj7 diag\$).ti,ab.
3	*CYSTIC FIBROSIS/di [Diagnosis]
4	or/1-3
5	exp *"SIGNS AND SYMPTOMS, RESPIRATORY"/
6	(symptom\$ adj3 respirat\$).ti,ab.
7	((Chronic\$ or recur\$) adj5 (lung adj3 infection?)).ti,ab.
8	exp PNEUMONIA/
9	pneumoni\$.ti,ab,kw.
10	(inflamm\$ adj3 (lung? or pulmonary)).ti,ab.
11	exp *RESPIRATORY TRACT DISEASES/ and CHRONIC DISEASE/
12	(chronic\$ adj3 respirat\$).ti,ab.
13	((Recurr\$ or chronic\$) adj2 cough\$).ti,ab.
14	FAILURE TO THRIVE/
15	GROWTH DISORDERS/
16	MALNUTRITION/
17	((fail\$ or falter\$) adj3 (thriv\$ or weight or grow\$)).ti,ab.
18	((grow\$ or weight or height or length) adj3 (disorder? or deficien\$ or poor\$ or retard\$ or restrict\$)).ti,ab.
19	(malnutrition\$ or underweight? or under weight? or wasting or stunting or stunted).ti,ab,kw.
20	exp "SIGNS AND SYMPTOMS, DIGESTIVE"/
21	exp MALABSORPTION SYNDROMES/

#	Searches
22	INTESTINAL ABSORPTION/
23	malabsorption.ti,ab.
24	(Blind Loop Syndrome or C?eliac Disease or Sprue or Lactose Intoleran\$ or Short Bowel Syndrome or Steatorrhea or Whipple Disease).ti,ab,kw.
25	INFERTILITY, MALE/
26	((Infertil\$ or Steril\$ or sub-fertil\$ or subfertil\$) adj10 (male? or men)).ti,ab.
27	(Aspermia or Asthenozoospermia or Azoospermia or Oligospermia or Sertoli Cell-Only Syndrome).ti,ab,kw.
28	exp PANCREATITIS/
29	pancreatitis.ti,ab,kw.
30	MECONIUM/
31	Meconium ileus.ti,ab,kw.
32	or/5-31
33	4 and 32
34	((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 (Diagnos\$ adj5 (doubt\$ or problem?))).ti,ab.
35	((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 (Diagnos\$ adj5 symptom?)).ti,ab.
36	((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 (sign? adj3 symptom?)).ti,ab.
37	((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 (Symptom? adj3 progress\$)).ti,ab.
38	((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj7 (Clinical adj2 (characteristic\$ or manifest\$))).ti,ab.
39	((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 Atypical presentation?).ti,ab.
40	((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj5 suspect\$).ti,ab.
41	((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 unscreen\$).ti,ab.
42	((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 ((miss\$ or never) adj3 (screen\$ or test\$))).ti,ab.
43	((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj5 (present\$ or manifest\$)).ti,ab.
44	diagnos\$.ab. /freq=2
45	43 and 44
46	CYSTIC FIBROSIS/
47	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
48	mucov\$.ti,ab.
49	or/46-48
50	DELAYED DIAGNOSIS/
51	*DIAGNOSTIC ERRORS/
52	or/50-51
53	49 and 52
54	33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 45 or 53

#### E.1.4 Database: Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects

Last searched on **EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to January 05, 2017, **EBM Reviews - Database of Abstracts of Reviews of Effects 1st Quarter 2015** on 10<sup>th</sup> January 2017.

#	Searches
1	(CYSTIC FIBROSIS and DIAGNOSIS).kw.
2	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj7 diag\$).ti,ab.
3	or/1-2
4	(SIGNS or SYMPTOMS).kw.
5	(symptom\$ adj3 respirat\$).ti,ab.
6	((Chronic\$ or recur\$) adj5 (lung adj3 infection?)).ti,ab.
7	PNEUMONIA.kw.
8	pneumoni\$.ti,ab.
9	(inflamm\$ adj3 (lung? or pulmonary)).ti,ab.
10	(RESPIRATORY TRACT DISEASES and CHRONIC DISEASE).kw.
11	(chronic\$ adj3 respirat\$).ti,ab.
12	((Recurr\$ or chronic\$) adj2 cough\$).ti,ab.
13	FAILURE TO THRIVE.kw.
14	GROWTH DISORDERS.kw.
15	MALNUTRITION.kw.
16	((fail\$ or falter\$) adj3 (thriv\$ or weight or grow\$)).ti,ab.
17	((grow\$ or weight or height or length) adj3 (disorder? or deficien\$ or poor\$ or retard\$ or restrict\$)).ti,ab.
18	(malnutrition\$ or underweight? or under weight? or wasting or stunting or stunted).ti,ab.
19	(SIGNS or SYMPTOMS).kw.
20	MALABSORPTION SYNDROMES.kw.
21	INTESTINAL ABSORPTION.kw.
22	malabsorption.ti,ab.
23	(Blind Loop Syndrome or C?eliac Disease or Sprue or Lactose Intoleran\$ or Short Bowel Syndrome or Steatorrhea or Whipple Disease).ti,ab.
24	INFERTILITY, MALE.kw.
25	((Infertil\$ or Steril\$ or sub-fertil\$ or subfertil\$) adj10 (male? or men)).ti,ab.
26	(Aspermia or Asthenozoospermia or Azoospermia or Oligospermia or Sertoli Cell-Only Syndrome).ti,ab.
27	PANCREATITIS.kw.
28	pancreatitis.ti,ab.
29	MECONIUM.kw.
30	Meconium ileus.ti,ab.
31	or/4-30
32	3 and 31
33	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 (Diagnos\$ adj5 (doubt\$ or problem?))).ti,ab.
34	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 (Diagnos\$ adj5 symptom?)).ti,ab.
35	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 (sign? adj3 symptom?)).ti,ab.
36	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 (Symptom? adj3

#	Searches
	progress\$)).ti,ab.
37	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj7 (Clinical adj2 (characteristic\$ or manifest\$))).ti,ab.
38	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 Atypical presentation?).ti,ab.
39	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj5 suspect\$).ti,ab.
40	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 ("no screen\$" or "not screen\$" or unscreen\$ or "no test\$" or "not test\$")).ti,ab.
41	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 ((miss\$ or never) adj3 (screen\$ or test\$))).ti,ab.
42	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj5 (present\$ or manifest\$)).ti,ab.
43	diagnos\$.ab. /freq=2
44	42 and 43
45	CYSTIC FIBROSIS.kw.
46	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
47	mucov\$.ti,ab.
48	or/45-47
49	DELAYED DIAGNOSIS.kw.
50	DIAGNOSTIC ERRORS.kw.
51	or/49-50
52	48 and 51
53	32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 44 or 52

### E.1.5 Database: Health Technology Assessment

Last searched on **EBM Reviews - Health Technology Assessment 4th Quarter 2016** on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).tw.
3	mucov\$.tw.
4	or/1-3
5	exp "SIGNS AND SYMPTOMS, RESPIRATORY"/
6	(symptom\$ adj3 respirat\$).tw.
7	((Chronic\$ or recur\$) adj5 (lung adj3 infection?)).tw.
8	exp PNEUMONIA/
9	pneumoni\$.tw.
10	(inflamm\$ adj3 (lung? or pulmonary)).tw.
11	exp RESPIRATORY TRACT DISEASES/ and CHRONIC DISEASE/
12	(chronic\$ adj3 respirat\$).tw.
13	((Recurr\$ or chronic\$) adj2 cough\$).tw.
14	FAILURE TO THRIVE/
15	GROWTH DISORDERS/
16	MALNUTRITION/
17	((fail\$ or falter\$) adj3 (thriv\$ or weight or grow\$)).tw.
18	((grow\$ or weight or height or length) adj3 (disorder? or deficien\$ or poor\$ or retard\$ or restrict\$)).tw.

#	Searches
19	(malnutrition\$ or underweight? or under weight? or wasting or stunting or stunted).tw.
20	exp "SIGNS AND SYMPTOMS, DIGESTIVE"/
21	exp MALABSORPTION SYNDROMES/
22	INTESTINAL ABSORPTION/
23	malabsorption.tw.
24	(Blind Loop Syndrome or C?eliac Disease or Sprue or Lactose Intoleran\$ or Short Bowel Syndrome or Steatorrhea or Whipple Disease).tw.
25	INFERTILITY, MALE/
26	((Infertil\$ or Steril\$ or sub-fertil\$ or subfertil\$) adj10 (male? or men)).tw.
27	(Aspermia or Asthenozoospermia or Azoospermia or Oligospermia or Sertoli Cell-Only Syndrome).tw.
28	exp PANCREATITIS/
29	pancreatitis.tw.
30	MECONIUM/
31	Meconium ileus.tw.
32	or/5-31
33	4 and 32
34	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 (Diagnos\$ adj5 (doubt\$ or problem?))).tw.
35	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 (Diagnos\$ adj5 symptom?)).tw.
36	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 (sign? adj3 symptom?)).tw.
37	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 (Symptom? adj3 progress\$)).tw.
38	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj7 (Clinical adj2 (characteristic\$ or manifest\$))).tw.
39	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 Atypical presentation?).tw.
40	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj5 suspect\$).tw.
41	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 ("no screen\$" or "not screen\$" or unscreen\$ or "no test\$" or "not test\$")).tw.
42	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 ((miss\$ or never) adj3 (screen\$ or test\$))).tw.
43	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj5 (present\$ or manifest\$)).tw.
44	diagnos\$.tw.
45	43 and 44
46	CYSTIC FIBROSIS/
47	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).tw.
48	mucov\$.tw.
49	or/46-48
50	DELAYED DIAGNOSIS/
51	DIAGNOSTIC ERRORS/
52	or/50-51
53	49 and 52
54	33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 45 or 53

## E.1.6 Database: Embase

Last searched on **Embase** 1974 to 2017 Week 01 on 4<sup>th</sup> January 2017.

#	Searches
1	*CYSTIC FIBROSIS/ and exp *DIAGNOSIS/
2	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj7 diag\$).ti,ab.
3	*CYSTIC FIBROSIS/di [Diagnosis]
4	or/1-3
5	PHYSICAL DISEASE BY BODY FUNCTION/
6	(symptom\$ adj3 respirat\$).ti.
7	(symptom\$ adj3 respirat\$).ab. /freq=2
8	((Chronic\$ or recur\$) adj5 (lung adj3 infection?)).ti,ab.
9	exp *PNEUMONIA/
10	pneumoni\$.ti.
11	pneumoni\$.ab. /freq=2
12	(inflamm\$ adj3 (lung? or pulmonary)).ti,ab.
13	exp RESPIRATORY TRACT DISEASE/ and CHRONIC DISEASE/
14	(chronic\$ adj3 respirat\$).ti,ab.
15	((Recurr\$ or chronic\$) adj2 cough\$).ti,ab.
16	*FAILURE TO THRIVE/
17	*GROWTH DISORDER/
18	*MALNUTRITION/
19	((fail\$ or falter\$) adj3 (thriv\$ or weight or grow\$)).ti.
20	((fail\$ or falter\$) adj3 (thriv\$ or weight or grow\$)).ab. /freq=2
21	((grow\$ or weight or height or length) adj3 (disorder? or deficien\$ or poor\$ or retard\$ or restrict\$)).ti,ab.
22	(malnutrition\$ or underweight? or under weight? or wasting or stunting or stunted).ti.
23	(malnutrition\$ or underweight? or under weight? or wasting or stunting or stunted).ab. /freq=2
24	PHYSICAL DISEASE BY BODY FUNCTION/
25	exp *MALABSORPTION/
26	*INTESTINE ABSORPTION/
27	malabsorption.ti.
28	malabsorption.ab. /freq=2
29	(Blind Loop Syndrome or C?eliac Disease or Sprue or Lactose Intoleran\$ or Short Bowel Syndrome or Steatorrhea or Whipple Disease).ti,ab.
30	*MALE INFERTILITY/
31	((Infertil\$ or Steril\$ or sub-fertil\$ or subfertil\$) adj10 (male? or men)).ti,ab.
32	(Aspermia or Asthenozoospermia or Azoospermia or Oligospermia or Sertoli Cell-Only Syndrome).ti,ab.
33	exp *PANCREATITIS/
34	pancreatitis.ti.
35	pancreatitis.ab. /freq=2
36	*MECONIUM/ or *MECONIUM ILIUS/
37	Meconium ileus.ti,ab.
38	or/5-37
39	4 and 38
40	(((((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)) or mucov\$) adj10 (Diagnos\$ adj5

#	Searches
	(doubt\$ or problem?)).ti,ab.
41	(((cystic or pancrea\$) adj2 (fibrosis or fibrocystic) or mucov\$) adj10 (Diagnos\$ adj5 symptom?)).ti,ab.
42	(((cystic or pancrea\$) adj2 (fibrosis or fibrocystic) or mucov\$) adj10 (sign? adj3 symptom?)).ti,ab.
43	(((cystic or pancrea\$) adj2 (fibrosis or fibrocystic) or mucov\$) adj10 (Symptom? adj3 progress\$)).ti,ab.
44	(((cystic or pancrea\$) adj2 (fibrosis or fibrocystic) or mucov\$) adj5 (Clinical adj2 (characteristic\$ or manifest\$))).ti,ab.
45	(((cystic or pancrea\$) adj2 (fibrosis or fibrocystic) or mucov\$) adj10 Atypical presentation?).ti,ab.
46	(((cystic or pancrea\$) adj2 (fibrosis or fibrocystic) or mucov\$) adj5 suspect\$).ti,ab.
47	(((cystic or pancrea\$) adj2 (fibrosis or fibrocystic) or mucov\$) adj10 ("no screen\$" or "not screen\$" or unscreen\$ or "no test\$" or "not test\$")).ti,ab.
48	(((cystic or pancrea\$) adj2 (fibrosis or fibrocystic) or mucov\$) adj10 ((miss\$ or never) adj3 (screen\$ or test\$))).ti,ab.
49	(((cystic or pancrea\$) adj2 (fibrosis or fibrocystic) or mucov\$) adj5 (present\$ or manifest\$)).ti,ab.
50	diagnos\$.ab. /freq=3
51	49 and 50
52	*CYSTIC FIBROSIS/
53	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
54	mucov\$.ti,ab.
55	or/52-54
56	*DELAYED DIAGNOSIS/
57	exp *DIAGNOSTIC ERROR/
58	or/56-57
59	55 and 58
60	39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 51 or 59
61	limit 60 to english language
62	letter.pt. or LETTER/
63	note.pt.
64	editorial.pt.
65	CASE REPORT/ or CASE STUDY/
66	(letter or comment*).ti.
67	or/62-66
68	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
69	67 not 68
70	ANIMAL/ not HUMAN/
71	NONHUMAN/
72	exp ANIMAL EXPERIMENT/
73	exp EXPERIMENTAL ANIMAL/
74	ANIMAL MODEL/
75	exp RODENT/
76	(rat or rats or mouse or mice).ti.
77	or/69-76
78	61 not 77

## E.2 What information and support should be given to children, young people and adults with cystic fibrosis?

### E.2.1 Database: Medline

Last searched on Ovid MEDLINE(R) 1946 to November Week 1 2016 on 10th November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	HEALTH EDUCATION/
6	exp CONSUMER HEALTH INFORMATION/
7	PATIENT EDUCATION AS TOPIC/
8	patient education handout.pt.
9	guideline.pt.
10	((information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruction\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$) adj3 (pamphlet\$ or leaflet\$ or booklet\$ or manual\$ or brochure\$ or publication\$ or handout\$ or electronic\$ or online or on-line or internet or website\$ or web site\$ or web page\$ or webpage\$ or app\$1 or video\$ or dvd\$ or audio\$)).ti,ab.
11	((information\$ or educat\$) adj3 (model\$ or program\$ or need\$ or requirement\$ or support\$ or seek\$ or access\$ or disseminat\$)).ti,ab.
12	(PUBLICATIONS/ or PAMPHLETS/ or POSTERS AS TOPIC/) and (patient\$ or famil\$ or parent? or parental or father\$ or paternal or mother\$ or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$).ti,ab.
13	(exp COUNSELING/ or DECISION SUPPORT TECHNIQUES/ or SOCIAL SUPPORT/) and (patient\$ or famil\$ or parent? or parental or father\$ or paternal or mother\$ or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$).ti.
14	((patient\$ or famil\$ or parent? or parental or father\$ or mother\$ or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti.
15	((patient\$ or famil\$ or parent? or parental or father\$ or paternal or mother\$ or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$) adj3 (pamphlet\$ or leaflet\$ or booklet\$ or manual\$ or brochure\$ or publication\$ or handout\$ or electronic\$ or online or on-line or internet or website\$ or web site\$ or web page\$ or webpage\$ or app\$1 or video\$ or dvd\$ or audio\$)).ti,ab.
16	((language\$ or age\$ or gender\$ or cultur\$ or person\$ or stage\$ of life or life stage\$ or lifestyle\$ or leisure) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti.
17	((pregnan\$ or fertil\$) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti,ab.
18	exp SELF-HELP GROUPS/
19	CHARITIES/ or charit\$.ti,ab.
20	HOTLINES/
21	exp TELEPHONE/

#	Searches
22	(hotline\$ or helpline\$ or telephone\$ or phone\$ or smartphone\$ or mobile\$).ti,ab.
23	exp INTERNET/
24	SOCIAL NETWORKING/
25	(social network\$ or social media\$ or facebook\$ or twitter or blog\$ or youtube).ti,ab.
26	exp PSYCHOTHERAPY/
27	((self help\$ or support\$ or counsel\$ or psycho\$) adj (group\$ or session\$ or program\$ or meeting\$ or therap\$)).ti,ab.
28	psychotherap\$.ti,ab.
29	STRESS, PSYCHOLOGICAL/pc
30	(checklist\$ or check list\$).ti,ab.
31	PROFESSIONAL-FAMILY RELATIONS/ or PROFESSIONAL-PATIENT RELATIONS/
32	PATIENT CARE TEAM/
33	(named contact or named person or named individual or point of contact or key worker\$).ti,ab.
34	exp PATIENT CARE PLANNING/
35	((timing or frequency or transition\$) and (inform\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or consult\$ or involvement or support\$ or counsel\$ or discuss\$)).ti,ab.
36	exp HOME CARE SERVICES/
37	home support\$.ti,ab.
38	home nurs\$.ti,ab.
39	outreach\$.ti,ab.
40	SCHOOLS/
41	SCHOOL NURSING/
42	((school\$ or education) adj3 (staff or teacher\$ or nurs\$ or healthcare or support\$)).ti,ab.
43	SOCIAL WELFARE/
44	SOCIAL SECURITY/
45	((social or disab\$ or income or unemploy\$) adj (security or aid or benefit\$ or credit\$ or welfare)).ti,ab.
46	or/5-45
47	and/4,46
48	limit 47 to english language
49	LETTER/
50	EDITORIAL/
51	NEWS/
52	exp HISTORICAL ARTICLE/
53	ANECDOTES AS TOPIC/
54	COMMENT/
55	CASE REPORT/
56	(letter or comment*).ti.
57	or/49-56
58	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
59	57 not 58
60	ANIMALS/ not HUMANS/
61	exp ANIMALS, LABORATORY/
62	exp ANIMAL EXPERIMENTATION/

#	Searches
63	exp MODELS, ANIMAL/
64	exp RODENTIA/
65	(rat or rats or mouse or mice).ti.
66	or/59-65
67	48 not 66

## E.2.2 Database: Medline In-Process & Other Non-Indexed Citations

Last searched on Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations November 09, 2016 on 10th November 2016.

#	Searches
1	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
2	mucov\$.ti,ab.
3	1 or 2
4	patient education handout.pt.
5	guideline.pt.
6	((information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruction\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$) adj3 (pamphlet\$ or leaflet\$ or booklet\$ or manual\$ or brochure\$ or publication\$ or handout\$ or electronic\$ or online or on-line or internet or website\$ or web site\$ or web page\$ or webpage or app\$1 or video\$ or dvd\$ or audio\$)).ti,ab.
7	((information\$ or educat\$) adj3 (model\$ or program\$ or need\$ or requirement\$ or support\$ or seek\$ or access\$ or disseminat\$)).ti,ab.
8	((patient\$ or famil\$ or parent? or parental or father* or paternal or mother* or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti.
9	((patient\$ or famil\$ or parent? or parental or father* or paternal or mother* or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$) adj3 (pamphlet\$ or leaflet\$ or booklet\$ or manual\$ or brochure\$ or publication\$ or handout\$ or electronic\$ or online or on-line or internet or website\$ or web site\$ or web page\$ or webpage\$ or app\$1 or video\$ or dvd\$ or audio\$)).ti,ab.
10	((language\$ or age\$ or gender\$ or cultur\$ or person\$ or stage\$ of life or life stage\$ or lifestyle\$ or leisure) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti.
11	((pregnan\$ or fertil\$) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti,ab.
12	charit\$.ti,ab.
13	(hotline\$ or helpline\$ or telephone\$ or phone\$ or smartphone\$ or mobile\$).ti,ab.
14	(social network\$ or social media\$ or facebook\$ or twitter or blog\$ or youtube).ti,ab.
15	((self help\$ or support\$ or counsel\$ or psycho\$) adj (group\$ or session\$ or program\$ or meeting\$ or therap\$)).ti,ab.
16	psychotherap\$.ti,ab.
17	(checklist\$ or check list\$).ti,ab.
18	patient care team.ti,ab.
19	(named contact or named person or named individual or point of contact or key

#	Searches
	worker\$.ti,ab.
20	((timing or frequency or transition\$) and (inform\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ involvement or support\$ or counsel\$ or discuss\$)).ti,ab.
21	home care.ti,ab.
22	home support\$.ti,ab.
23	home nurs\$.ti,ab.
24	outreach\$.ti,ab.
25	((school\$ or education) adj3 (staff or teacher\$ or nurs\$ or healthcare or support\$)).ti,ab.
26	((social or disab\$ or income or unemploy\$) adj (security or aid or benefit\$ or credit\$ or welfare)).ti,ab.
27	or/4-26
28	3 and 27

### E.2.3 Database: Cochrane Central Register of Controlled Trials

Last searched on **EBM Reviews - Cochrane Central Register of Controlled Trials**  
October 2016 on 10<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	HEALTH EDUCATION/
6	exp CONSUMER HEALTH INFORMATION/
7	PATIENT EDUCATION AS TOPIC/
8	patient education handout.pt.
9	guideline.pt.
10	((information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruction\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$) adj3 (pamphlet\$ or leaflet\$ or booklet\$ or manual\$ or brochure\$ or publication\$ or handout\$ or electronic\$ or online or on-line or internet or website\$ or web site\$ or web page\$ or webpage or app\$1 or video\$ or dvd\$ or audio\$)).ti,ab.
11	((information\$ or educat\$) adj3 (model\$ or program\$ or need\$ or requirement\$ or support\$ or seek\$ or access\$ or disseminat\$)).ti,ab.
12	(PUBLICATIONS/ or PAMPHLETS/ or POSTERS AS TOPIC/) and (patient\$ or famil\$ or parent? or parental or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$).ti,ab.
13	(exp COUNSELING/ or DECISION SUPPORT TECHNIQUES/ or SOCIAL SUPPORT/) and (patient\$ or famil\$ or parent? or parental or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$).ti.
14	((patient\$ or famil\$ or parent? or parental or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti.
15	((patient\$ or famil\$ or parent? or parental or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$) adj3 (pamphlet\$ or leaflet\$ or booklet\$ or manual\$ or brochure\$ or publication\$ or handout\$ or electronic\$ or online or on-line or

#	Searches
	internet or website\$ or web site\$ or web page\$ or webpage\$ or app\$1 or video\$ or dvd\$ or audio\$)).ti,ab.
16	((language\$ or age\$ or gender\$ or cultur\$ or person\$ or stage\$ of life or life stage\$ or lifestyle\$ or leisure) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti.
17	((pregnan\$ or fertil\$) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti,ab.
18	exp SELF-HELP GROUPS/
19	CHARITIES/ or charit\$.ti,ab.
20	HOTLINES/
21	exp TELEPHONE/
22	(hotline\$ or helpline\$ or telephone\$ or phone\$ or smartphone\$ or mobile\$).ti,ab.
23	exp INTERNET/
24	SOCIAL NETWORKING/
25	(social network\$ or social media\$ or facebook\$ or twitter or blog\$ or youtube).ti,ab.
26	exp PSYCHOTHERAPY/
27	((self help\$ or support\$ or counsel\$ or psycho\$) adj (group\$ or session\$ or program\$ or meeting\$ or therap\$)).ti,ab.
28	psychotherap\$.ti,ab.
29	STRESS, PSYCHOLOGICAL/pc
30	(checklist\$ or check list\$).ti,ab.
31	PROFESSIONAL-FAMILY RELATIONS/ or PROFESSIONAL-PATIENT RELATIONS/
32	PATIENT CARE TEAM/
33	(named contact or named person or named individual or point of contact or key worker\$).ti,ab.
34	exp PATIENT CARE PLANNING/
35	((timing or frequency or transition\$) and (inform\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or consult\$ or involvement or support\$ or counsel\$ or discuss\$)).ti,ab.
36	exp HOME CARE SERVICES/
37	home support\$.ti,ab.
38	home nurs\$.ti,ab.
39	outreach\$.ti,ab.
40	SCHOOLS/
41	SCHOOL NURSING/
42	((school\$ or education) adj3 (staff or teacher\$ or nurs\$ or healthcare or support\$)).ti,ab.
43	SOCIAL WELFARE/
44	SOCIAL SECURITY/
45	((social or disab\$ or income or unemploy\$) adj (security or aid or benefit\$ or credit\$ or welfare)).ti,ab.
46	or/5-45
47	and/4,46
48	limit 47 to english language

## E.2.4 Database: Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects

Last searched on **EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to November 09, 2016, **EBM Reviews - Database of Abstracts of Reviews of Effects 1st Quarter 2015** on 10<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS.kw.
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	HEALTH EDUCATION.kw.
6	CONSUMER HEALTH INFORMATION.kw.
7	PATIENT EDUCATION AS TOPIC.kw.
8	((information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruction\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$) adj3 (pamphlet\$ or leaflet\$ or booklet\$ or manual\$ or brochure\$ or publication\$ or handout\$ or electronic\$ or online or on-line or internet or website\$ or web site\$ or web page\$ or webpage or app\$1 or video\$ or dvd\$ or audio\$)).ti,ab.
9	((information\$ or educat\$) adj3 (model\$ or program\$ or need\$ or requirement\$ or support\$ or seek\$ or access\$ or disseminat\$)).ti,ab.
10	(PUBLICATIONS or PAMPHLETS or POSTERS AS TOPIC).kw. and (patient\$ or famil\$ or parent? or parental or father* or paternal or mother* or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$).ti,ab.
11	(COUNSELING or DECISION SUPPORT TECHNIQUES or SOCIAL SUPPORT).kw. and (patient\$ or famil\$ or parent? or parental or father* or paternal or mother* or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$).ti.
12	((patient\$ or famil\$ or parent? or parental or father* or paternal or mother* or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti.
13	((patient\$ or famil\$ or parent? or parental or father* or paternal or mother* or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$) adj3 (pamphlet\$ or leaflet\$ or booklet\$ or manual\$ or brochure\$ or publication\$ or handout\$ or electronic\$ or online or on-line or internet or website\$ or web site\$ or web page\$ or webpage\$ or app\$1 or video\$ or dvd\$ or audio\$)).ti,ab.
14	((language\$ or age\$ or gender\$ or cultur\$ or person\$ or stage\$ of life or life stage\$ or lifestyle\$ or leisure) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti.
15	((pregnan\$ or fertil\$) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti,ab.
16	SELF-HELP GROUPS.kw.
17	CHARITIES.kw. or charit\$.ti,ab.
18	HOTLINES.kw.
19	TELEPHONE.kw.
20	(hotline\$ or helpline\$ or telephone\$ or phone\$ or smartphone\$ or mobile\$).ti,ab.
21	INTERNET.kw.
22	SOCIAL NETWORKING.kw.
23	(social network\$ or social media\$ or facebook\$ or twitter or blog\$ or youtube).ti,ab.

#	Searches
24	PSYCHOTHERAPY.kw.
25	((self help\$ or support\$ or counsel\$ or psycho\$) adj (group\$ or session\$ or program\$ or meeting\$ or therap\$)).ti,ab.
26	psychotherap\$.ti,ab.
27	STRESS, PSYCHOLOGICAL.kw.
28	(checklist\$ or check list\$).ti,ab.
29	(PROFESSIONAL-FAMILY RELATIONS or PROFESSIONAL-PATIENT RELATIONS).kw.
30	PATIENT CARE TEAM.kw.
31	(named contact or named person or named individual or point of contact or key worker\$).ti,ab.
32	PATIENT CARE PLANNING.kw.
33	((timing or frequency or transition\$) and (inform\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or consult\$ or involvement or support\$ or counsel\$ or discuss\$)).ti,ab.
34	HOME CARE SERVICES.kw.
35	home support\$.ti,ab.
36	home nurs\$.ti,ab.
37	outreach\$.ti,ab.
38	SCHOOLS.kw.
39	SCHOOL NURSING.kw.
40	((school\$ or education) adj3 (staff or teacher\$ or nurs\$ or healthcare or support\$)).ti,ab.
41	SOCIAL WELFARE.kw.
42	SOCIAL SECURITY.kw.
43	((social or disab\$ or income or unemploy\$) adj (security or aid or benefit\$ or credit\$ or welfare)).ti,ab.
44	or/5-43
45	4 and 44

### E.2.5 Database: Health Technology Assessment

Last searched on **EBM Reviews - Health Technology Assessment 4th Quarter 2016** on 8<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	exp HEALTH EDUCATION/
6	PATIENT EDUCATION AS TOPIC/
7	((information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruction\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$) adj3 (pamphlet\$ or leaflet\$ or booklet\$ or manual\$ or brochure\$ or publication\$ or handout\$ or electronic\$ or online or on-line or internet or website\$ or web site\$ or web page\$ or webpage or app\$1 or video\$ or dvd\$ or audio\$)).ti,ab.
8	((information\$ or educat\$) adj3 (model\$ or program\$ or need\$ or requirement\$ or support\$ or seek\$ or access\$ or disseminat\$)).ti,ab.

#	Searches
9	(PUBLICATIONS/ or PAMPHLETS/ or POSTERS AS TOPIC/) and (patient\$ or famil\$ or parent? or parental or father* or paternal or mother* or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$).ti,ab.
10	(exp COUNSELING/ or DECISION SUPPORT TECHNIQUES/ or SOCIAL SUPPORT/) and (patient\$ or famil\$ or parent? or parental or father* or paternal or mother* or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$).ti.
11	((patient\$ or famil\$ or parent? or parental or father* or paternal or mother* or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti.
12	((patient\$ or famil\$ or parent? or parental or father* or paternal or mother* or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$) adj3 (pamphlet\$ or leaflet\$ or booklet\$ or manual\$ or brochure\$ or publication\$ or handout\$ or electronic\$ or online or on-line or internet or website\$ or web site\$ or web page\$ or webpage\$ or app\$1 or video\$ or dvd\$ or audio\$)).ti,ab.
13	((language\$ or age\$ or gender\$ or cultur\$ or person\$ or stage\$ of life or life stage\$ or lifestyle\$ or leisure) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti.
14	((pregnan\$ or fertil\$) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti,ab.
15	exp SELF-HELP GROUPS/
16	exp CHARITIES/ or charit\$.ti,ab.
17	HOTLINES/
18	exp TELEPHONE/
19	(hotline\$ or helpline\$ or telephone\$ or phone\$ or smartphone\$ or mobile\$).ti,ab.
20	exp INTERNET/
21	(social network\$ or social media\$ or facebook\$ or twitter or blog\$ or youtube).ti,ab.
22	exp PSYCHOTHERAPY/
23	((self help\$ or support\$ or counsel\$ or psycho\$) adj (group\$ or session\$ or program\$ or meeting\$ or therap\$)).ti,ab.
24	psychotherap\$.ti,ab.
25	STRESS, PSYCHOLOGICAL/pc
26	(checklist\$ or check list\$).ti,ab.
27	PROFESSIONAL-FAMILY RELATIONS/ or PROFESSIONAL-PATIENT RELATIONS/
28	PATIENT CARE TEAM/
29	(named contact or named person or named individual or point of contact or key worker\$).ti,ab.
30	exp PATIENT CARE PLANNING/
31	((timing or frequency or transition\$) and (inform\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or consult\$ or involvement or support\$ or counsel\$ or discuss\$)).ti,ab.
32	exp HOME CARE SERVICES/
33	home support\$.ti,ab.
34	home nurs\$.ti,ab.
35	outreach\$.ti,ab.
36	SCHOOLS/
37	SCHOOL NURSING/

#	Searches
38	((school\$ or education) adj3 (staff or teacher\$ or nurs\$ or healthcare or support\$)).ti,ab.
39	exp SOCIAL WORK/
40	exp SOCIAL WELFARE/
41	((social or disab\$ or income or unemploy\$) adj (security or aid or benefit\$ or credit\$ or welfare)).ti,ab.
42	or/5-41
43	4 and 42

## E.2.6 Database: Embase

Last searched on **Embase** 1974 to 2016 Week 45 on 10<sup>th</sup> November 2016.

#	Searches
1	cystic fibrosis/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	health education/
6	consumer health information/
7	patient information/
8	patient education/
9	((information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruction\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$) adj3 (pamphlet\$ or leaflet\$ or booklet\$ or manual\$ or brochure\$ or publication\$ or handout\$ or electronic\$ or online or on-line or internet or website\$ or web site\$ or web page\$ or webpage or app\$1 or video\$ or dvd\$ or audio\$)).ti,ab.
10	((information\$ or educat\$) and (model\$ or program\$ or need\$ or requirement\$ or support\$ or seek\$ or access\$ or disseminat\$)).ti.
11	PUBLICATION/ and (patient\$ or famil\$ or parent? or parental or father* or paternal or mother* or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$).ti.
12	(exp COUNSELING/ or DECISION SUPPORT SYSTEM/ or SOCIAL SUPPORT/) and (patient\$ or famil\$ or parent? or parental or father* or paternal or mother* or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$).ti.
13	((patient\$ or famil\$ or parent? or parental or father* or paternal or mother* or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti.
14	((patient\$ or famil\$ or parent? or parental or father* or paternal or mother* or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$) adj3 (pamphlet\$ or leaflet\$ or booklet\$ or manual\$ or brochure\$ or publication\$ or handout\$ or electronic\$ or online or on-line or internet or website\$ or web site\$ or web page\$ or webpage\$ or app\$1 or video\$ or dvd\$ or audio\$)).ti,ab.
15	((language\$ or age\$ or gender\$ or cultur\$ or person\$ or stage\$ of life or life stage\$ or lifestyle\$ or leisure) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti.
16	((pregnan\$ or fertil\$) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti,ab.
17	self help/

#	Searches
18	charit\$.ti.
19	telephone/
20	mobile phone/
21	mobile application/
22	(hotline\$ or helpline\$ or telephone\$ or phone\$ or smartphone\$ or mobile\$).ti.
23	internet/
24	social network/
25	(social network\$ or social media\$ or facebook\$ or twitter or blog\$ or youtube).ti,ab.
26	exp psychotherapy/
27	((self help\$ or support\$ or counsel\$ or psycho\$) adj (group\$ or session\$ or program\$ or meeting\$ or therap\$)).ti,ab.
28	psychotherap\$.ti,ab.
29	mental stress/pc [Prevention]
30	(checklist\$ or check list\$).ti.
31	human relation/
32	doctor patient relation/
33	(named contact or named person or named individual or point of contact or key worker\$).ti,ab.
34	patient care planning/
35	((timing or frequency or transition\$) and (inform\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or consult\$ or involvement or support\$ or counsel\$ or discuss\$)).ti.
36	exp home care/
37	home support\$.ti,ab.
38	home nurs\$.ti,ab.
39	outreach\$.ti,ab.
40	community care/
41	school health education/ or school health service/ or school health nursing/
42	((school\$ or education) adj3 (staff or teacher\$ or nurs\$ or healthcare or support\$)).ti,ab.
43	school/
44	social welfare/
45	social security/
46	((social or disab\$ or income or unemploy\$) adj (security or aid or benefit\$ or credit\$ or welfare)).ti,ab.
47	or/5-46
48	4 and 47
49	letter.pt. or LETTER/
50	note.pt.
51	editorial.pt.
52	CASE REPORT/ or CASE STUDY/
53	(letter or comment*).ti.
54	or/49-53
55	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
56	54 not 55
57	ANIMAL/ not HUMAN/
58	NONHUMAN/

#	Searches
59	exp ANIMAL EXPERIMENT/
60	exp EXPERIMENTAL ANIMAL/
61	ANIMAL MODEL/
62	exp RODENT/
63	(rat or rats or mouse or mice).ti.
64	or/56-63
65	48 not 64
66	limit 65 to english language

## E.2.7 Database: PsycINFO

Last searched on **PsycINFO 1967 to October 2016** on 10<sup>th</sup> November 2016.

#	Searches
1	cystic fibrosis/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	health education/
6	client education/
7	Patients/ and Information/
8	((information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruction\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$) adj3 (pamphlet\$ or leaflet\$ or booklet\$ or manual\$ or brochure\$ or publication\$ or handout\$ or electronic\$ or online or on-line or internet or website\$ or web site\$ or web page\$ or webpage or app\$1 or video\$ or dvd\$ or audio\$)).ti,ab.
9	((information\$ or educat\$) adj3 (model\$ or program\$ or need\$ or requirement\$ or support\$ or seek\$ or access\$ or disseminat\$)).ti,ab.
10	exp printed communications media/ or exp reading materials/
11	(exp COUNSELING/ or exp COUNSELORS/ or exp FAMILY THERAPY/ or exp DECISION MAKING/ or SOCIAL SUPPORT/) and (patient\$ or famil\$ or parent? or parental or father* or paternal or mother* or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$).ti.
12	((patient\$ or famil\$ or parent? or parental or father* or paternal or mother* or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti.
13	((patient\$ or famil\$ or parent? or parental or father* or paternal or mother* or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$) adj3 (pamphlet\$ or leaflet\$ or booklet\$ or manual\$ or brochure\$ or publication\$ or handout\$ or electronic\$ or online or on-line or internet or website\$ or web site\$ or web page\$ or webpage\$ or app\$1 or video\$ or dvd\$ or audio\$)).ti,ab.
14	((language\$ or age\$ or gender\$ or cultur\$ or person\$ or stage\$ of life or life stage\$ or lifestyle\$ or leisure) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti.
15	((pregnan\$ or fertil\$) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti,ab.
16	SUPPORT GROUPS/

#	Searches
17	nonprofit organizations/
18	charit\$.ti,ab.
19	hot line services/
20	exp telephone systems/
21	(hotline\$ or helpline\$ or telephone\$ or phone\$ or smartphone\$ or mobile\$).ti,ab.
22	exp internet/
23	online social networks/
24	(social network\$ or social media\$ or facebook\$ or twitter or blog\$ or youtube).ti,ab.
25	exp PSYCHOTHERAPY/
26	((self help\$ or support\$ or counsel\$ or psycho\$) adj (group\$ or session\$ or program\$ or meeting\$ or therap\$)).ti,ab.
27	psychotherap\$.ti,ab.
28	psychological stress/ or "stress and coping measures"/
29	(checklist\$ or check list\$).ti,ab.
30	(named contact or named person or named individual or point of contact or key worker\$).ti,ab.
31	exp treatment planning/
32	((timing or frequency or transition\$) and (inform\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or consult\$ or involvement or support\$ or counsel\$ or discuss\$)).ti,ab.
33	home care/ or adult day care/ or home visiting programs/
34	home support\$.ti,ab.
35	home nurs\$.ti,ab.
36	outreach\$.ti,ab.
37	exp OUTREACH PROGRAMS/
38	((school\$ or education) adj3 (staff or teacher\$ or nurs\$ or healthcare or support\$)).ti,ab.
39	exp schools/
40	school nurses/
41	exp Community Welfare Services/ or exp "Welfare Services (Government)"/
42	social security/
43	((social or disab\$ or income or unemploy\$) adj (security or aid or benefit\$ or credit\$ or welfare)).ti,ab.
44	or/5-43
45	4 and 44
46	limit 45 to english language

## E.2.8 Database: CINAHL

Last searched on **CINHAL** on 8<sup>th</sup> November 2016.

Search ID#	Search Terms
S44	S5 AND S43
S43	S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42
S42	TI ((social or disab* or income or unemploy*) N1 (security or aid or benefit* or credit* or welfare)) or AB ((social or disab* or income or unemploy*) N1 (security or aid or benefit*

Search ID#	Search Terms
	or credit* or welfare))
S41	(MH "Economic and Social Security")
S40	MH SOCIAL WELFARE
S39	TI ((school* or education) N3 (staff or teacher* or nurs* or healthcare or support*)) or AB ((school* or education) N3 (staff or teacher* or nurs* or healthcare or support*))
S38	MH SCHOOLS+
S37	TI outreach* or AB outreach*
S36	TI home nurs* or AB home nurs*
S35	TI home support* or AB home support*
S34	(MH "Home Health Care+")
S33	TI ((timing or frequency or transition*) and (inform* or educat* or learn* or train* or program* or advi?e* or instruct* or teach* or knowledge or understanding or misunderstanding or communicat* or miscommunicat* or consult* or involvement or support* or counsel* or discuss*)) or AB ((timing or frequency or transition*) and (inform* or educat* or learn* or train* or program* or advi?e* or instruct* or teach* or knowledge or understanding or misunderstanding or communicat* or miscommunicat* or consult* or involvement or support* or counsel* or discuss*))
S32	(MH "Patient Care Plans+")
S31	TI (named contact or named person or named individual or point of contact or key worker*) or AB (named contact or named person or named individual or point of contact or key worker*)
S30	(MH "Multidisciplinary Care Team+")
S29	(MH "Professional-Patient Relations+") OR (MH "Professional-Family Relations")
S28	TI (checklist* or check list*) or AB (checklist* or check list*)
S27	(MH "Stress, Psychological+/PC")
S26	TI psychotherap*
S25	TI ((self help* or support* or counsel* or psycho*) N1 (group* or session* or program* or meeting* or therap*)) or AB ((self help* or support* or counsel* or psycho*) N1 (group* or session* or program* or meeting* or therap*))
S24	(MH "Psychotherapy+")
S23	TI (social network* or social media* or facebook* or twitter or blog* or youtube) or AB (social network* or social media* or facebook* or twitter or blog* or youtube)
S22	(MH "Social Networks")
S21	MH INTERNET
S20	TI (hotline* or helpline* or telephone* or phone* or smartphone* or mobile*)
S19	(MH "Telephone Information Services")
S18	MH CHARITIES OR TI charit*
S17	(MH "Psychotherapy, Group+")
S16	TI ((pregnan* or fertil*) N3 (information* or educat* or learn* or train* or program* or advi?e* or instruct* or teach* or knowledge or understanding or misunderstanding or communicat* or miscommunicat* or involvement or support* or counsel*)) or AB ((pregnan* or fertil*) N3 (information* or educat* or learn* or train* or program* or advi?e* or instruct* or teach* or knowledge or understanding or misunderstanding or communicat* or miscommunicat* or involvement or support* or counsel*))
S15	TI ((language* or age* or gender* or cultur* or person* or stage* of life or life stage* or lifestyle* or leisure) N3 (information* or educat* or learn* or train* or program* or advi?e* or instruct* or teach* or knowledge or understanding or misunderstanding or communicat* or miscommunicat* or involvement or support* or counsel*)) or AB ((language* or age* or gender* or cultur* or person* or stage* of life or life stage* or lifestyle* or leisure) N3 (information* or educat* or learn* or train* or program* or advi?e* or instruct* or teach* or knowledge or understanding or misunderstanding or communicat* or miscommunicat* or involvement or support* or counsel*))

Search ID#	Search Terms
	or instruct* or teach* or knowledge or understanding or misunderstanding or communicat* or miscommunicat* or involvement or support* or counsel*)
S14	TI ((patient* or famil* or parent? or parental or father* or mother* or grandparent* or grandfather* or grandmother* or caregiver* or carer*) N3 (pamphlet* or leaflet* or booklet* or manual* or brochure* or publication* or handout* or electronic* or online or on-line or internet or website* or web site* or web page* or webpage* or app*1 or video* or dvd* or audio*)) or AB ((patient* or famil* or parent? or parental or father* or paternal or mother* or maternal or or grandparent* or grandfather* or grandmother* or caregiver* or carer*) N3 (pamphlet* or leaflet* or booklet* or manual* or brochure* or publication* or handout* or electronic* or online or on-line or internet or website* or web site* or web page* or webpage* or app*1 or video* or dvd* or audio*))
S13	TI ((patient* or famil* or parent? or parental or father* or paternal or mother* or maternal or or grandparent* or grandfather* or grandmother* or caregiver* or carer*) N3 (information* or educat* or learn* or train* or program* or advi?e* or instruct* or teach* or knowledge or understanding or misunderstanding or communicat* or miscommunicat* or involvement or support* or counsel*))
S12	(MH COUNSELING or MH DECISION SUPPORT TECHNIQUES or MH SOCIAL SUPPORT) and TI (patient* or famil* or parent? or parental or father* or paternal or mother* or maternal or grandparent* or grandfather* or grandmother* or caregiver* or carer*)
S11	(MH PUBLICATIONS/ or MH PAMPHLETS) and TI (patient* or famil* or parent* or parental or father* or paternal or mother* or maternal or grandparent* or grandfather* or grandmother* or caregiver* or carer*)
S10	TI ((information* or educat*) N3 (model* or program* or need* or requirement* or support* or seek* or access* or disseminat*))
S9	TI ((information* or educat* or learn* or train* or program* or advi?e* or instruction* or teach* or knowledge or understanding or misunderstanding or communicat* or miscommunicat* or involvement or support* or counsel*) N3 (pamphlet* or leaflet* or booklet* or manual* or brochure* or publication* or handout* or electronic* or online or on-line or internet or website* or web site* or web page* or webpage* or app*1 or video* or dvd* or audio*))
S8	MH PATIENT EDUCATION
S7	MH CONSUMER HEALTH INFORMATION
S6	MH HEALTH EDUCATION
S5	S1 or S2 or S3 or S4
S4	TI mucov* OR AB mucov*
S3	AB ((cystic or pancrea*) N2 (fibrosis or fibrocystic))
S2	TI ((cystic or pancrea*) N2 (fibrosis or fibrocystic))
S1	MH CYSTIC FIBROSIS

### E.2.9 Database: AMED

Last searched on **AMED 1985 to October 2016** on 10<sup>th</sup> November 2016.

#	Searches
1	cystic fibrosis/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	Health education/
6	exp patient education/
7	((information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruction\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or

#	Searches
	miscommunicat\$ or involvement or support\$ or counsel\$) adj3 (pamphlet\$ or leaflet\$ or booklet\$ or manual\$ or brochure\$ or publication\$ or handout\$ or electronic\$ or online or on-line or internet or website\$ or web site\$ or web page\$ or webpage\$ or app\$1 or video\$ or dvd\$ or audio\$)).ti,ab.
8	((information\$ or educat\$) adj3 (model\$ or program\$ or need\$ or requirement\$ or support\$ or seek\$ or access\$ or disseminat\$)).ti,ab.
9	exp Publications/ and (patient\$ or famil\$ or parent? or parental or father\$ or paternal or mother\$ or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$).ti,ab.
10	(exp COUNSELING/ or DECISION MAKING/ or SOCIAL SUPPORT/) and (patient\$ or famil\$ or parent? or parental or father\$ or paternal or mother\$ or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$).ti,ab.
11	((patient\$ or famil\$ or parent? or parental or father\$ or mother\$ or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti.
12	((patient\$ or famil\$ or parent? or parental or father\$ or paternal or mother\$ or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$) adj3 (pamphlet\$ or leaflet\$ or booklet\$ or manual\$ or brochure\$ or publication\$ or handout\$ or electronic\$ or online or on-line or internet or website\$ or web site\$ or web page\$ or webpage\$ or app\$1 or video\$ or dvd\$ or audio\$)).ti,ab.
13	((language\$ or age\$ or gender\$ or cultur\$ or person\$ or stage\$ of life or life stage\$ or lifestyle\$ or leisure) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti.
14	((pregnan\$ or fertil\$) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti,ab.
15	Self help groups/
16	CHARITIES/ or charit\$.ti,ab.
17	exp communications media/
18	(hotline\$ or helpline\$ or telephone\$ or phone\$ or smartphone\$ or mobile\$).ti,ab.
19	(internet or social network\$ or social media\$ or facebook\$ or twitter or blog\$ or youtube).ti,ab.
20	exp psychotherapy/
21	((self help\$ or support\$ or counsel\$ or psycho\$) adj (group\$ or session\$ or program\$ or meeting\$ or therap\$)).ti,ab.
22	psychotherap\$.ti,ab.
23	stress psychological/
24	(checklist\$ or check list\$).ti,ab.
25	professional family relations/ or exp professional patient relations/
26	patient care team/
27	(named contact or named person or named individual or point of contact or key worker\$).ti,ab.
28	patient care planning/
29	((timing or frequency or transition\$) and (inform\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or consult\$ or involvement or support\$ or counsel\$ or discuss\$)).ti,ab.
30	exp home care services/
31	home support\$.ti,ab.

#	Searches
32	home nurs\$.ti,ab.
33	outreach\$.ti,ab.
34	schools/
35	((school\$ or education) adj3 (staff or teacher\$ or nurs\$ or healthcare or support\$)).ti,ab.
36	school health services/
37	social welfare/
38	social security/
39	((social or disab\$ or income or unemploy\$) adj (security or aid or benefit\$ or credit\$ or welfare)).ti,ab.
40	or/5-39
41	4 and 40
42	limit 41 to english language

### E.2.10 Database: HMIC

Last searched on **HMIC 1979 to September 2016** on 10<sup>th</sup> November 2016.

#	Searches
1	cystic fibrosis/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	Health education/
6	exp patient education/
7	((information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruction\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$) adj3 (pamphlet\$ or leaflet\$ or booklet\$ or manual\$ or brochure\$ or publication\$ or handout\$ or electronic\$ or online or on-line or internet or website\$ or web site\$ or web page\$ or webpage\$ or app\$1 or video\$ or dvd\$ or audio\$)).ti,ab.
8	((information\$ or educat\$) adj3 (model\$ or program\$ or need\$ or requirement\$ or support\$ or seek\$ or access\$ or disseminat\$)).ti,ab.
9	exp Publications/ and (patient\$ or famil\$ or parent? or parental or father\$ or paternal or mother\$ or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$).ti,ab.
10	(exp COUNSELING/ or DECISION MAKING/ or SOCIAL SUPPORT/) and (patient\$ or famil\$ or parent? or parental or father\$ or paternal or mother\$ or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$).ti,ab.
11	((patient\$ or famil\$ or parent? or parental or father\$ or mother\$ or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti.
12	((patient\$ or famil\$ or parent? or parental or father\$ or paternal or mother\$ or maternal or grandparent\$ or grandfather\$ or grandmother\$ or caregiver\$ or carer\$) adj3 (pamphlet\$ or leaflet\$ or booklet\$ or manual\$ or brochure\$ or publication\$ or handout\$ or electronic\$ or online or on-line or internet or website\$ or web site\$ or web page\$ or webpage\$ or app\$1 or video\$ or dvd\$ or audio\$)).ti,ab.
13	((language\$ or age\$ or gender\$ or cultur\$ or person\$ or stage\$ of life or life stage\$ or lifestyle\$ or leisure) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti.

#	Searches
14	((pregnan\$ or fertil\$) adj3 (information\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or involvement or support\$ or counsel\$)).ti,ab.
15	Self help groups/
16	CHARITIES/ or charit\$.ti,ab.
17	INTERNET/ or INTERNET WEBSITES/
18	SOCIAL NETWORKING/
19	(hotline\$ or helpline\$ or telephone\$ or phone\$ or smartphone\$ or mobile\$).ti,ab.
20	(internet or social network\$ or social media\$ or facebook\$ or twitter or blog\$ or youtube).ti,ab.
21	exp psychotherapy/
22	((self help\$ or support\$ or counsel\$ or psycho\$) adj (group\$ or session\$ or program\$ or meeting\$ or therap\$)).ti,ab.
23	psychotherap\$.ti,ab.
24	exp STRESS/
25	(checklist\$ or check list\$).ti,ab.
26	PATIENT EMPOWERMENT/
27	patient care team/
28	(named contact or named person or named individual or point of contact or key worker\$).ti,ab.
29	exp HEALTH PLANS/
30	((timing or frequency or transition\$) and (inform\$ or educat\$ or learn\$ or train\$ or program\$ or advi?e\$ or instruct\$ or teach\$ or knowledge or understanding or misunderstanding or communicat\$ or miscommunicat\$ or consult\$ or involvement or support\$ or counsel\$ or discuss\$)).ti,ab.
31	exp home care/
32	home support\$.ti,ab.
33	home nurs\$.ti,ab.
34	outreach\$.ti,ab.
35	schools/
36	((school\$ or education) adj3 (staff or teacher\$ or nurs\$ or healthcare or support\$)).ti,ab.
37	school health services/
38	social welfare/
39	social security/
40	((social or disab\$ or income or unemploy\$) adj (security or aid or benefit\$ or credit\$ or welfare)).ti,ab.
41	or/5-40
42	4 and 41

## E.3 Service delivery

### E.3.1 What is the effectiveness of different models of care (for example, specialist centre, shared care [delivered by a Network CF Clinic which is part of an agreed designated network with a Specialist CF Centre], community, telehealth and/or home care for people with CF?

- Database: Medline

Last searched on **Ovid MEDLINE(R)** 1946 to December Week 1 2016 on 5<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	"DELIVERY OF HEALTH CARE"/
6	HEALTH SERVICES ADMINISTRATION/
7	MODELS, ORGANIZATIONAL/
8	MODELS, NURSING/
9	((care or healthcare) adj3 (organi\$ or deliv\$)).ab,ti.
10	((care or healthcare or organi\$ or nursing or nurse?) adj3 (model? or design\$)).ab,ti.
11	(special\$ adj3 (center? or centre? or clinic?)).ab,ti.
12	exp TELEMEDICINE/
13	(telehealth\$ or tele health\$ or telemedicine\$ or tele medicine\$ or teleconsult\$ or tele consult\$).ab,ti.
14	(Remote\$ adj3 monitor\$).ab,ti.
15	((share? or network\$) adj3 (care or healthcare or center? or centre? or clinic? or service?)).ab,ti.
16	HOME CARE SERVICES/
17	HOME HEALTH NURSING/
18	HOME INFUSION THERAPY/
19	((home? or domicil\$) adj3 (care or healthcare or center? or centre? or clinic? or service?)).ab,ti.
20	(hospital? adj2 home?).ab,ti.
21	((home? or domicil\$) adj3 (Infusion therap\$ or Intravenous\$ or IV)).ab,ti.
22	(outreach adj3 (care or healthcare or center? or centre? or clinic? or service?)).ab,ti.
23	COMMUNITY HEALTH SERVICES/
24	exp COMMUNITY HEALTH NURSING/
25	CHILD HEALTH SERVICES/
26	(communit\$ adj3 (care or healthcare or center? or centre? or clinic? or service?)).ab,ti.
27	((nursing or nurse?) adj3 (communit\$ or home? or domicil\$ or school?)).ab,ti.
28	PALLIATIVE CARE/
29	(palliative adj3 (care or healthcare or service?)).ab,ti.
30	HEALTH SERVICES ACCESSIBILITY/
31	(access\$ adj3 (care or healthcare or center? or centre? or clinic? or service?)).ab,ti.
32	or/5-31
33	4 and 32
34	limit 33 to english language
35	LETTER/
36	EDITORIAL/
37	NEWS/
38	exp HISTORICAL ARTICLE/
39	ANECDOTES AS TOPIC/
40	COMMENT/
41	CASE REPORT/
42	(letter or comment*).ti.

#	Searches
43	or/35-42
44	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
45	43 not 44
46	ANIMALS/ not HUMANS/
47	exp ANIMALS, LABORATORY/
48	exp ANIMAL EXPERIMENTATION/
49	exp MODELS, ANIMAL/
50	exp RODENTIA/
51	(rat or rats or mouse or mice).ti.
52	or/45-51
53	34 not 52

- Database: Medline In-Process & Other Non-Indexed Citations

Last searched on **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations** January 04, 2017 on 5<sup>th</sup> January 2017.

#	Searches
1	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
2	mucov\$.ti,ab.
3	or/1-2
4	((care or healthcare) adj3 (organi\$ or deliv\$)).ab,ti.
5	((care or healthcare or organi\$ or nursing or nurse?) adj3 (model? or design\$)).ab,ti.
6	(special\$ adj3 (center? or centre? or clinic?)).ab,ti.
7	(telehealth\$ or tele health\$ or telemedicine\$ or tele medicine\$ or teleconsult\$ or tele consult\$).ab,ti.
8	(Remote\$ adj3 monitor\$).ab,ti.
9	((share? or network\$) adj3 (care or healthcare or center? or centre? or clinic? or service?)).ab,ti.
10	((home? or domicil\$) adj3 (care or healthcare or center? or centre? or clinic? or service?)).ab,ti.
11	(hospital? adj2 home?).ab,ti.
12	((home? or domicil\$) adj3 (Infusion therap\$ or Intravenous\$ or IV)).ab,ti.
13	(outreach adj3 (care or healthcare or center? or centre? or clinic? or service?)).ab,ti.
14	(communit\$ adj3 (care or healthcare or center? or centre? or clinic? or service?)).ab,ti.
15	((nursing or nurse?) adj3 (communit\$ or home? or domicil\$ or school?)).ab,ti.
16	(palliative adj3 (care or healthcare or service?)).ab,ti.
17	(access\$ adj3 (care or healthcare or center? or centre? or clinic? or service?)).ab,ti.
18	or/4-17
19	3 and 18

- Database: Cochrane Central Register of Controlled Trials

Last searched on **EBM Reviews - Cochrane Central Register of Controlled Trials** November 2016 on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab,kw.
3	mucov\$.ti,ab,kw.
4	or/1-3

#	Searches
5	"DELIVERY OF HEALTH CARE"/
6	HEALTH SERVICES ADMINISTRATION/
7	MODELS, ORGANIZATIONAL/
8	MODELS, NURSING/
9	((care or healthcare) adj3 (organi\$ or deliv\$)).ti,ab,kw.
10	((care or healthcare or organi\$ or nursing or nurse?) adj3 (model? or design\$)).ti,ab,kw.
11	(special\$ adj3 (center? or centre? or clinic?)).ti,ab,kw.
12	exp TELEMEDICINE/
13	(telehealth\$ or tele health\$ or telemedicine\$ or tele medicine\$ or teleconsult\$ or tele consult\$).ti,ab,kw.
14	(Remote\$ adj3 monitor\$).ti,ab,kw.
15	((share? or network\$) adj3 (care or healthcare or center? or centre? or clinic? or service?)).ti,ab,kw.
16	HOME CARE SERVICES/
17	HOME HEALTH NURSING/
18	HOME INFUSION THERAPY/
19	((home? or domicil\$) adj3 (care or healthcare or center? or centre? or clinic? or service?)).ti,ab,kw.
20	(hospital? adj2 home?).ti,ab,kw.
21	((home? or domicil\$) adj3 (Infusion therap\$ or Intravenous\$ or IV)).ti,ab,kw.
22	(outreach adj3 (care or healthcare or center? or centre? or clinic? or service?)).ti,ab,kw.
23	COMMUNITY HEALTH SERVICES/
24	exp COMMUNITY HEALTH NURSING/
25	CHILD HEALTH SERVICES/
26	(communit\$ adj3 (care or healthcare or center? or centre? or clinic? or service?)).ti,ab,kw.
27	((nursing or nurse?) adj3 (communit\$ or home? or domicil\$ or school?)).ti,ab,kw.
28	PALLIATIVE CARE/
29	(palliative adj3 (care or healthcare or service?)).ti,ab,kw.
30	HEALTH SERVICES ACCESSIBILITY/
31	(access\$ adj3 (care or healthcare or center? or centre? or clinic? or service?)).ti,ab,kw.
32	or/5-31
33	4 and 32

- Database: Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects

Last searched on **EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to January 05, 2017, **EBM Reviews - Database of Abstracts of Reviews of Effects** 1st Quarter 2015 on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS.kw.
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).tw,tx.
3	mucov\$.tw,tx.
4	or/1-3
5	"DELIVERY OF HEALTH CARE".kw.
6	HEALTH SERVICES ADMINISTRATION.kw.
7	MODELS, ORGANIZATIONAL.kw.

#	Searches
8	MODELS, NURSING.kw.
9	((care or healthcare) adj3 (organi\$ or deliv\$)).tw,tx.
10	((care or healthcare or organi\$ or nursing or nurse?) adj3 (model? or design\$)).tw,tx.
11	(special\$ adj3 (center? or centre? or clinic?)).tw,tx.
12	TELEMEDICINE.kw.
13	(telehealth\$ or tele health\$ or telemedicine\$ or tele medicine\$ or teleconsult\$ or tele consult\$).tw,tx.
14	(Remote\$ adj3 monitor\$).tw,tx.
15	((share? or network\$) adj3 (care or healthcare or center? or centre? or clinic? or service?)).tw,tx.
16	HOME CARE SERVICES.kw.
17	HOME HEALTH NURSING.kw.
18	HOME INFUSION THERAPY.kw.
19	((home? or domicil\$) adj3 (care or healthcare or center? or centre? or clinic? or service?)).tw,tx.
20	(hospital? adj2 home?).tw,tx.
21	((home? or domicil\$) adj3 (Infusion therap\$ or Intravenous\$ or IV)).tw,tx.
22	(outreach adj3 (care or healthcare or center? or centre? or clinic? or service?)).tw,tx.
23	COMMUNITY HEALTH SERVICES.kw.
24	COMMUNITY HEALTH NURSING.kw.
25	CHILD HEALTH SERVICES.kw.
26	(communit\$ adj3 (care or healthcare or center? or centre? or clinic? or service?)).tw,tx.
27	((nursing or nurse?) adj3 (communit\$ or home? or domicil\$ or school?)).tw,tx.
28	PALLIATIVE CARE.kw.
29	(palliative adj3 (care or healthcare or service?)).tw,tx.
30	HEALTH SERVICES ACCESSIBILITY.kw.
31	(access\$ adj3 (care or healthcare or center? or centre? or clinic? or service?)).tw,tx.
32	or/5-31
33	4 and 32

- Database: Health Technology Assessment

Last searched on **EBM Reviews - Health Technology Assessment 4th Quarter 2016** on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).tw.
3	mucov\$.tw.
4	or/1-3
5	"DELIVERY OF HEALTH CARE"/
6	HEALTH SERVICES ADMINISTRATION/
7	MODELS, ORGANIZATIONAL/
8	MODELS, NURSING/
9	((care or healthcare) adj3 (organi\$ or deliv\$)).tw.
10	((care or healthcare or organi\$ or nursing or nurse?) adj3 (model? or design\$)).tw.
11	(special\$ adj3 (center? or centre? or clinic?)).tw.
12	exp TELEMEDICINE/
13	(telehealth\$ or tele health\$ or telemedicine\$ or tele medicine\$ or teleconsult\$ or tele

#	Searches
	consult\$).tw.
14	(Remote\$ adj3 monitor\$).tw.
15	((share? or network\$) adj3 (care or healthcare or center? or centre? or clinic? or service?)).tw.
16	HOME CARE SERVICES/
17	HOME HEALTH NURSING/
18	HOME INFUSION THERAPY/
19	((home? or domicil\$) adj3 (care or healthcare or center? or centre? or clinic? or service?)).tw.
20	(hospital? adj2 home?).tw.
21	((home? or domicil\$) adj3 (Infusion therap\$ or Intravenous\$ or IV)).tw.
22	(outreach adj3 (care or healthcare or center? or centre? or clinic? or service?)).tw.
23	COMMUNITY HEALTH SERVICES/
24	exp COMMUNITY HEALTH NURSING/
25	CHILD HEALTH SERVICES/
26	(communit\$ adj3 (care or healthcare or center? or centre? or clinic? or service?)).tw.
27	((nursing or nurse?) adj3 (communit\$ or home? or domicil\$ or school?)).tw.
28	PALLIATIVE CARE/
29	(palliative adj3 (care or healthcare or service?)).tw.
30	HEALTH SERVICES ACCESSIBILITY/
31	(access\$ adj3 (care or healthcare or center? or centre? or clinic? or service?)).tw.
32	or/5-31
33	4 and 32

- Database: Embase

Last searched on **Embase** 1974 to 2017 Week 01 on 4<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	*HEALTH CARE DELIVERY/
6	*HEALTH CARE ORGANIZATION/
7	*"ORGANIZATION AND MANAGEMENT"/
8	((care or healthcare) adj2 (organi\$ or deliv\$)).ab,ti.
9	((care or healthcare or organi\$ or nursing or nurse?) adj2 (model? or design\$)).ab,ti.
10	(special\$ adj2 (center? or centre? or clinic?)).ab,ti.
11	*TELEMEDICINE/
12	(telehealth\$ or tele health\$ or telemedicine\$ or tele medicine\$ or teleconsult\$ or tele consult\$).ab,ti.
13	(Remote\$ adj3 monitor\$).ab,ti.
14	((share? or network\$) adj3 (care or healthcare or center? or centre? or clinic? or service?)).ab,ti.
15	*HOME CARE/
16	VISITING NURSING SERVICE/
17	HOME INTRAVENOUS THERAPY/
18	((home? or domicil\$) adj2 (care or healthcare or center? or centre? or clinic? or

#	Searches
	service?)).ab,ti.
19	(hospital? adj2 home?).ab,ti.
20	((home? or domicil\$) adj2 (Infusion therap\$ or Intravenous\$ or IV)).ab,ti.
21	(outreach adj3 (care or healthcare or center? or centre? or clinic? or service?)).ab,ti.
22	*COMMUNITY CARE/
23	*COMMUNITY HEALTH NURSING/
24	*CHILD HEALTH CARE/
25	(communit\$ adj3 (care or healthcare or center? or centre? or clinic? or service?)).ab,ti.
26	((nursing or nurse?) adj3 (communit\$ or home? or domicil\$ or school?)).ab,ti.
27	*PALLIATIVE THERAPY/
28	(palliative adj3 (care or healthcare or service?)).ab,ti.
29	*HEALTH CARE DELIVERY/
30	(access\$ adj3 (care or healthcare or center? or centre? or clinic? or service?)).ab,ti.
31	or/5-30
32	4 and 31
33	limit 32 to english language
34	letter.pt. or LETTER/
35	note.pt.
36	editorial.pt.
37	CASE REPORT/ or CASE STUDY/
38	(letter or comment*).ti.
39	or/34-38
40	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
41	39 not 40
42	ANIMAL/ not HUMAN/
43	NONHUMAN/
44	exp ANIMAL EXPERIMENT/
45	exp EXPERIMENTAL ANIMAL/
46	ANIMAL MODEL/
47	exp RODENT/
48	(rat or rats or mouse or mice).ti.
49	or/41-48
50	33 not 49

- Database: CINAHL

Last searched on **CINAHL** 1981 present on 11<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea*) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov*.ti,ab.
4	or/1-3
5	*HEALTH CARE DELIVERY/
6	* QUALITY MANAGEMENT, ORGANIZATIONAL/
7	((care or healthcare) adj2 (organi* or deliv*)).ab,ti.
8	((care or healthcare or organi* or nursing or nurse*) adj2 (model* or design*)).ab,ti.
9	(special* adj2 (center* or centre* or clinic*)).ab,ti.

#	Searches
10	exp *TELEMEDICINE/
11	(telehealth* or "tele health*" or telemedicine* or "tele medicine*" or teleconsult* or "tele consult*").ab,ti.
12	(Remote* adj2 monitor*).ab,ti.
13	((share* or network*) adj2 (care or healthcare or center* or centre* or clinic* or service*)).ab,ti.
14	*HOME HEALTH CARE/
15	*HOME NURSING, PROFESSIONAL/
16	*HOME INTRAVENOUS THERAPY/
17	((home* or domicil*) adj2 (care or healthcare or center* or centre* or clinic* or service*)).ab,ti.
18	(hospital* adj2 home*).ab,ti.
19	((home* or domicil*) adj2 ("Infusion therap*" or Intravenous* or IV)).ab,ti.
20	(outreach adj2 (care or healthcare or center* or centre* or clinic* or service*)).ab,ti.
21	*COMMUNITY HEALTH SERVICES/
22	*COMMUNITY HEALTH NURSING/
23	*CHILD HEALTH SERVICES/
24	(communit* adj2 (care or healthcare or center* or centre* or clinic* or service*)).ab,ti.
25	((nursing or nurse*) adj2 (communit* or home* or domicil* or school*)).ab,ti.
26	*PALLIATIVE CARE/
27	(palliative adj2 (care or healthcare or service*)).ab,ti.
28	*HEALTH SERVICES ACCESSIBILITY/
29	(access* adj2 (care or healthcare or center* or centre* or clinic* or service*)).ab,ti.
30	or/5-29
31	4 and 30 [LIMIT TO: (LANGUAGE ENGLISH)]

### E.3.2 What is the clinical and cost-effectiveness of multidisciplinary teams of various compositions?

- Database: Medline

Last searched on **Ovid MEDLINE(R)** 1946 to December Week 1 2016 on 5<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	PATIENT CARE TEAM/
6	((patient? or medical or health) adj1 care team).ab,ti.
7	healthcare team?.ab,ti.
8	((multidisciplinary or multi-disciplinary or multiprofession\$ or multi-profession\$ or integrated or network\$) adj3 (team? or staff\$ or task force? or approach\$ or program\$ or system? or panel? or forum? or care or manag\$ or service?)).ab,ti.
9	mdt?.ab,ti.
10	((interdisciplinary or inter-disciplinary or interprofession\$ or inter-profession\$) adj3 (team? or staff\$ or task force? or approach\$ or program\$ or system? or panel? or forum? or care or manag\$ or service?)).ab,ti.
11	((transdisciplinary or trans-disciplinary or transprofession\$ or trans-profession\$) adj3 (team? or staff\$ or task force? or approach\$ or program\$ or system? or panel? or forum?

#	Searches
	or care or manag\$ or service?)).ab,ti.
12	network meeting?.ti,ab.
13	INTERDISCIPLINARY COMMUNICATION/
14	((interdisciplinary or inter-disciplinary or interprofession\$ or inter-profession\$) adj3 (communic\$ or collaborat\$ or relation\$)).ab,ti.
15	((multidisciplinary or multi-disciplinary or multiprofession\$ or multi-profession\$) adj3 (communic\$ or collaborat\$ or relation\$)).ab,ti.
16	((transdisciplinary or trans-disciplinary or transprofession\$ or trans-profession\$) adj3 (communic\$ or collaborat\$ or relation\$)).ab,ti.
17	((co-ordinat\$ or coordinat\$ or network\$) adj3 (care or service? or practice?)).ab,ti.
18	or/5-17
19	4 and 18
20	limit 19 to english language
21	LETTER/
22	EDITORIAL/
23	NEWS/
24	exp HISTORICAL ARTICLE/
25	ANECDOTES AS TOPIC/
26	COMMENT/
27	CASE REPORT/
28	(letter or comment*).ti.
29	or/21-28
30	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
31	29 not 30
32	ANIMALS/ not HUMANS/
33	exp ANIMALS, LABORATORY/
34	exp ANIMAL EXPERIMENTATION/
35	exp MODELS, ANIMAL/
36	exp RODENTIA/
37	(rat or rats or mouse or mice).ti.
38	or/31-37
39	20 not 38

- Database: Medline In-Process & Other Non-Indexed Citations

Last searched on **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations** January 04, 2017 on 5<sup>th</sup> January 2017.

#	Searches
1	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
2	mucov\$.ti,ab.
3	or/1-2
4	((patient? or medical or health) adj1 care team).ab,ti.
5	healthcare team?.ab,ti.
6	((multidisciplinary or multi-disciplinary or multiprofession\$ or multi-profession\$ or integrated or network\$) adj3 (team? or staff\$ or task force? or approach\$ or program\$ or system? or panel? or forum? or care or manag\$ or service?)).ab,ti.
7	mdt?.ab,ti.
8	((interdisciplinary or inter-disciplinary or interprofession\$ or inter-profession\$) adj3 (team? or staff\$ or task force? or approach\$ or program\$ or system? or panel? or forum?

#	Searches
	or care or manag\$ or service?)).ab,ti.
9	((transdisciplinary or trans-disciplinary or transprofession\$ or trans-profession\$) adj3 (team? or staff\$ or task force? or approach\$ or program\$ or system? or panel? or forum? or care or manag\$ or service?)).ab,ti.
10	network meeting?.ti,ab.
11	((interdisciplinary or inter-disciplinary or interprofession\$ or inter-profession\$) adj3 (communic\$ or collaborat\$ or relation\$)).ab,ti.
12	((multidisciplinary or multi-disciplinary or multiprofession\$ or multi-profession\$) adj3 (communic\$ or collaborat\$ or relation\$)).ab,ti.
13	((transdisciplinary or trans-disciplinary or transprofession\$ or trans-profession\$) adj3 (communic\$ or collaborat\$ or relation\$)).ab,ti.
14	((co-ordinat\$ or coordinat\$ or network\$) adj3 (care or service? or practice?)).ab,ti.
15	or/4-14
16	3 and 15

- Database: Cochrane Central Register of Controlled Trials

Last searched on **EBM Reviews - Cochrane Central Register of Controlled Trials**  
November 2016 on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ab,ti,kw.
3	mucov\$.ab,ti,kw.
4	or/1-3
5	PATIENT CARE TEAM/
6	((patient? or medical or health) adj1 care team).ab,ti,kw.
7	healthcare team?.ab,ti,kw.
8	((multidisciplinary or multi-disciplinary or multiprofession\$ or multi-profession\$ or integrated or network\$) adj3 (team? or staff\$ or task force? or approach\$ or program\$ or system? or panel? or forum? or care or manag\$ or service?)).ab,ti,kw.
9	mdt?.ab,ti,kw.
10	((interdisciplinary or inter-disciplinary or interprofession\$ or inter-profession\$) adj3 (team? or staff\$ or task force? or approach\$ or program\$ or system? or panel? or forum? or care or manag\$ or service?)).ab,ti,kw.
11	((transdisciplinary or trans-disciplinary or transprofession\$ or trans-profession\$) adj3 (team? or staff\$ or task force? or approach\$ or program\$ or system? or panel? or forum? or care or manag\$ or service?)).ab,ti,kw.
12	network meeting?.ab,ti,kw.
13	INTERDISCIPLINARY COMMUNICATION/
14	((interdisciplinary or inter-disciplinary or interprofession\$ or inter-profession\$) adj3 (communic\$ or collaborat\$ or relation\$)).ab,ti,kw.
15	((multidisciplinary or multi-disciplinary or multiprofession\$ or multi-profession\$) adj3 (communic\$ or collaborat\$ or relation\$)).ab,ti,kw.
16	((transdisciplinary or trans-disciplinary or transprofession\$ or trans-profession\$) adj3 (communic\$ or collaborat\$ or relation\$)).ab,ti,kw.
17	((co-ordinat\$ or coordinat\$ or network\$) adj3 (care or service? or practice?)).ab,ti,kw.
18	or/5-17
19	4 and 18

- Database: Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects

Last searched on **EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to January 05, 2017, **EBM Reviews - Database of Abstracts of Reviews of Effects** 1st Quarter 2015 on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS.kw.
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).tx,tw.
3	mucov\$.tx,tw.
4	or/1-3
5	PATIENT CARE TEAM.kw.
6	((patient? or medical or health) adj1 care team).tx,tw.
7	healthcare team?.tx,tw.
8	((multidisciplinary or multi-disciplinary or multiprofession\$ or multi-profession\$ or integrated or network\$) adj3 (team? or staff\$ or task force? or approach\$ or program\$ or system? or panel? or forum? or care or manag\$ or service?)).tx,tw.
9	mdt?.tx,tw.
10	((interdisciplinary or inter-disciplinary or interprofession\$ or inter-profession\$) adj3 (team? or staff\$ or task force? or approach\$ or program\$ or system? or panel? or forum? or care or manag\$ or service?)).tx,tw.
11	((transdisciplinary or trans-disciplinary or transprofession\$ or trans-profession\$) adj3 (team? or staff\$ or task force? or approach\$ or program\$ or system? or panel? or forum? or care or manag\$ or service?)).tx,tw.
12	network meeting?.tx,tw.
13	INTERDISCIPLINARY COMMUNICATION.kw.
14	((interdisciplinary or inter-disciplinary or interprofession\$ or inter-profession\$) adj3 (communic\$ or collaborat\$ or relation\$)).tx,tw.
15	((multidisciplinary or multi-disciplinary or multiprofession\$ or multi-profession\$) adj3 (communic\$ or collaborat\$ or relation\$)).tx,tw.
16	((transdisciplinary or trans-disciplinary or transprofession\$ or trans-profession\$) adj3 (communic\$ or collaborat\$ or relation\$)).tx,tw.
17	((co-ordinat\$ or coordinat\$ or network\$) adj3 (care or service? or practice?)).tx,tw.
18	or/5-17
19	4 and 18

- Database: Health Technology Assessment

Last searched on **EBM Reviews - Health Technology Assessment** 4th Quarter 2016 on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).tw.
3	mucov\$.tw.
4	or/1-3
5	PATIENT CARE TEAM/
6	((patient? or medical or health) adj1 care team).tw.
7	healthcare team?.tw.
8	((multidisciplinary or multi-disciplinary or multiprofession\$ or multi-profession\$ or integrated or network\$) adj3 (team? or staff\$ or task force? or approach\$ or program\$ or system? or panel? or forum? or care or manag\$ or service?)).tw.
9	mdt?.tw.
10	((interdisciplinary or inter-disciplinary or interprofession\$ or inter-profession\$) adj3 (team? or staff\$ or task force? or approach\$ or program\$ or system? or panel? or forum? or care or manag\$ or service?)).tw.

#	Searches
11	((transdisciplinary or trans-disciplinary or transprofession\$ or trans-profession\$) adj3 (team? or staff\$ or task force? or approach\$ or program\$ or system? or panel? or forum? or care or manag\$ or service?)).tw.
12	network meeting?.tw.
13	INTERDISCIPLINARY COMMUNICATION/
14	((interdisciplinary or inter-disciplinary or interprofession\$ or inter-profession\$) adj3 (communic\$ or collaborat\$ or relation\$)).tw.
15	((multidisciplinary or multi-disciplinary or multiprofession\$ or multi-profession\$) adj3 (communic\$ or collaborat\$ or relation\$)).tw.
16	((transdisciplinary or trans-disciplinary or transprofession\$ or trans-profession\$) adj3 (communic\$ or collaborat\$ or relation\$)).tw.
17	((co-ordinat\$ or coordinat\$ or network\$) adj3 (care or service? or practice?)).tw.
18	or/5-17
19	4 and 18

- Database: Embase

Last searched on **Embase** 1974 to 2017 Week 01 on 4<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	MULTIDISCIPLINARY TEAM CARE/
6	((patient? or medical or health) adj1 care team).ab,ti.
7	healthcare team?.ab,ti.
8	((multidisciplinary or multi-disciplinary or multiprofession\$ or multi-profession\$ or integrated or network\$) adj3 (team? or staff\$ or task force? or program\$ or system? or panel? or forum? or care or manag\$ or service?)).ab,ti.
9	mdt?.ab,ti.
10	((interdisciplinary or inter-disciplinary or interprofession\$ or inter-profession\$) adj3 (team? or staff\$ or task force? or approach\$ or program\$ or system? or panel? or forum? or care or manag\$ or service?)).ab,ti.
11	((transdisciplinary or trans-disciplinary or transprofession\$ or trans-profession\$) adj3 (team? or staff\$ or task force? or approach\$ or program\$ or system? or panel? or forum? or care or manag\$ or service?)).ab,ti.
12	network meeting?.ti,ab.
13	*INTERDISCIPLINARY COMMUNICATION/
14	((interdisciplinary or inter-disciplinary or interprofession\$ or inter-profession\$) adj3 (communic\$ or collaborat\$ or relation\$)).ab,ti.
15	((multidisciplinary or multi-disciplinary or multiprofession\$ or multi-profession\$) adj3 (communic\$ or collaborat\$ or relation\$)).ab,ti.
16	((transdisciplinary or trans-disciplinary or transprofession\$ or trans-profession\$) adj3 (communic\$ or collaborat\$ or relation\$)).ab,ti.
17	((co-ordinat\$ or coordinat\$ or network\$) adj3 (care or service? or practice?)).ab,ti.
18	or/5-17
19	4 and 18
20	limit 19 to english language
21	letter.pt. or LETTER/
22	note.pt.

#	Searches
23	editorial.pt.
24	CASE REPORT/ or CASE STUDY/
25	(letter or comment*).ti.
26	or/21-25
27	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
28	26 not 27
29	ANIMAL/ not HUMAN/
30	NONHUMAN/
31	exp ANIMAL EXPERIMENT/
32	exp EXPERIMENTAL ANIMAL/
33	ANIMAL MODEL/
34	exp RODENT/
35	(rat or rats or mouse or mice).ti.
36	or/28-35
37	20 not 36

## E.4 What parts of the transition from children's to adult services are most important for young people with cystic fibrosis and their family members and carers?

### E.4.1 Database: Medline

Last searched on Ovid MEDLINE(R) 1946 to October Week 4 2016 on 10th November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	exp CONTINUITY OF PATIENT CARE/
6	(transition\$ and (service? or care or clinic? or setting\$ or healthcare or hospital? or center\$ or centre\$ or facilit\$ or unit? or department\$ or institution\$ or agenc\$ or hospice? or provider? or program\$ or "adult orient\$" or communit\$ or outpatient\$ or outreach)).ti,ab.
7	((transfer\$ or handoff or handover or "hand over") and (service\$ or care or clinic? or healthcare or setting\$ or hospital? or center\$ or centre\$ or facilit\$ or unit? or department\$ or institution\$ or agenc\$ or hospice\$ or provider\$ or communit\$ or outpatient\$ or outreach) and adult\$).ti,ab.
8	(transition\$ adj3 (coordinat\$ or framework? or manag\$ or prepar\$ or plan\$ or protocol\$ or support\$ or trajector\$ or pathway\$ or process\$ or readiness or timing or partnership\$ or program\$ or training or educat\$ or strateg\$ or failure\$ or barrier\$ or system?)).ti,ab.
9	(transition\$ and (MDT\$ or multidisciplinary team\$ or multiprofession\$ or interdisciplinar\$ or key worker\$ or consultant\$ or clinician\$ or specialist\$ or p?ediatrician\$ or social worker\$ or lead\$ or professional\$ or rehabilitation or staff or nurse\$ or therapist\$ or multiagenc\$ or agenc\$)).ti,ab.
10	(transition\$ and (communicat\$ or written or writing or verbal\$ or email\$ or electronic\$ or contact\$)).ti,ab.
11	(transition\$ and (admin\$ or record\$ or appointment\$ or checklist\$ or check list\$ or summar\$ or information or booklet\$ or pamphlet\$ or passport\$)).ti,ab.
12	((transition\$ and ("continued care" or "continuing care" or (continuity adj2 care))) adj5

#	Searches
	(adult\$ or p?ediatric\$ or child\$ or adolescent\$ or family or families or carer\$).ti,ab.
13	(LIFESpan or Moving on well).ti,ab.
14	or/5-13
15	PATIENT CARE PLANNING/ and (adult\$ or p?ediatric\$ or child\$ or adolescent\$ or family or families or carer\$).ti.
16	"SURVEYS AND QUESTIONNAIRES"/ or HEALTH CARE SURVEYS/
17	NEEDS ASSESSMENT/
18	16 or 17
19	(survey\$ or questionnaire\$).ti,ab.
20	18 or 19
21	15 and 20
22	14 or 21
23	4 and 22
24	limit 23 to english language
25	LETTER/
26	EDITORIAL/
27	NEWS/
28	exp HISTORICAL ARTICLE/
29	ANECDOTES AS TOPIC/
30	COMMENT/
31	CASE REPORT/
32	(letter or comment*).ti.
33	or/25-32
34	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
35	33 not 34
36	ANIMALS/ not HUMANS/
37	exp ANIMALS, LABORATORY/
38	exp ANIMAL EXPERIMENTATION/
39	exp MODELS, ANIMAL/
40	exp RODENTIA/
41	(rat or rats or mouse or mice).ti.
42	or/35-41
43	24 not 42

#### E.4.2 Database: Medline In-Process & Other Non-Indexed Citations

Last searched on Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations November 09, 2016 on 10th November 2016.

#	Searches
1	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
2	mucov\$.ti,ab.
3	1 or 2
4	(transition\$ and (service? or care or clinic? or setting\$ or healthcare or hospital? or center\$ or centre\$ or facilit\$ or unit? or department\$ or institution\$ or agenc\$ or hospice? or provider? or program\$ or "adult orient\$" or communit\$ or outpatient\$ or outreach)).ti,ab.
5	((transfer\$ or handoff or handover or "hand over") and (service\$ or care or clinic? or healthcare or setting\$ or hospital? or center\$ or centre\$ or facilit\$ or unit? or

#	Searches
	department\$ or institution\$ or agenc\$ or hospice\$ or provider\$ or communit\$ or outpatient\$ or outreach) and adult\$).ti,ab.
6	(transition\$ adj3 (coordinat\$ or framework? or manag\$ or prepar\$ or plan\$ or protocol\$ or support\$ or trajector\$ or pathway\$ or process\$ or readiness or timing or partnership\$ or program\$ or training or educat\$ or strateg\$ or failure\$ or barrier\$ or system?)).ti,ab.
7	(transition\$ and (MDT\$ or multidisciplinary team\$ or multiprofession\$ or interdisciplinar\$ or key worker\$ or consultant\$ or clinician\$ or specialist\$ or p?ediatrician\$ or social worker\$ or lead\$ or professional\$ or rehabilitation or staff or nurse\$ or therapist\$ or multiagenc\$ or agenc\$)).ti,ab.
8	(transition\$ and (communicat\$ or written or writing or verbal\$ or email\$ or electronic\$ or contact\$)).ti,ab.
9	(transition\$ and (admin\$ or record\$ or appointment\$ or checklist\$ or check list\$ or summar\$ or information or booklet\$ or pamphlet\$ or passport\$)).ti,ab.
10	((transition\$ and ("continued care" or "continuing care" or (continuity adj2 care))) adj5 (adult\$ or p?ediatric\$ or child\$ or adolescent\$ or family or families or carer\$)).ti,ab.
11	(LIFESpan or Moving on well).ti,ab.
12	or/4-11
13	(patient\$ adj2 plan\$).ti,ab. and (adult\$ or p?ediatric\$ or child\$ or adolescent\$ or family or families or carer\$).ti.
14	(survey\$ or questionnaire\$).ti,ab.
15	13 or 14
16	12 or 15
17	3 and 16
18	limit 17 to english language

### E.4.3 Database: Cochrane Central Register of Controlled Trials

Last searched on **EBM Reviews - Cochrane Central Register of Controlled Trials**  
October 2016 on 10<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	exp CONTINUITY OF PATIENT CARE/
6	(transition\$ and (service? or care or clinic? or setting\$ or healthcare or hospital? or center\$ or centre\$ or facilit\$ or unit? or department\$ or institution\$ or agenc\$ or hospice? or provider? or program\$ or "adult orient\$" or communit\$ or outpatient\$ or outreach)).ti,ab.
7	((transfer\$ or handoff or handover or "hand over") and (service\$ or care or clinic? or healthcare or setting\$ or hospital? or center\$ or centre\$ or facilit\$ or unit? or department\$ or institution\$ or agenc\$ or hospice\$ or provider\$ or communit\$ or outpatient\$ or outreach) and adult\$).ti,ab.
8	(transition\$ adj3 (coordinat\$ or framework? or manag\$ or prepar\$ or plan\$ or protocol\$ or support\$ or trajector\$ or pathway\$ or process\$ or readiness or timing or partnership\$ or program\$ or training or educat\$ or strateg\$ or failure\$ or barrier\$ or system?)).ti,ab.
9	(transition\$ and (MDT\$ or multidisciplinary team\$ or multiprofession\$ or interdisciplinar\$ or key worker\$ or consultant\$ or clinician\$ or specialist\$ or p?ediatrician\$ or social worker\$ or lead\$ or professional\$ or rehabilitation or staff or nurse\$ or therapist\$ or multiagenc\$ or agenc\$)).ti,ab.
10	(transition\$ and (communicat\$ or written or writing or verbal\$ or email\$ or electronic\$ or contact\$)).ti,ab.

#	Searches
11	(transition\$ and (admin\$ or record\$ or appointment\$ or checklist\$ or check list\$ or summar\$ or information or booklet\$ or pamphlet\$ or passport\$)).ti,ab.
12	((transition\$ and ("continued care" or "continuing care" or (continuity adj2 care))) adj5 (adult\$ or p?ediatric\$ or child\$ or adolescent\$ or family or families or carer\$)).ti,ab.
13	(LIFEsplan or Moving on well).ti,ab.
14	or/5-13
15	PATIENT CARE PLANNING/ and (adult\$ or p?ediatric\$ or child\$ or adolescent\$ or family or families or carer\$).ti.
16	"SURVEYS AND QUESTIONNAIRES"/ or HEALTH CARE SURVEYS/
17	NEEDS ASSESSMENT/
18	16 or 17
19	(survey\$ or questionnaire\$).ti,ab.
20	18 or 19
21	15 and 20
22	14 or 21
23	4 and 22
24	limit 23 to english language

#### E.4.4 Database: Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects

Last searched on **EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to November 09, 2016, **EBM Reviews - Database of Abstracts of Reviews of Effects 1st Quarter 2015** on 10<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS.kw.
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	CONTINUITY OF PATIENT CARE.kw.
6	(transition\$ and (service? or care or clinic? or setting\$ or healthcare or hospital? or center\$ or centre\$ or facilit\$ or unit? or department\$ or institution\$ or agenc\$ or hospice? or provider? or program\$ or "adult orient\$" or communit\$ or outpatient\$ or outreach)).ti,ab.
7	((transfer\$ or handoff or handover or "hand over") and (service\$ or care or clinic? or healthcare or setting\$ or hospital? or center\$ or centre\$ or facilit\$ or unit? or department\$ or institution\$ or agenc\$ or hospice\$ or provider\$ or communit\$ or outpatient\$ or outreach) and adult\$).ti,ab.
8	(transition\$ adj3 (coordinat\$ or framework? or manag\$ or prepar\$ or plan\$ or protocol\$ or support\$ or trajector\$ or pathway\$ or process\$ or readiness or timing or partnership\$ or program\$ or training or educat\$ or strateg\$ or failure\$ or barrier\$ or system?)).ti,ab.
9	(transition\$ and (MDT\$ or multidisciplinary team\$ or multiprofession\$ or interdisciplinar\$ or key worker\$ or consultant\$ or clinician\$ or specialist\$ or p?ediatrician\$ or social worker\$ or lead\$ or professional\$ or rehabilitation or staff or nurse\$ or therapist\$ or multiagenc\$ or agenc\$)).ti,ab.
10	(transition\$ and (communicat\$ or written or writing or verbal\$ or email\$ or electronic\$ or contact\$)).ti,ab.
11	(transition\$ and (admin\$ or record\$ or appointment\$ or checklist\$ or check list\$ or summar\$ or information or booklet\$ or pamphlet\$ or passport\$)).ti,ab.
12	((("continued care" or "continuing care" or (continuity adj2 care)) adj5 (adult\$ or p?ediatric\$ or child\$ or adolescent\$ or family or families or carer\$)).ti,ab.

#	Searches
13	(LIFESpan or Moving on well).ti,ab.
14	or/5-13
15	PATIENT CARE PLANNING.kw. and (adult\$ or p?ediatric\$ or child\$ or adolescent\$ or family or families or carer\$).ti.
16	("SURVEYS AND QUESTIONNAIRES" or HEALTH CARE SURVEYS).kw.
17	NEEDS ASSESSMENT.kw.
18	16 or 17
19	(survey\$ or questionnaire\$).ti,ab.
20	18 or 19
21	15 and 20
22	14 or 21
23	4 and 22

#### E.4.5 Database: Health Technology Assessment

Last searched on **EBM Reviews - Health Technology Assessment 4th Quarter 2016** on 10<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	exp CONTINUITY OF PATIENT CARE/
6	(transition\$ and (service? or care or clinic? or setting\$ or healthcare or hospital? or center\$ or centre\$ or facilit\$ or unit? or department\$ or institution\$ or agenc\$ or hospice? or provider? or program\$ or "adult orient\$" or communit\$ or outpatient\$ or outreach)).ti,ab.
7	((transfer\$ or handoff or handover or "hand over") and (service\$ or care or clinic? or healthcare or setting\$ or hospital? or center\$ or centre\$ or facilit\$ or unit? or department\$ or institution\$ or agenc\$ or hospice\$ or provider\$ or communit\$ or outpatient\$ or outreach) and adult\$).ti,ab.
8	(transition\$ adj3 (coordinat\$ or framework? or manag\$ or prepar\$ or plan\$ or protocol\$ or support\$ or trajector\$ or pathway\$ or process\$ or readiness or timing or partnership\$ or program\$ or training or educat\$ or strateg\$ or failure\$ or barrier\$ or system?)).ti,ab.
9	(transition\$ and (MDT\$ or multidisciplinary team\$ or multiprofession\$ or interdisciplinary\$ or key worker\$ or consultant\$ or clinician\$ or specialist\$ or p?ediatrician\$ or social worker\$ or lead\$ or professional\$ or rehabilitation or staff or nurse\$ or therapist\$ or multiagenc\$ or agenc\$)).ti,ab.
10	(transition\$ and (communicat\$ or written or writing or verbal\$ or email\$ or electronic\$ or contact\$)).ti,ab.
11	(transition\$ and (admin\$ or record\$ or appointment\$ or checklist\$ or check list\$ or summar\$ or information or booklet\$ or pamphlet\$ or passport\$)).ti,ab.
12	((transition\$ and ("continued care" or "continuing care" or (continuity adj2 care))) adj5 (adult\$ or p?ediatric\$ or child\$ or adolescent\$ or family or families or carer\$)).ti,ab.
13	(LIFESpan or Moving on well).ti,ab.
14	or/5-13
15	PATIENT CARE PLANNING/ and (adult\$ or p?ediatric\$ or child\$ or adolescent\$ or family or families or carer\$).ti.
16	"SURVEYS AND QUESTIONNAIRES"/ or HEALTH CARE SURVEYS/
17	NEEDS ASSESSMENT/

#	Searches
18	16 or 17
19	(survey\$ or questionnaire\$).ti,ab.
20	18 or 19
21	15 and 20
22	14 or 21
23	4 and 22
24	limit 23 to english language

#### E.4.6 Database: Embase

Last searched on **Embase** 1974 to 2016 Week 45 on 10<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	transition to adult care/
6	(transition\$ and (service? or care or clinic? or setting\$ or healthcare or hospital? or center\$ or centre\$ or facilit\$ or unit? or department\$ or institution\$ or agenc\$ or hospice? or provider? or program\$ or "adult orient\$" or communit\$ or outpatient\$ or outreach)).ti,ab.
7	((transfer\$ or handoff or handover or "hand over") and (service\$ or care or clinic? or healthcare or setting\$ or hospital? or center\$ or centre\$ or facilit\$ or unit? or department\$ or institution\$ or agenc\$ or hospice\$ or provider\$ or communit\$ or outpatient\$ or outreach) and adult\$).ti,ab.
8	(transition\$ adj3 (coordinat\$ or framework? or manag\$ or prepar\$ or plan\$ or protocol\$ or support\$ or trajector\$ or pathway\$ or process\$ or readiness or timing or partnership\$ or program\$ or training or educat\$ or strateg\$ or failure\$ or barrier\$ or system?)).ti,ab.
9	(transition\$ and (MDT\$ or multidisciplinary team\$ or multiprofession\$ or interdisciplinar\$ or key worker\$ or consultant\$ or clinician\$ or specialist\$ or p?ediatrician\$ or social worker\$ or lead\$ or professional\$ or rehabilitation or staff or nurse\$ or therapist\$ or multiagenc\$ or agenc\$)).ti,ab.
10	(transition\$ and (communicat\$ or written or writing or verbal\$ or email\$ or electronic\$ or contact\$)).ti,ab.
11	(transition\$ and (admin\$ or record\$ or appointment\$ or checklist\$ or check list\$ or summar\$ or information or booklet\$ or pamphlet\$ or passport\$)).ti,ab.
12	((transition\$ and ("continued care" or "continuing care" or (continuity adj2 care))) adj5 (adult\$ or p?ediatric\$ or child\$ or adolescent\$ or family or families or carer\$)).ti,ab.
13	(LIFEsplan or Moving on well).ti,ab.
14	or/5-13
15	PATIENT CARE PLANNING/ and (adult\$ or p?ediatric\$ or child\$ or adolescent\$ or family or families or carer\$).ti.
16	QUESTIONNAIRE/ or HEALTH CARE SURVEY/
17	NEEDS ASSESSMENT/
18	16 or 17
19	(survey\$ or questionnaire\$).ti,ab.
20	18 or 19
21	15 and 20
22	14 or 21
23	4 and 22

#	Searches
24	limit 23 to english language
25	letter.pt. or LETTER/
26	note.pt.
27	editorial.pt.
28	CASE REPORT/ or CASE STUDY/
29	(letter or comment*).ti.
30	or/25-29
31	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
32	30 not 31
33	ANIMAL/ not HUMAN/
34	NONHUMAN/
35	exp ANIMAL EXPERIMENT/
36	exp EXPERIMENTAL ANIMAL/
37	ANIMAL MODEL/
38	exp RODENT/
39	(rat or rats or mouse or mice).ti.
40	or/32-39
41	ot 40

## E.5 What are the non-lower-respiratory complications of cystic fibrosis in infants, children, young people and adults?

### E.5.1 Database: Medline

Last searched on Ovid MEDLINE(R) 1946 to October Week 4 2016 on 8th November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	1 or 2 or 3
5	PREVALENCE/
6	INCIDENCE/
7	exp MODELS, STATISTICAL/
8	(prevalen\$ or incidence? or model\$ or rate? or epidemiolog\$).ti.
9	((prevalen\$ or incidence? or transversal\$) adj3 (study or studies)).ti,ab.
10	COHORT STUDIES/
11	(cohort adj3 (study or studies)).ti,ab.
12	(Cohort adj3 analy\$).ti,ab.
13	FOLLOW-UP STUDIES/
14	(Follow\$ up adj3 (study or studies)).ti,ab.
15	LONGITUDINAL STUDIES/
16	longitudinal\$.ti,ab.
17	PROSPECTIVE STUDIES/
18	prospective\$.ti,ab.

#	Searches
19	RETROSPECTIVE STUDIES/
20	retrospective\$.ti,ab.
21	CROSS-SECTIONAL STUDIES/
22	cross-sectional\$.ti,ab.
23	MULTICENTER STUDIES/
24	((multicent\$ or multi\$ cent\$) adj3 (study or studies)).ti,ab.
25	REGISTRIES/
26	(registr\$ or register?).ti,ab.
27	or/5-26
28	AGE FACTORS/
29	AGE OF ONSET/
30	TIME TO TREATMENT/
31	(age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).ti,ab.
32	(disease adj3 (duration or onset)).ti,ab.
33	or/28-32
34	27 or 33
35	Malnutrition/ep
36	malnutrition.ti.
37	nutritional deficienc\$.ab,ti.
38	*Nutritional Status/
39	nutrition\$ status.ab,ti.
40	or/35-39
41	Growth Disorders/
42	(Impair\$ adj2 growth).ab,ti.
43	stature.ab,ti.
44	height velocity.ab,ti.
45	stunt\$.ab,ti.
46	or/41-45
47	Puberty, Delayed/
48	(puberty adj2 delay\$).ab,ti.
49	Sexual Maturation/
50	(sexual adj2 matur\$).ab,ti.
51	or/47-50
52	Distal Intestinal Obstruction Syndrome.ab,ti.
53	DIOS.ab,ti.
54	Intestinal Obstruction/
55	(Intestin\$ adj2 Obstruct\$).ab,ti.
56	or/52-55
57	exp Abdominal Pain/
58	(abdom\$ adj2 pain\$).ti,ab.
59	exp Gastrointestinal Diseases/co
60	Intussusception/
61	intus?usception?.ab,ti.
62	(intestin\$ adj2 invagination?).ab,ti.
63	or/57-62

#	Searches
64	Meconium/ and Ileus/
65	(meconium and ileus).ab,ti.
66	(bowel\$ adj2 obstruct\$).ab,ti.
67	64 or 65 or 66
68	Intestinal Volvulus/
69	volvulus.ab,ti.
70	68 or 69
71	Diabetes Mellitus/ep
72	Diabetes Mellitus, Type 1/ep
73	Diabetes Mellitus, Type 2/ep
74	Diabetes Complications/
75	Hyperglycemia/ep
76	Hypoglycemia/ep
77	Glucose Intolerance/ep
78	*Insulin Resistance/
79	(relate\$ adj2 diabet\$).ab,ti.
80	CFRD.ab,ti.
81	or/71-80
82	RESPIRATORY TRACT INFECTIONS/ep
83	Respiratory Tract Diseases/ep
84	((upper respiratory or upper airway\$ or (larynx\$ or glottis\$ or epiglottis\$ or subglottis\$ or oropharynx\$ or tonsil\$ or hypopharynx\$ or pharynx\$ or throat or vocal cord or vocal fold or voice box or nasopharynx\$ or paranasal or nasal or nose or sinus or sinonasal or nasosinus)) adj1 (disease\$ or disorder\$ or dysfunction\$ or adduction\$ or paralysis\$)).ab,ti.
85	Nose Diseases/co, ep
86	Paranasal Sinus Diseases/co, ep
87	Nasal Polyps/
88	(Nasal adj2 polyp\$).ab,ti.
89	exp Rhinitis/co, ep
90	(chronic rhinitis or chronic rhinitides or (chronic adj2 catarrh)).ab,ti.
91	exp Sinusitis/co, ep
92	chronic sinusitis.ab,ti.
93	chronic rhinosinusitis.ab,ti.
94	sinus hypoplasia.ab,ti.
95	Pharyngeal Diseases/co, ep
96	Nasopharyngeal Diseases/co, ep
97	Laryngeal Diseases/co, ep
98	exp Vocal Cord Dysfunction/
99	Vocal Cord Paralysis/
100	exp Voice Disorders/co
101	or/82-100
102	Musculoskeletal Diseases/
103	musculoskeletal.ab,ti.
104	Osteoarthropathy, Secondary Hypertrophic/
105	(hypertrophic adj2 osteoarthropath\$ adj2 pulmonary).ab,ti.

#	Searches
106	(finger? adj2 club\$).ab,ti.
107	Kyphosis/
108	kyphos?s.ab,ti.
109	Scoliosis/
110	scolios?s.ab,ti.
111	Joint Diseases/
112	(joint? adj2 disease?).ab,ti.
113	Arthralgia/
114	arthralgia?.ab,ti.
115	Polyarthralgia?.ab,ti.
116	(joint? adj2 pain?).ab,ti.
117	Synovitis/
118	synoviti\$.ab,ti.
119	Arthritis/
120	arthriti\$.ab,ti.
121	Bone Density/
122	(Bone? adj2 (densit\$ or content?)).ab,ti.
123	Osteoporosis/
124	or/102-123
125	Urinary Incontinence, Stress/
126	(stress adj2 incontinen\$).ab,ti.
127	125 or 126
128	Bartter Syndrome/
129	pseudo bartter\$ syndrome.ab,ti.
130	pseudobartter\$ syndrome.ab,ti.
131	128 or 129 or 130
132	exp Renal Insufficiency/
133	exp kidney diseases/
134	((kidney\$ or renal) adj2 (complicat\$ or disease\$ or insufficien\$ or fail\$ or dysfunction\$ or amyloidosis or stone\$ or impair\$)).ab,ti.
135	nephrolithiasis.ab,ti.
136	nephrocalcinosis.ab,ti.
137	nephritis.ab,ti.
138	or/132-137
139	Liver Diseases/
140	(liver adj2 disease?).ab,ti.
141	(liver adj2 dysfunction?).ab,ti.
142	Liver Cirrhosis/
143	(liver adj2 cirrhos?s).ab,ti.
144	(liver adj2 fibros?s).ab,ti.
145	(hepatic adj2 cirrhos?s).ab,ti.
146	Hypertension, Portal/
147	(portal adj2 hypertension?).ab,ti.
148	cruveilhier baumgarten syndrome.ab,ti.
149	or/139-148
150	Exocrine Pancreatic Insufficiency/

#	Searches
151	(exocrine adj2 pancreatic adj2 insufficienc\$).ab,ti.
152	150 or 151
153	Infertility/
154	Infertility, Male/
155	Aspermia/
156	Asthenozoospermia/
157	Azoospermia/
158	Oligospermia/
159	Sertoli Cell-Only Syndrome/
160	Infertility, Female/
161	sterility.ab,ti.
162	subfertility.ab,ti.
163	sub-fertility.ab,ti.
164	infertility.ab,ti.
165	Aspermia.ab,ti.
166	Asthenozoospermia.ab,ti.
167	Azoospermia.ab,ti.
168	Oligospermia.ab,ti.
169	sertoli cell only syndrome.ab,ti.
170	germinal cell aplasia.ab,ti.
171	del castillo syndrome.ab,ti.
172	or/153-171
173	4 and 34 and 40
174	4 and 34 and 46
175	4 and 34 and 51
176	4 and 34 and 56
177	4 and 34 and 63
178	4 and 34 and 67
179	4 and 34 and 70
180	4 and 34 and 81
181	4 and 34 and 101
182	4 and 34 and 124
183	4 and 34 and 127
184	4 and 34 and 131
185	4 and 34 and 138
186	4 and 34 and 149
187	4 and 34 and 152
188	4 and 34 and 172
189	or/173-188
190	limit 189 to english language
191	LETTER/
192	EDITORIAL/
193	NEWS/
194	exp HISTORICAL ARTICLE/
195	ANECDOTES AS TOPIC/

#	Searches
196	COMMENT/
197	CASE REPORT/
198	(letter or comment* or abstracts).ti.
199	or/191-198
200	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
201	199 not 200
202	ANIMALS/ not HUMANS/
203	exp ANIMALS, LABORATORY/
204	exp ANIMAL EXPERIMENTATION/
205	exp MODELS, ANIMAL/
206	exp RODENTIA/
207	(rat or rats or mouse or mice).ti.
208	or/201-207
209	190 not 208

### E.5.2 Database: Medline In-Process & Other Non-Indexed Citations

Last searched on Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations November 07, 2016 on 8th November 2016.

#	Searches
1	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
2	mucov\$.ti,ab.
3	1 or 2
4	malnutrition.ti.
5	nutritional deficienc\$.ab,ti.
6	nutrition\$ status.ab,ti.
7	or/4-6
8	(Impair\$ adj2 growth).ab,ti.
9	stature.ab,ti.
10	height velocity.ab,ti.
11	stunt\$.ab,ti.
12	or/8-11
13	(puberty adj2 delay\$).ab,ti.
14	matur\$.ab,ti.
15	13 or 14
16	Distal Intestinal Obstruction Syndrome.ab,ti.
17	DIOS.ab,ti.
18	(Intestin\$ adj2 Obstruct\$).ab,ti.
19	or/16-18
20	(abdom\$ adj2 pain\$).ti,ab.
21	intus?usception?.ab,ti.
22	(intestin\$ adj2 invagination?).ab,ti.
23	or/20-22
24	(meconium and ileus).ab,ti.
25	(bowel\$ adj2 obstruct\$).ab,ti.
26	24 or 25

#	Searches
27	volvulus.ab,ti.
28	(relate\$ adj2 diabet\$).ab,ti.
29	CFRD.ab,ti.
30	29 or "30".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
31	((upper respiratory or upper airway\$ or (larynx\$ or glottis\$ or epiglottis\$ or subglottis\$ or oropharynx\$ or tonsil\$ or hypopharynx\$ or pharynx\$ or throat or vocal cord or vocal fold or voice box or nasopharynx\$ or paranasal or nasal or nose or sinus or sinonasal or nasosinus)) adj1 (disease\$ or disorder\$ or dysfunction\$ or adduction\$ or paralys\$)).ab,ti.
32	(Nasal adj2 polyp\$).ab,ti.
33	(chronic rhinitis or chronic rhinitides or (chronic adj2 catarrh)).ab,ti.
34	nasosinusitis.ab,ti.
35	chronic sinusitis.ab,ti.
36	chronic rhinosinusitis.ab,ti.
37	sinus hypoplasia.ab,ti.
38	or/31-37
39	musculoskeletal.ab,ti.
40	(hypertrophic adj2 osteoarthropath\$ adj2 pulmonary).ab,ti.
41	(finger? adj2 club\$).ab,ti.
42	kyphos?s.ab,ti.
43	scolios?s.ab,ti.
44	(joint? adj2 disease?).ab,ti.
45	arthralgia?.ab,ti.
46	(joint? adj2 pain?).ab,ti.
47	synoviti\$.ab,ti.
48	arthriti\$.ab,ti.
49	(Bone? adj2 (densit\$ or content\$)).ab,ti.
50	or/39-49
51	(stress adj2 incontinen\$).ab,ti.
52	((kidney\$ or renal) adj2 (complicat\$ or disease\$ or insufficien\$ or fail\$ or dysfunction\$ or amyloidosis or stone\$ or impair\$)).ab,ti.
53	nephrolithiasis.ab,ti.
54	nephrocalcinosis.ab,ti.
55	nephritis.ab,ti.
56	or/52-55
57	(liver adj2 disease?).ab,ti.
58	(liver adj2 dysfunction?).ab,ti.
59	(liver adj2 cirrhos?s).ab,ti.
60	(liver adj2 fibros?s).ab,ti.
61	(hepatic adj2 cirrhos?s).ab,ti.
62	(portal adj2 hypertension?).ab,ti.
63	cruveilhier baumgarten syndrome.ab,ti.
64	(exocrine adj2 pancreatic adj2 insufficienc\$).ab,ti.
65	or/57-64
66	sterility.ab,ti.

#	Searches
67	subfertility.ab,ti.
68	sub-fertility.ab,ti.
69	infertility.ab,ti.
70	Aspermia.ab,ti.
71	Asthenozoospermia.ab,ti.
72	Azoospermia.ab,ti.
73	Oligospermia.ab,ti.
74	sertoli cell only syndrome.ab,ti.
75	germinal cell aplasia.ab,ti.
76	del castillo syndrome.ab,ti.
77	or/66-76
78	3 and 7
79	3 and 12
80	3 and 15
81	3 and 19
82	3 and 23
83	3 and 26
84	3 and 27
85	3 and 30
86	3 and 38
87	3 and 50
88	3 and 51
89	3 and 56
90	3 and 65
91	or/78-90

### E.5.3 Database: Cochrane Central Register of Controlled Trials

Last searched on **EBM Reviews - Cochrane Central Register of Controlled Trials**  
October 2016 on 8<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS.kw.
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	1 or 2 or 3
5	Malnutrition.kw.
6	malnutrition.ti.
7	nutritional deficienc\$.ab,ti.
8	Nutritional Status.kw.
9	nutrition\$ status.ab,ti.
10	or/5-9
11	Growth Disorders.kw.
12	(Impair\$ adj2 growth).ab,ti.
13	stature.ab,ti.
14	height velocity.ab,ti.
15	stunt\$.ab,ti.

#	Searches
16	or/11-15
17	Puberty.kw.
18	(puberty adj2 delay\$).ab,ti.
19	Maturation.kw.
20	matur\$.ab,ti.
21	or/17-20
22	Distal Intestinal Obstruction Syndrome.ab,ti.
23	DIOS.ab,ti.
24	Intestinal Obstruction.kw.
25	(Intestin\$ adj2 Obstruct\$).ab,ti.
26	or/22-25
27	Abdominal Pain.kw.
28	(abdom\$ adj2 pain\$).ti,ab.
29	Gastrointestinal Diseases.kw.
30	Intussusception.kw.
31	intus?usception?.ab,ti.
32	(intestin\$ adj2 invagination?).ab,ti.
33	or/27-32
34	(Meconium and Ileus).kw.
35	(meconium and ileus).ab,ti.
36	(bowel\$ adj2 obstruct\$).ab,ti.
37	34 or 35 or 36
38	(intestinal or intestine or intestines).kw.
39	volvulus.ab,ti.
40	38 or 39
41	Diabetes Mellitus.kw.
42	Diabetes Mellitus, Type 1.kw.
43	Diabetes Mellitus, Type 2.kw.
44	Diabetes Complications.kw.
45	Hyperglycemia.kw.
46	Hypoglycemia.kw.
47	Glucose Intolerance.kw.
48	Insulin Resistance.kw.
49	(relate\$ adj2 diabet\$).ab,ti.
50	CFRD.ab,ti.
51	or/41-50
52	RESPIRATORY TRACT INFECTIONS.kw.
53	Respiratory Tract Diseases.kw.
54	((upper respiratory or upper airway\$ or (larynx\$ or glottis\$ or epiglottis\$ or subglottis\$ or oropharynx\$ or tonsil\$ or hypopharynx\$ or pharynx\$ or throat or vocal cord or vocal fold or voice box or nasopharynx\$ or paranasal or nasal or nose or sinus or sinonasal or nasosinus)) adj1 (disease\$ or disorder\$ or dysfunction\$ or adduction\$ or paralysis\$)).ab,ti.
55	Nose Diseases.kw.
56	(nasal and polyps).kw.
57	(Nasal adj2 polyp\$).ab,ti.

#	Searches
58	Rhinitis.kw.
59	(chronic rhinitis or chronic rhinitides or (chronic adj2 catarrh)).ab,ti.
60	Sinusitis.kw.
61	chronic sinusitis.ab,ti.
62	chronic rhinosinusitis.ab,ti.
63	sinus hypoplasia.ab,ti.
64	Pharyngeal Diseases.kw.
65	nasosinusitis.kw.
66	Laryngeal Diseases.kw.
67	Vocal Cord.kw.
68	Vocal Cord Paralysis.kw.
69	Voice Disorders.kw.
70	or/52-69
71	Musculoskeletal Diseases.kw.
72	musculoskeletal.ab,ti.
73	(hypertrophic adj2 osteoarthropath\$ adj2 pulmonary).ab,ti.
74	(finger? adj2 club\$).ab,ti.
75	Kyphosis.kw.
76	kyphos?s.ab,ti.
77	Scoliosis.kw.
78	scolios?s.ab,ti.
79	Joint Diseases.kw.
80	(joint? adj2 disease?).ab,ti.
81	Arthralgia.kw.
82	arthralgia?.ab,ti.
83	(joint? adj2 pain?).ab,ti.
84	Synovitis.kw.
85	synoviti\$.ab,ti.
86	Arthritis.kw.
87	arthriti\$.ab,ti.
88	Bone Density.kw.
89	(Bone? adj2 (densit\$ or content?)).ab,ti.
90	Osteoporosis.kw.
91	or/71-90
92	Urinary Incontinence, Stress.kw.
93	(stress adj2 incontinen\$).ab,ti.
94	92 or 93
95	Renal Insufficiency.kw.
96	Kidney diseases.kw.
97	((kidney\$ or renal) adj2 (complicat\$ or disease\$ or insufficien\$ or fail\$ or dysfunction\$ or amyloidosis or stone\$ or impair\$)).ab,ti.
98	nephrolithiasis.ab,ti.
99	nephrocalcinosis.ab,ti.
100	nephritis.ab,ti.
101	or/95-100
102	Liver Diseases.kw.

#	Searches
103	(liver adj2 disease?).ab,ti.
104	(liver adj2 dysfunction?).ab,ti.
105	Liver Cirrhosis.kw.
106	(liver adj2 cirrhos?s).ab,ti.
107	(liver adj2 fibros?s).ab,ti.
108	(hepatic adj2 cirrhos?s).ab,ti.
109	Hypertension, Portal.kw.
110	(portal adj2 hypertension?).ab,ti.
111	cruveilhier baumgarten syndrome.ab,ti.
112	or/102-111
113	Exocrine Pancreatic Insufficiency.kw.
114	(exocrine adj2 pancreatic adj2 insufficienc\$).ab,ti.
115	113 or 114
116	Infertility.kw.
117	Infertility, Male.kw.
118	Asthenozoospermia.kw.
119	Azoospermia.kw.
120	Oligospermia.kw.
121	Infertility, Female.kw.
122	sterility.ab,ti.
123	subfertility.ab,ti.
124	sub-fertility.ab,ti.
125	infertility.ab,ti.
126	Aspermia.ab,ti.
127	Asthenozoospermia.ab,ti.
128	Azoospermia.ab,ti.
129	Oligospermia.ab,ti.
130	sertoli cell only syndrome.ab,ti.
131	germinal cell aplasia.ab,ti.
132	del castillo syndrome.ab,ti.
133	or/116-132
134	4 and 10
135	4 and 16
136	4 and 21
137	4 and 26
138	4 and 33
139	4 and 37
140	4 and 40
141	4 and 51
142	4 and 70
143	4 and 91
144	4 and 94
145	4 and 101
146	4 and 112
147	4 and 115

#	Searches
148	4 and 133
149	or/134-148

#### E.5.4 Database: Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects

Last searched on **EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to November 07, 2016, **EBM Reviews - Database of Abstracts of Reviews of Effects 1st Quarter 2015** on 8<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS.kw.
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	1 or 2 or 3
5	Malnutrition.kw.
6	malnutrition.ti.
7	nutritional deficienc\$.ab,ti.
8	Nutritional Status.kw.
9	nutrition\$ status.ab,ti.
10	or/5-9
11	Growth Disorders.kw.
12	(Impair\$ adj2 growth).ab,ti.
13	stature.ab,ti.
14	height velocity.ab,ti.
15	stunt\$.ab,ti.
16	or/11-15
17	Puberty.kw.
18	(puberty adj2 delay\$.ab,ti.
19	Maturation.kw.
20	matur\$.ab,ti.
21	or/17-20
22	Distal Intestinal Obstruction Syndrome.ab,ti.
23	DIOS.ab,ti.
24	Intestinal Obstruction.kw.
25	(Intestin\$ adj2 Obstruct\$).ab,ti.
26	or/22-25
27	Abdominal Pain.kw.
28	(abdom\$ adj2 pain\$).ti,ab.
29	Gastrointestinal Diseases.kw.
30	Intussusception.kw.
31	intus?usception?.ab,ti.
32	(intestin\$ adj2 invagination?).ab,ti.
33	or/27-32
34	(Meconium and Ileus).kw.
35	(meconium and ileus).ab,ti.
36	(bowel\$ adj2 obstruct\$).ab,ti.

#	Searches
37	34 or 35 or 36
38	(intestinal or intestine or intestines).kw.
39	volvulus.ab,ti.
40	38 or 39
41	Diabetes Mellitus.kw.
42	Diabetes Mellitus, Type 1.kw.
43	Diabetes Mellitus, Type 2.kw.
44	Diabetes Complications.kw.
45	Hyperglycemia.kw.
46	Hypoglycemia.kw.
47	Glucose Intolerance.kw.
48	Insulin Resistance.kw.
49	(relate\$ adj2 diabet\$).ab,ti.
50	CFRD.ab,ti.
51	or/41-50
52	RESPIRATORY TRACT INFECTIONS.kw.
53	Respiratory Tract Diseases.kw.
54	((upper respiratory or upper airway\$ or (larynx\$ or glottis\$ or epiglottis\$ or subglottis\$ or oropharynx\$ or tonsil\$ or hypopharynx\$ or pharynx\$ or throat or vocal cord or vocal fold or voice box or nasopharynx\$ or paranasal or nasal or nose or sinus or sinonasal or nasosinus)) adj1 (disease\$ or disorder\$ or dysfunction\$ or adduction\$ or paralysis\$)).ab,ti.
55	Nose Diseases.kw.
56	Paranasal Sinus Diseases.kw.
57	(nasal and polyps).kw.
58	(Nasal adj2 polyp\$).ab,ti.
59	Rhinitis.kw.
60	(chronic rhinitis or chronic rhinitides or (chronic adj2 catarrh)).ab,ti.
61	Sinusitis.kw.
62	chronic sinusitis.ab,ti.
63	chronic rhinosinusitis.ab,ti.
64	sinus hypoplasia.ab,ti.
65	Pharyngeal Diseases.kw.
66	nasopharyngitis.kw.
67	Laryngeal Diseases.kw.
68	Vocal Cord Dysfunction.kw.
69	Vocal Cord Paralysis.kw.
70	Voice Disorders.kw.
71	or/52-70
72	Musculoskeletal Diseases.kw.
73	musculoskeletal.ab,ti.
74	(hypertrophic adj2 osteoarthropath\$ adj2 pulmonary).ab,ti.
75	(finger? adj2 club\$).ab,ti.
76	Kyphosis.kw.
77	kyphos?s.ab,ti.
78	Scoliosis.kw.

#	Searches
79	scolios?s.ab,ti.
80	Joint Diseases.kw.
81	(joint? adj2 disease?).ab,ti.
82	Arthralgia.kw.
83	arthralgia?.ab,ti.
84	(joint? adj2 pain?).ab,ti.
85	Synovitis.kw.
86	synoviti\$.ab,ti.
87	Arthritis.kw.
88	arthriti\$.ab,ti.
89	Bone Density.kw.
90	(Bone? adj2 (densit\$ or content?)).ab,ti.
91	Osteoporosis.kw.
92	or/72-91
93	Urinary Incontinence, Stress.kw.
94	(stress adj2 incontinen\$).ab,ti.
95	93 or 94
96	Renal Insufficiency.kw.
97	Kidney diseases.kw.
98	((kidney\$ or renal) adj2 (complicat\$ or disease\$ or insufficien\$ or fail\$ or dysfunction\$ or amyloidosis or stone\$ or impair\$)).ab,ti.
99	nephrolithiasis.ab,ti.
100	nephrocalcinosis.ab,ti.
101	nephritis.ab,ti.
102	or/96-101
103	Liver Diseases.kw.
104	(liver adj2 disease?).ab,ti.
105	(liver adj2 dysfunction?).ab,ti.
106	Liver Cirrhosis.kw.
107	(liver adj2 cirrhos?s).ab,ti.
108	(liver adj2 fibros?s).ab,ti.
109	(hepatic adj2 cirrhos?s).ab,ti.
110	Hypertension, Portal.kw.
111	(portal adj2 hypertension?).ab,ti.
112	cruveilhier baumgarten syndrome.ab,ti.
113	or/103-112
114	Exocrine Pancreatic Insufficiency.kw.
115	(exocrine adj2 pancreatic adj2 insufficienc\$).ab,ti.
116	114 or 115
117	Infertility.kw.
118	Infertility, Male.kw.
119	Asthenozoospermia.kw.
120	Azoospermia.kw.
121	Oligospermia.kw.
122	Infertility, Female.kw.
123	sterility.ab,ti.

#	Searches
124	subfertility.ab,ti.
125	sub-fertility.ab,ti.
126	infertility.ab,ti.
127	Aspermia.ab,ti.
128	Asthenozoospermia.ab,ti.
129	Azoospermia.ab,ti.
130	Oligospermia.ab,ti.
131	sertoli cell only syndrome.ab,ti.
132	germinal cell aplasia.ab,ti.
133	del castillo syndrome.ab,ti.
134	or/117-133
135	4 and 10
136	4 and 16
137	4 and 21
138	4 and 26
139	4 and 33
140	4 and 37
141	4 and 40
142	4 and 51
143	4 and 71
144	4 and 92
145	4 and 95
146	4 and 102
147	4 and 113
148	4 and 116
149	4 and 134
150	or/135-149

### E.5.5 Database: Health Technology Assessment

Last searched on **EBM Reviews - Health Technology Assessment 4th Quarter 2016** on 8<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	1 or 2 or 3
5	Malnutrition/
6	malnutrition.ti.
7	nutritional deficienc\$.ab,ti.
8	Nutritional Status/
9	nutrition\$ status.ab,ti.
10	or/5-9
11	Growth Disorders/
12	(Impair\$ adj2 growth).ab,ti.
13	stature.ab,ti.

#	Searches
14	height velocity.ab,ti.
15	stunt\$.ab,ti.
16	or/11-15
17	Puberty, Delayed/
18	(puberty adj2 delay\$).ab,ti.
19	Sexual Maturation/
20	(sexual adj2 matur\$).ab,ti.
21	or/17-20
22	Distal Intestinal Obstruction Syndrome.ab,ti.
23	DIOS.ab,ti.
24	Intestinal Obstruction/
25	(Intestin\$ adj2 Obstruct\$).ab,ti.
26	or/22-25
27	exp Abdominal Pain/
28	(abdom\$ adj2 pain\$).ti,ab.
29	exp Gastrointestinal Diseases/
30	Intussusception/
31	intus?usception?.ab,ti.
32	(intestin\$ adj2 invagination?).ab,ti.
33	or/27-32
34	Meconium/ and Ileus/
35	(meconium and ileus).ab,ti.
36	(bowel\$ adj2 obstruct\$).ab,ti.
37	34 or 35 or 36
38	Intestinal Volvulus/
39	volvulus.ab,ti.
40	38 or 39
41	Diabetes Mellitus/
42	Diabetes Mellitus, Type 1/
43	Diabetes Mellitus, Type 2/
44	Diabetes Complications/
45	Hyperglycemia/
46	Hypoglycemia/
47	Glucose Intolerance/
48	Insulin Resistance/
49	(relate\$ adj2 diabet\$).ab,ti.
50	CFRD.ab,ti.
51	or/41-50
52	RESPIRATORY TRACT INFECTIONS/
53	Respiratory Tract Diseases/
54	((upper respiratory or upper airway\$ or (larynx\$ or glottis\$ or epiglottis\$ or subglottis\$ or oropharynx\$ or tonsil\$ or hypopharynx\$ or pharynx\$ or throat or vocal cord or vocal fold or voice box or nasopharynx\$ or paranasal or nasal or nose or sinus or sinonasal or nasosinus)) adj1 (disease\$ or disorder\$ or dysfunction\$ or adduction\$ or paralys\$)).ab,ti.
55	Nose Diseases/
56	Paranasal Sinus Diseases/

#	Searches
57	Nasal Polyps/
58	(Nasal adj2 polyp\$).ab,ti.
59	exp Rhinitis/
60	(chronic rhinitis or chronic rhinitides or (chronic adj2 catarrh)).ab,ti.
61	exp Sinusitis/
62	chronic sinusitis.ab,ti.
63	chronic rhinosinusitis.ab,ti.
64	sinus hypoplasia.ab,ti.
65	Pharyngeal Diseases/
66	Nasopharyngeal Diseases/
67	Laryngeal Diseases/
68	exp Vocal Cord Dysfunction/
69	Vocal Cord Paralysis/
70	exp Voice Disorders/
71	or/52-70
72	Musculoskeletal Diseases/
73	musculoskeletal.ab,ti.
74	Osteoarthropathy, Secondary Hypertrophic/
75	(hypertrophic adj2 osteoarthropath\$ adj2 pulmonary).ab,ti.
76	(finger? adj2 club\$).ab,ti.
77	Kyphosis/
78	kyphos?s.ab,ti.
79	Scoliosis/
80	scolios?s.ab,ti.
81	Joint Diseases/
82	(joint? adj2 disease?).ab,ti.
83	Arthralgia/
84	arthralgia?.ab,ti.
85	Polyarthralgia?.ab,ti.
86	(joint? adj2 pain?).ab,ti.
87	Synovitis/
88	synoviti\$.ab,ti.
89	Arthritis/
90	arthriti\$.ab,ti.
91	Bone Density/
92	(Bone? adj2 (densit\$ or content?)).ab,ti.
93	Osteoporosis/
94	or/72-93
95	Urinary Incontinence, Stress/
96	(stress adj2 incontinen\$).ab,ti.
97	95 or 96
98	Bartter Syndrome/
99	pseudo bartter\$ syndrome.ab,ti.
100	pseudobartter\$ syndrome.ab,ti.
101	98 or 99 or 100

#	Searches
102	exp Renal Insufficiency/
103	exp kidney diseases/
104	((kidney\$ or renal) adj2 (complicat\$ or disease\$ or insufficien\$ or fail\$ or dysfunction\$ or amyloidosis or stone\$ or impair\$)).ab,ti.
105	nephrolithiasis.ab,ti.
106	nephrocalcinosis.ab,ti.
107	nephritis.ab,ti.
108	or/102-107
109	Liver Diseases/
110	(liver adj2 disease?).ab,ti.
111	(liver adj2 dysfunction?).ab,ti.
112	Liver Cirrhosis/
113	(liver adj2 cirrhos?s).ab,ti.
114	(liver adj2 fibros?s).ab,ti.
115	(hepatic adj2 cirrhos?s).ab,ti.
116	Hypertension, Portal/
117	(portal adj2 hypertension?).ab,ti.
118	cruveilhier baumgarten syndrome.ab,ti.
119	or/109-118
120	Exocrine Pancreatic Insufficiency/
121	(exocrine adj2 pancreatic adj2 insufficienc\$).ab,ti.
122	120 or 121
123	Infertility/
124	Infertility, Male/
125	Aspermia/
126	Asthenozoospermia/
127	Azoospermia/
128	Oligospermia/
129	Sertoli Cell-Only Syndrome/
130	Infertility, Female/
131	sterility.ab,ti.
132	subfertility.ab,ti.
133	sub-fertility.ab,ti.
134	infertility.ab,ti.
135	Aspermia.ab,ti.
136	Asthenozoospermia.ab,ti.
137	Azoospermia.ab,ti.
138	Oligospermia.ab,ti.
139	sertoli cell only syndrome.ab,ti.
140	germinal cell aplasia.ab,ti.
141	del castillo syndrome.ab,ti.
142	or/123-141
143	4 and 10
144	4 and 16
145	4 and 21
146	4 and 26

#	Searches
147	4 and 33
148	4 and 37
149	4 and 40
150	4 and 51
151	4 and 71
152	4 and 94
153	4 and 97
154	4 and 101
155	4 and 108
156	4 and 119
157	4 and 122
158	4 and 142
159	or/143-158
160	limit 159 to english language

### E.5.6 Database: Embase

Last searched on **Embase** 1974 to 2016 Week 45 on 8<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	mucov\$.ti,ab.
3	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
4	or/1-3
5	EPIDEMIOLOGY/
6	epidemiolog\$.tw.
7	PREVALENCE/
8	prevalence.tw.
9	cross sectional.tw.
10	INCIDENCE/
11	incidence.tw.
12	or/5-11
13	exp CASE CONTROL STUDY/
14	(case\$ adj2 control\$).tw.
15	cohort analysis/
16	cohort.tw.
17	LONGITUDINAL STUDY/
18	longitudinal\$.ti,ab.
19	FOLLOW UP/
20	(Follow\$ up adj3 (study or studies)).ti,ab.
21	PROSPECTIVE STUDY/
22	prospective\$.ti,ab.
23	retrospective study/
24	retrospective\$.ti,ab.
25	CROSS-SECTIONAL STUDY/
26	cross-sectional\$.ti,ab.
27	"MULTICENTER STUDY (TOPIC)"/

#	Searches
28	((multicent\$ or multi\$ cent\$) adj3 (study or studies)).ti,ab.
29	REGISTER/
30	(registr\$ or register?).ti,ab.
31	or/13-30
32	AGE/
33	ONSET AGE/
34	TIME TO TREATMENT/
35	(age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).ti,ab.
36	(disease adj3 (duration or onset)).ti,ab.
37	or/32-36
38	12 or 31 or 37
39	EXP MALNUTRITION/co, ep [Complication, Epidemiology]
40	malnutrition.ti.
41	nutritional deficienc\$.ab,ti.
42	EXP NUTRITIONAL STATUS/
43	nutrition\$ status.ab,ti.
44	or/39-43
45	GROWTH DISORDER/
46	(Impair\$ adj2 growth).ab,ti.
47	stature.ab,ti.
48	height velocity.ab,ti.
49	stunt\$.ab,ti.
50	or/45-49
51	DELAYED PUBERTY/
52	(puberty adj2 delay\$).ab,ti.
53	SEXUAL MATURATION/
54	(sexual adj2 matur\$).ab,ti.
55	or/51-54
56	Distal Intestinal Obstruction Syndrome.ab,ti.
57	DIOS.ab,ti.
58	EXP INTESTINE OBSTRUCTION/co, ep [Complication, Epidemiology]
59	(Intestin\$ adj2 Obstruct\$).ab,ti.
60	intus?usception?.ab,ti.
61	(intestin\$ adj2 invagination?).ab,ti.
62	EXP GASTROINTESTINAL DISEASE/co, ep [Complication, Epidemiology]
63	EXP ABDOMINAL PAIN/co, ep [Complication, Epidemiology]
64	(abdom\$ adj2 pain\$).ti,ab.
65	(intest\$ adj2 volvulus).ab,ti.
66	MECONIUM ILEUS/
67	(meconium and ileus).ab,ti.
68	(bowel\$ adj2 obstruct\$).ab,ti.
69	or/56-68
70	DIABETES MELLITUS/co, ep [Complication, Epidemiology]
71	HYPERGLYCEMIA/co, ep [Complication, Epidemiology]
72	HYPOGLYCEMIA/co, ep [Complication, Epidemiology]

#	Searches
73	GLUCOSE INTOLERANCE/co, ep [Complication, Epidemiology]
74	INSULIN RESISTANCE/co, ep [Complication, Epidemiology]
75	(relate\$ adj2 diabet\$).ab,ti.
76	CFRD.ab,ti.
77	or/70-76
78	EXP UPPER RESPIRATORY TRACT INFECTION/co, ep [Complication, Epidemiology]
79	((upper respiratory or upper airway\$ or (larynx\$ or glottis\$ or epiglottis\$ or subglottis\$ or oropharynx\$ or tonsil\$ or hypopharynx\$ or pharynx\$ or throat or vocal cord or vocal fold or voice box or nasopharynx\$ or paranasal or nasal or nose or sinus or sinonasal or nasosinus)) adj1 (disease\$ or disorder\$ or dysfunction\$ or adduction\$ or paralysis\$)).ab,ti.
80	NOSE DISEASE/co, ep [Complication, Epidemiology]
81	PARANASAL SINUS DISEASE/co, ep [Complication, Epidemiology]
82	NOSE POLYP/co, ep [Complication, Epidemiology]
83	(Nasal adj2 polyp\$).ab,ti.
84	EXP RHINITIS/co, ep [Complication, Epidemiology]
85	(chronic rhinitis or chronic rhinitides or (chronic adj2 catarrh)).ab,ti.
86	CHRONIC SINUSITIS/co, ep [Complication, Epidemiology]
87	CHRONIC RHINOSINUSITIS/co, ep [Complication, Epidemiology]
88	PARANASAL SINUSITIS/co, ep [Complication, Epidemiology]
89	(chronic adj (sinusitis or rhinosinusitis)).ab,ti.
90	sinus hypoplasia.ab,ti.
91	PHARYNX DISEASE/co, ep [Complication, Epidemiology]
92	LARYNX DISORDER/co, ep [Complication, Epidemiology]
93	VOCAL CORD DISORDER/co, ep [Complication, Epidemiology]
94	VOCAL CORD PARALYSIS/co, ep [Complication, Epidemiology]
95	VOICE DISORDER/co, ep [Complication, Epidemiology]
96	or/78-95
97	MUSCULOSKELETAL DISEASE/co, ep [Complication, Epidemiology]
98	musculoskeletal.ab,ti.
99	HYPERTROPHIC OSTEOARTHROPATHY/
100	(hypertrophic adj2 osteoarthropath\$ adj2 pulmonary).ab,ti.
101	(finger? adj2 club\$).ab,ti.
102	KYPHOSIS/
103	kyphos?s.ab,ti.
104	EXP SCOLIOSIS/co, ep [Complication, Epidemiology]
105	scolios?s.ab,ti.
106	ARTHROPATHY/co, ep [Complication, Epidemiology]
107	(joint? adj2 disease?).ab,ti.
108	ARTHRALGIA/co, ep [Complication, Epidemiology]
109	arthralgia?.ab,ti.
110	Polyarthralgia?.ab,ti.
111	(joint? adj2 pain?).ab,ti.
112	SYNOVITIS/co, ep [Complication, Epidemiology]
113	synoviti\$.ab,ti.
114	ARTHRITIS/co, ep [Complication, Epidemiology]

#	Searches
115	arthriti\$.ab,ti.
116	BONE DENSITY/
117	(Bone? adj2 (densit\$ or content?)).ab,ti.
118	OSTEOPOROSIS/co, ep [Complication, Epidemiology]
119	or/97-118
120	STRESS INCONTINENCE/
121	(stress adj2 incontinen\$).ab,ti.
122	120 or 121
123	BARTTER SYNDROME/
124	pseudo bartter\$ syndrome.ab,ti.
125	pseudobartter\$ syndrome.ab,ti.
126	123 or 124 or 125
127	EXP KIDNEY DISEASE/co, ep [Complication, Epidemiology]
128	((kidney\$ or renal) adj2 (complicat\$ or disease\$ or insufficien\$ or fail\$ or dysfunction\$ or amyloidosis or stone\$ or impair\$)).ab,ti.
129	nephrolithiasis.ab,ti.
130	nephrocalcinosis.ab,ti.
131	nephritis.ab,ti.
132	or/127-131
133	LIVER DISEASE/co, ep [Complication, Epidemiology]
134	(liver adj2 disease?).ab,ti.
135	(liver adj2 dysfunction?).ab,ti.
136	LIVER CIRRHOSIS/co, ep [Complication, Epidemiology]
137	(liver adj2 cirrhos?s).ab,ti.
138	(liver adj2 fibros?s).ab,ti.
139	(hepatic adj2 cirrhos?s).ab,ti.
140	PORTAL HYPERTENSION/
141	(portal adj2 hypertension?).ab,ti.
142	cruveilhier baumgarten syndrome.ab,ti.
143	or/133-142
144	PANCREAS EXOCRINE INSUFFICIENCY/
145	(exocrine adj2 pancreatic adj2 insufficienc\$).ab,ti.
146	144 or 145
147	EXP INFERTILITY/co, ep [Complication, Epidemiology]
148	MALE INFERTILITY/
149	ASPERMIA/
150	ASTHENOSPERMIA/
151	AZOOSPERMIA/
152	OLIGOSPERMIA/
153	SERTOLI CELL ONLY SYNDROME/
154	FEMALE INFERTILITY/
155	sterility.ab,ti.
156	subfertility.ab,ti.
157	sub-fertility.ab,ti.
158	infertility.ab,ti.
159	Aspermia.ab,ti.

#	Searches
160	Asthenozoospermia.ab,ti.
161	Azoospermia.ab,ti.
162	Oligospermia.ab,ti.
163	sertoli cell only syndrome.ab,ti.
164	germinal cell aplasia.ab,ti.
165	del castillo syndrome.ab,ti.
166	or/147-163
167	4 and 38 and 44
168	4 and 38 and 50
169	4 and 38 and 56
170	4 and 38 and 61
171	4 and 38 and 75
172	4 and 38 and 83
173	4 and 38 and 102
174	4 and 38 and 125
175	4 and 38 and 132
176	4 and 38 and 138
177	4 and 38 and 150
178	4 and 38 and 153
179	4 and 38 and 172
180	or/167-179
181	letter.pt. or LETTER/
182	note.pt.
183	editorial.pt.
184	CASE REPORT/ or CASE STUDY/
185	(letter or comment*).ti.
186	or/181-185
187	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
188	186 not 187
189	ANIMAL/ not HUMAN/
190	NONHUMAN/
191	exp ANIMAL EXPERIMENT/
192	exp EXPERIMENTAL ANIMAL/
193	ANIMAL MODEL/
194	exp RODENT/
195	(rat or rats or mouse or mice).ti.
196	or/188-195
197	180 not 196

## E.6 Pulmonary monitoring

### E.6.1 What is the value of the following investigative strategies in monitoring the onset of pulmonary disease in people with CF without clinical signs or symptoms of lung disease?

- Non-invasive microbiological investigation- induced sputum samples, cough swab, throat swab, and nasopharyngeal aspiration

- Invasive microbiological investigation- bronchoalveolar lavage
- Lung physiological function tests- Cardiopulmonary exercise testing, Spirometry and Lung Clearance Index
- Imaging techniques- Chest x-ray and CT scan

### E.6.2 What is the value of the following investigative strategies in monitoring evolving pulmonary disease in people with established lung disease?

- Non-invasive microbiological investigation- induced sputum samples, cough swab, throat swab, and nasopharyngeal aspiration
- Invasive microbiological investigation- bronchoalveolar lavage
- Lung physiological function tests- Cardiopulmonary exercise testing, Spirometry and Lung Clearance Index
- Imaging techniques- Chest x-ray and CT scan
- Evolving pulmonary disease defined as decline in lung function (based on FEV1), increased exacerbations and/or infections, (symptom based?) and CT changes.

### E.6.3 What is the added value of imaging and invasive microbiological testing in addition to non-invasive microbiological testing and lung function tests in monitoring the response to treatment following an acute exacerbation?

- Database: Medline

Last searched on **Ovid MEDLINE(R)** 1946 to October Week 3 2016 on 2<sup>nd</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	exp *RESPIRATORY TRACT INFECTIONS/
6	exp *BACTERIAL INFECTIONS/
7	exp *PNEUMONIA/
8	exp *STAPHYLOCOCCUS AUREUS/
9	exp *PSEUDOMONAS AERUGINOSA/
10	exp *LUNG/pa, pp [Pathology, Physiopathology]
11	((lung? or pulmonar? or respirat\$ or airway?) adj (disease? or dysfunction\$ or obstruct\$ or inflam\$ or infect\$ or pathol\$)).ti.
12	((bacteria\$ or mycobacteria\$) adj infect\$).ti.
13	pneumoni\$.ti.
14	(staphylococcus aureus or s aureus or pseudomonas aeruginosa or p aeruginosa).ti.
15	or/5-14
16	exp "SENSITIVITY AND SPECIFICITY"/
17	(sensitivity or specificity).ti,ab.
18	((pre test or pretest or post test or posttest) adj probability).ti,ab.
19	(predictive value\$ or PPV or NPV).ti,ab.
20	likelihood ratio\$.ti,ab.
21	LIKELIHOOD FUNCTIONS/
22	(ROC curve\$ or AUC).ti,ab.
23	diagnos\$.ti.
24	(diagnos\$ adj2 (performance\$ or accurac\$ or utilit\$ or value\$ or efficien\$ or

#	Searches
	effectiveness)).ti,ab.
25	gold standard.ab.
26	di.fs.
27	or/16-26
28	*DIAGNOSTIC TECHNIQUES, RESPIRATORY SYSTEM/
29	((lung? or pulmonar? or respirat\$ or airway?) adj3 (disease? or dysfunction\$ or obstruct\$ or inflam\$ or infect\$ or pathol\$ or microbiolog\$ or bacteri\$ or pathogen?) adj3 (monitor\$ or investigat\$ or test\$ or assess\$ or measure\$ or exam\$ or cultur\$ or marker? or onset or detect\$ or indicat\$)).ti,ab.
30	or/28-29
31	SPUTUM/
32	((cough or throat or pharyn\$ or oral or oropharyn\$ or sputum or airway?) adj3 (swab? or culture\$ or sampl\$)).ti,ab.
33	(sputum adj1 induc\$).ti,ab.
34	(sputum adj2 analys\$).ti,ab.
35	exp BRONCHOALVEOLAR LAVAGE/
36	BRONCHOSCOPY/
37	((bronch\$ or lung? or pulmonar? or respirat\$) adj3 lavage).ti,ab.
38	(BAL or BALF).ti,ab.
39	(nasopharyn\$ adj3 aspirat\$).ti,ab.
40	exp RESPIRATORY FUNCTION TESTS/
41	BREATH TESTS/
42	EXERCISE TEST/
43	((lung? or pulmonar? or respirat\$ or airway?) adj3 function test?).ti,ab.
44	(lung clearance index\$ or forced expiratory volume? or spiromet\$ or spirogra\$ or broncospiro\$ or cardiopulmonary exercise test?).ti,ab.
45	(LCI or FEV or FEV1 or CPEX or CPX or CPET).ti,ab.
46	exp RADIOGRAPHY, THORACIC/
47	exp RESPIRATORY SYSTEM/ra [Radiography]
48	((chest? or thora\$) adj3 (xray or x ray or radiogra\$)).ti,ab.
49	CXR.ti,ab.
50	exp TOMOGRAPHY, X-RAY COMPUTED/
51	(CT scan\$ or CAT scan\$ or xray CT or x ray CT or HRCT).ti,ab.
52	((xray or x ray or comput\$) adj3 tomogra\$).ti,ab.
53	exp MAGNETIC RESONANCE IMAGING/
54	(MRI or NMRI).ti,ab.
55	((magnetic resonance or MR or MTC or MT or NMR or magneti#ation transfer or spin or chemical shift) adj2 (imag\$ or tomogra\$)).ti,ab.
56	or/31-55
57	4 and 15 and 27 and 56
58	4 and 30 and 56
59	*CYSTIC FIBROSIS/ and exp *RESPIRATORY TRACT INFECTIONS/di, mi, ra [Diagnosis, Microbiology, Radiography]
60	*CYSTIC FIBROSIS/ and exp *BACTERIAL INFECTIONS/di, mi, ra [Diagnosis, Microbiology, Radiography]
61	*CYSTIC FIBROSIS/ and exp *PNEUMONIA/di, mi, ra [Diagnosis, Microbiology, Radiography]
62	or/57-61

#	Searches
63	limit 62 to english language
64	LETTER/
65	EDITORIAL/
66	NEWS/
67	exp HISTORICAL ARTICLE/
68	ANECDOTES AS TOPIC/
69	COMMENT/
70	CASE REPORT/
71	(letter or comment*).ti.
72	or/64-71
73	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
74	72 not 73
75	ANIMALS/ not HUMANS/
76	exp ANIMALS, LABORATORY/
77	exp ANIMAL EXPERIMENTATION/
78	exp MODELS, ANIMAL/
79	exp RODENTIA/
80	(rat or rats or mouse or mice).ti.
81	or/74-80
82	63 not 81

- Medline In-Process & Other Non-Indexed Citations

Last searched on **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations** October 31, 2016 on 2<sup>nd</sup> November 2016.

#	Searches
1	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
2	mucov\$.ti,ab.
3	or/1-2
4	((lung? or pulmonar? or respirat\$ or airway?) adj (disease? or dysfunction\$ or obstruct\$ or inflam\$ or infect\$ or pathol\$)).ti.
5	((bacteria\$ or mycobacteria\$) adj infect\$).ti.
6	pneumoni\$.ti.
7	(staphylococcus aureus or s aureus or pseudomonas aeruginosa or p aeruginosa).ti.
8	or/4-7
9	(sensitivity or specificity).ti,ab.
10	((pre test or pretest or post test or posttest) adj probability).ti,ab.
11	(predictive value\$ or PPV or NPV).ti,ab.
12	likelihood ratio\$.ti,ab.
13	(ROC curve\$ or AUC).ti,ab.
14	diagnos\$.ti.
15	(diagnos\$ adj2 (performance\$ or accurac\$ or utilit\$ or value\$ or efficien\$ or effectiveness)).ti,ab.
16	gold standard.ab.
17	or/9-16
18	((lung? or pulmonar? or respirat\$ or airway?) adj3 (disease? or dysfunction\$ or obstruct\$ or inflam\$ or infect\$ or pathol\$ or microbiolog\$ or bacteri\$ or pathogen?) adj3 (monitor\$ or investigat\$ or test\$ or assess\$ or measure\$ or exam\$ or cultur\$ or marker? or onset

#	Searches
	or detect\$ or indicat\$).ti,ab.
19	((cough or throat or pharyn\$ or oral or oropharyn\$ or sputum or airway?) adj3 (swab? or culture\$ or sampl\$)).ti,ab.
20	(sputum adj1 induc\$).ti,ab.
21	(sputum adj2 analys\$).ti,ab.
22	((bronch\$ or lung? or pulmonar? or respirat\$) adj3 lavage).ti,ab.
23	(BAL or BALF).ti,ab.
24	(nasopharyn\$ adj3 aspirat\$).ti,ab.
25	((lung? or pulmonar? or respirat\$ or airway?) adj3 function test?).ti,ab.
26	(lung clearance index\$ or forced expiratory volume? or spiromet\$ or spirogra\$ or broncospiro\$ or cardiopulmonary exercise test?).ti,ab.
27	(LCI or FEV or FEV1 or CPEX or CPX or CPET).ti,ab.
28	((chest? or thora\$) adj3 (xray or x ray or radiogra\$)).ti,ab.
29	CXR.ti,ab.
30	(CT scan\$ or CAT scan\$ or xray CT or x ray CT or HRCT).ti,ab.
31	((xray or x ray or comput\$) adj3 tomogra\$).ti,ab.
32	(MRI or NMRI).ti,ab.
33	((magnetic resonance or MR or MTC or MT or NMR or magneti#ation transfer or spin or chemical shift) adj2 (imag\$ or tomogra\$)).ti,ab.
34	or/19-33
35	3 and 8 and 17 and 34
36	4 and 18 and 34
37	or/35-36

- Database: Cochrane Central Register of Controlled Trials

Last searched on **EBM Reviews - Cochrane Central Register of Controlled Trials**  
September 2016 on 2<sup>nd</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab,kw.
3	mucov\$.ti,ab.
4	or/1-3
5	exp *RESPIRATORY TRACT INFECTIONS/
6	exp *BACTERIAL INFECTIONS/
7	exp *PNEUMONIA/
8	exp *STAPHYLOCOCCUS AUREUS/
9	exp *PSEUDOMONAS AERUGINOSA/
10	exp *LUNG/pa, pp [Pathology, Physiopathology]
11	((lung? or pulmonar? or respirat\$ or airway?) adj2 (disease? or dysfunction\$ or obstruct\$ or inflam\$ or infect\$ or pathol\$)).ti,kw.
12	((bacteria\$ or mycobacteria\$) adj infect\$).ti,kw.
13	pneumoni\$.ti.
14	(staphylococcus aureus or s aureus or pseudomonas aeruginosa or p aeruginosa).ti,kw.
15	or/5-14
16	exp "SENSITIVITY AND SPECIFICITY"/
17	(sensitivity or specificity).ti,ab,kw.
18	((pre test or pretest or post test or posttest) adj probability).ti,ab.

#	Searches
19	(predictive value\$ or PPV or NPV).ti,ab.
20	likelihood ratio\$.ti,ab.
21	LIKELIHOOD FUNCTIONS/ or STATISTICAL MODEL.kw.
22	(ROC curve\$ or AUC).ti,ab.
23	diagnos\$.ti.
24	(diagnos\$ adj2 (performance\$ or accurac\$ or utilit\$ or value\$ or efficien\$ or effectiveness)).ti,ab,kw.
25	gold standard.ab.
26	di.fs.
27	or/16-26
28	*DIAGNOSTIC TECHNIQUES, RESPIRATORY SYSTEM/ or RESPIRATORY TRACT EXAMINATION.kw.
29	((lung? or pulmonar? or respirat\$ or airway?) adj3 (disease? or dysfunction\$ or obstruct\$ or inflam\$ or infect\$ or pathol\$ or microbiolog\$ or bacteri\$ or pathogen?) adj3 (monitor\$ or investigat\$ or test\$ or assess\$ or measure\$ or exam\$ or cultur\$ or marker? or onset or detect\$ or indicat\$)).ti,ab.
30	or/28-29
31	SPUTUM/ or SPUTUM EXAMINATION.kw.
32	((cough or throat or pharyn\$ or oral or oropharyn\$ or sputum or airway?) adj3 (swab? or culture\$ or sampl\$)).ti,ab,kw.
33	(sputum adj1 induc\$.ti,ab.
34	(sputum adj2 analys\$.ti,ab,kw.
35	exp BRONCHOALVEOLAR LAVAGE/
36	BRONCHOSCOPY/ or RESPIRATORY TRACT ASPIRATION PROCEDURE.kw.
37	((bronch\$ or lung? or pulmonar? or respirat\$) adj3 lavage).ti,ab,kw.
38	(BAL or BALF).ti,ab.
39	(nasopharyn\$ adj3 aspirat\$.ti,ab.
40	exp RESPIRATORY FUNCTION TESTS/ or RESPIRATORY TRACT PARAMETERS.kw.
41	BREATH TESTS/ or BREATH ANALYSIS.kw.
42	EXERCISE TEST/
43	((lung? or pulmonar? or respirat\$ or airway?) adj3 function test?).ti,ab,kw.
44	(lung clearance index\$ or forced expiratory volume? or spiromet\$ or spirogra\$ or broncospiro\$ or cardiopulmonary exercise test?).ti,ab,kw.
45	(LCI or FEV or FEV1 or CPEX or CPX or CPET).ti,ab.
46	exp RADIOGRAPHY, THORACIC/
47	exp RESPIRATORY SYSTEM/ra [Radiography]
48	((chest? or thora\$) adj3 (xray or x ray or radiogra\$)).ti,ab,kw.
49	CXR.ti,ab.
50	exp TOMOGRAPHY, X-RAY COMPUTED/
51	(CT scan\$ or CAT scan\$ or xray CT or x ray CT or HRCT).ti,ab.
52	((xray or x ray or comput\$) adj3 tomogra\$).ti,ab,kw.
53	exp MAGNETIC RESONANCE IMAGING/
54	(MRI or NMRI).ti,ab.
55	((magnetic resonance or MR or MTC or MT or NMR or magneti#ation transfer or spin or chemical shift) adj2 (imag\$ or tomogra\$)).ti,ab,kw.
56	or/31-55
57	4 and 15 and 27 and 56

#	Searches
58	4 and 30 and 56
59	CYSTIC FIBROSIS/ and exp RESPIRATORY TRACT INFECTIONS/di, mi, ra [Diagnosis, Microbiology, Radiography]
60	CYSTIC FIBROSIS/ and exp BACTERIAL INFECTIONS/di, mi, ra [Diagnosis, Microbiology, Radiography]
61	CYSTIC FIBROSIS/ and exp PNEUMONIA/di, mi, ra [Diagnosis, Microbiology, Radiography]
62	or/57-61

- Database: Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects

Last searched on **EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to October 26, 2016, **EBM Reviews - Database of Abstracts of Reviews of Effects** 1st Quarter 2015 on 2<sup>nd</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS.kw.
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).tw,tx.
3	mucov\$.tw,tx.
4	or/1-3
5	RESPIRATORY TRACT INFECTIONS.kw.
6	BACTERIAL INFECTIONS.kw.
7	PNEUMONIA.kw.
8	STAPHYLOCOCCUS AUREUS.kw.
9	PSEUDOMONAS AERUGINOSA.kw.
10	LUNG?.kw.
11	((lung? or pulmonar? or respirat\$ or airway?) adj (disease? or dysfunction\$ or obstruct\$ or inflam\$ or infect\$ or pathol\$)).ti.
12	((bacteria\$ or mycobacteria\$) adj infect\$).ti.
13	pneumoni\$.ti.
14	(staphylococcus aureus or s aureus or pseudomonas aeruginosa or p aeruginosa).ti.
15	or/5-14
16	"SENSITIVITY AND SPECIFICITY".kw.
17	(sensitivity or specificity).tw,tx.
18	((pre test or pretest or post test or posttest) adj probability).tw,tx.
19	(predictive value\$ or PPV or NPV).tw,tx.
20	likelihood ratio\$.tw,tx.
21	LIKELIHOOD FUNCTIONS.kw.
22	(ROC curve\$ or AUC).tw,tx.
23	diagnos\$.ti.
24	(diagnos\$ adj2 (performance\$ or accurac\$ or utilit\$ or value\$ or efficien\$ or effectiveness)).tw,tx.
25	gold standard.tw,tx.
26	or/16-25
27	DIAGNOSTIC TECHNIQUES, RESPIRATORY SYSTEM.kw.
28	((lung? or pulmonar? or respirat\$ or airway?) adj3 (disease? or dysfunction\$ or obstruct\$ or inflam\$ or infect\$ or pathol\$ or microbiolog\$ or bacteri\$ or pathogen?) adj3 (monitor\$ or investigat\$ or test\$ or assess\$ or measure\$ or exam\$ or cultur\$ or marker? or onset or detect\$ or indicat\$)).tw,tx.

#	Searches
29	or/27-28
30	SPUTUM.kw.
31	((cough or throat or pharyn\$ or oral or oropharyn\$ or sputum or airway?) adj3 (swab? or culture\$ or sampl\$)).tw,tx.
32	(sputum adj1 induc\$).tw,tx.
33	(sputum adj2 analys\$).tw,tx.
34	BRONCHOALVEOLAR LAVAGE.kw.
35	BRONCHOSCOPY.kw.
36	((bronch\$ or lung? or pulmonar? or respirat\$) adj3 lavage).tw,tx.
37	(BAL or BALF).tw,tx.
38	(nasopharyn\$ adj3 aspirat\$).tw,tx.
39	RESPIRATORY FUNCTION TESTS.kw.
40	BREATH TESTS.kw.
41	EXERCISE TEST.kw.
42	((lung? or pulmonar? or respirat\$ or airway?) adj3 function test?).tw,tx.
43	(lung clearance index\$ or forced expiratory volume? or spiromet\$ or spirogra\$ or broncospiro\$ or cardiopulmonary exercise test?).tw,tx.
44	(LCI or FEV or FEV1 or CPEX or CPX or CPET).tw,tx.
45	RADIOGRAPHY, THORACIC.kw.
46	((chest? or thora\$) adj3 (xray or x ray or radiogra\$)).tw,tx.
47	CXR.tw,tx.
48	TOMOGRAPHY, X-RAY COMPUTED.kw.
49	(CT scan\$ or CAT scan\$ or xray CT or x ray CT or HRCT).tw,tx.
50	((xray or x ray or comput\$) adj3 tomogra\$).tw,tx.
51	MAGNETIC RESONANCE IMAGING.kw.
52	(MRI or NMRI).tw,tx.
53	((magnetic resonance or MR or MTC or MT or NMR or magneti#ation transfer or spin or chemical shift) adj2 (imag\$ or tomogra\$)).tw,tx.
54	or/30-53
55	4 and 15 and 26 and 54
56	4 and 29 and 54
57	or/55-56

- Database: Health Technology Assessment

Last searched on **EBM Reviews - Health Technology Assessment 3<sup>rd</sup> Quarter 2016** on 2<sup>nd</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).tw.
3	mucov\$.tw.
4	or/1-3
5	exp *RESPIRATORY TRACT INFECTIONS/
6	exp *BACTERIAL INFECTIONS/
7	exp *PNEUMONIA/
8	exp *STAPHYLOCOCCUS AUREUS/
9	exp *PSEUDOMONAS AERUGINOSA/
10	exp *LUNG/pa, pp [Pathology, Physiopathology]

#	Searches
11	((lung? or pulmonar? or respirat\$ or airway?) adj (disease? or dysfunction\$ or obstruct\$ or inflam\$ or infect\$ or pathol\$)).ti.
12	((bacteria\$ or mycobacteria\$) adj infect\$).ti.
13	pneumoni\$.ti.
14	(staphylococcus aureus or s aureus or pseudomonas aeruginosa or p aeruginosa).ti.
15	or/5-14
16	exp "SENSITIVITY AND SPECIFICITY"/
17	(sensitivity or specificity).tw.
18	((pre test or pretest or post test or posttest) adj probability).tw.
19	(predictive value\$ or PPV or NPV).tw.
20	likelihood ratio\$.tw.
21	LIKELIHOOD FUNCTIONS/
22	(ROC curve\$ or AUC).tw.
23	diagnos\$.tw.
24	(diagnos\$ adj2 (performance\$ or accurac\$ or utilit\$ or value\$ or efficien\$ or effectiveness)).tw.
25	gold standard.tw.
26	di.fs.
27	or/16-26
28	*DIAGNOSTIC TECHNIQUES, RESPIRATORY SYSTEM/
29	((lung? or pulmonar? or respirat\$ or airway?) adj3 (disease? or dysfunction\$ or obstruct\$ or inflam\$ or infect\$ or pathol\$ or microbiolog\$ or bacteri\$ or pathogen?) adj3 (monitor\$ or investigat\$ or test\$ or assess\$ or measure\$ or exam\$ or cultur\$ or marker? or onset or detect\$ or indicat\$)).tw.
30	or/28-29
31	SPUTUM/
32	((cough or throat or pharyn\$ or oral or oropharyn\$ or sputum or airway?) adj3 (swab? or culture\$ or sampl\$)).tw.
33	(sputum adj1 induc\$).tw.
34	(sputum adj2 analys\$).tw.
35	exp BRONCHOALVEOLAR LAVAGE/
36	BRONCHOSCOPY/
37	((bronch\$ or lung? or pulmonar? or respirat\$) adj3 lavage).tw.
38	(BAL or BALF).tw.
39	(nasopharyn\$ adj3 aspirat\$).tw.
40	exp RESPIRATORY FUNCTION TESTS/
41	BREATH TESTS/
42	EXERCISE TEST/
43	((lung? or pulmonar? or respirat\$ or airway?) adj3 function test?).tw.
44	(lung clearance index\$ or forced expiratory volume? or spiromet\$ or spirogra\$ or broncospiro\$ or cardiopulmonary exercise test?).tw.
45	(LCI or FEV or FEV1 or CPEX or CPX or CPET).tw.
46	exp RADIOGRAPHY, THORACIC/
47	exp RESPIRATORY SYSTEM/ra [Radiography]
48	((chest? or thora\$) adj3 (xray or x ray or radiogra\$)).tw.
49	CXR.tw.
50	exp TOMOGRAPHY, X-RAY COMPUTED/

#	Searches
51	(CT scan\$ or CAT scan\$ or xray CT or x ray CT or HRCT).tw.
52	((xray or x ray or comput\$) adj3 tomogra\$).tw.
53	exp MAGNETIC RESONANCE IMAGING/
54	(MRI or NMRI).tw.
55	((magnetic resonance or MR or MTC or MT or NMR or magneti#ation transfer or spin or chemical shift) adj2 (imag\$ or tomogra\$)).tw.
56	or/31-55
57	4 and 15 and 27 and 56
58	4 and 30 and 56

- Database: Embase

Last searched on **Embase** 1974 to 2016 Week 44 on 2<sup>nd</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	exp *LUNG DISEASE/
6	exp *RESPIRATORY TRACT INFLAMMATION/
7	exp *RESPIRATORY TRACT INFECTION/
8	exp *BACTERIAL INFECTION/
9	exp *STAPHYLOCOCCUS AUREUS/
10	exp *PSEUDOMONAS AERUGINOSA/
11	((lung? or pulmonar? or respirat\$ or airway?) adj (disease? or dysfunction\$ or obstruct\$ or inflam\$ or infect\$ or pathol\$)).ti.
12	((bacteri\$ or mycobacteria\$) adj infect\$).ti.
13	pneumoni\$.ti.
14	(staphylococcus aureus or s aureus or pseudomonas aeruginosa or p aeruginosa).ti.
15	or/5-14
16	"SENSITIVITY AND SPECIFICITY"/
17	(sensitivity or specificity).ti,ab.
18	((pre test or pretest or post test or posttest) adj probability).ti,ab.
19	(predictive value\$ or PPV or NPV).ti,ab.
20	likelihood ratio\$.ti,ab.
21	STATISTICAL MODEL/
22	(ROC curve\$ or AUC).ti,ab.
23	diagnos\$.ti.
24	(diagnos\$ adj2 (performance\$ or accurac\$ or utilit\$ or value\$ or efficien\$ or effectiveness)).ti,ab.
25	gold standard.ab.
26	*DIAGNOSTIC ACCURACY/ or DIAGNOSTIC TEST ACCURACY STUDY/
27	di.fs.
28	or/16-27
29	*RESPIRATORY TRACT EXAMINATION/
30	((lung? or pulmonar? or respirat\$ or airway?) adj3 (disease? or dysfunction\$ or obstruct\$ or inflam\$ or infect\$ or pathol\$ or microbiolog\$ or bacteri\$ or pathogen?) adj3 (monitor\$ or investigat\$ or test\$ or assess\$ or measure\$ or exam\$ or cultur\$ or marker? or onset

#	Searches
	or detect\$ or indicat\$)).ti,ab.
31	or/29-30
32	exp SPUTUM EXAMINATION/
33	((cough or throat or pharyn\$ or oral or oropharyn\$ or sputum or airway?) adj3 (swab? or culture\$ or sampl\$)).ti,ab.
34	(sputum adj1 induc\$).ti,ab.
35	(sputum adj2 analys\$).ti,ab.
36	LUNG LAVAGE/
37	exp RESPIRATORY TRACT ASPIRATION PROCEDURE/
38	((bronch\$ or lung? or pulmonar? or respirat\$) adj3 lavage).ti,ab.
39	(BAL or BALF).ti,ab.
40	(nasopharyn\$ adj3 aspirat\$).ti,ab.
41	exp LUNG FUNCTION TEST/
42	exp RESPIRATORY TRACT PARAMETERS/
43	exp BREATH ANALYSIS/
44	((lung? or pulmonar? or respirat\$ or airway?) adj3 function test?).ti,ab.
45	(lung clearance index\$ or forced expiratory volume? or spiromet\$ or spirogra\$ or broncospiro\$ or cardiopulmonary exercise test?).ti,ab.
46	(LCI or FEV or FEV1 or CPEX or CPX or CPET).ti,ab.
47	THORAX RADIOGRAPHY/
48	((chest? or thora\$) adj3 (xray or x ray or radiogra\$)).ti,ab.
49	CXR.ti,ab.
50	exp COMPUTER ASSISTED TOMOGRAPHY/
51	(CT scan\$ or CAT scan\$ or xray CT or x ray CT or HRCT).ti,ab.
52	((xray or x ray or comput\$) adj3 tomogra\$).ti,ab.
53	exp NUCLEAR MAGNETIC RESONANCE IMAGING/
54	(MRI or NMRI).ti,ab.
55	((magnetic resonance or MR or MTC or MT or NMR or magneti#ation transfer or spin or chemical shift) adj2 (imag\$ or tomogra\$)).ti,ab.
56	or/32-55
57	and/4,15,28,56
58	and/4,31,56
59	*CYSTIC FIBROSIS/ and exp *LUNG DISEASE/di [Diagnosis]
60	*CYSTIC FIBROSIS/ and exp *RESPIRATORY TRACT INFLAMMATION/di [Diagnosis]
61	*CYSTIC FIBROSIS/ and exp *RESPIRATORY TRACT INFECTION/di [Diagnosis]
62	*CYSTIC FIBROSIS/ and exp *BACTERIAL INFECTION/di [Diagnosis]
63	or/57-62
64	limit 63 to english language
65	letter.pt. or LETTER/
66	note.pt.
67	editorial.pt.
68	CASE REPORT/ or CASE STUDY/
69	(letter or comment*).ti.
70	or/65-69
71	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
72	70 not 71

#	Searches
73	ANIMAL/ not HUMAN/
74	NONHUMAN/
75	exp ANIMAL EXPERIMENT/
76	exp EXPERIMENTAL ANIMAL/
77	ANIMAL MODEL/
78	exp RODENT/
79	(rat or rats or mouse or mice).ti.
80	or/72-79
81	64 not 80

## E.7 What is the effectiveness of airway clearance techniques [chest physiotherapy] in people with cystic fibrosis?

### E.7.1 Database: Medline

Last searched on **Ovid MEDLINE(R)** 1946 to December Week 1 2016 on 5<sup>th</sup> January 2017.

#	Searches
1	META-ANALYSIS/
2	META-ANALYSIS AS TOPIC/
3	(meta analy* or metanaly* or metaanaly*).ti,ab.
4	((systematic* or evidence*) adj2 (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	or/1-9
11	randomized controlled trial.pt.
12	controlled clinical trial.pt.
13	pragmatic clinical trial.pt.
14	randomi#ed.ab.
15	placebo.ab.
16	randomly.ab.
17	CLINICAL TRIALS AS TOPIC/
18	trial.ti.
19	or/11-18
20	or/10,19
21	CYSTIC FIBROSIS/
22	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
23	mucov\$.ti,ab.
24	or/21-23
25	exp PHYSICAL THERAPY MODALITIES/ or exp AIRWAY MANAGEMENT/ or exp AIRWAY OBSTRUCTION/th [Therapy]
26	((physiotherap\$ or physical therap\$ or massage therap\$) adj3 (chest\$ or thora\$)).ti,ab.

#	Searches
27	((mucoc\$ or mucus or airway\$) adj3 clear\$).ti,ab.
28	exp DRAINAGE, POSTURAL/
29	exp PERCUSSION/
30	exp COUGH/
31	(chest adj3 (shak\$ or percussion or clap\$)).ti,ab.
32	(huff\$ or percussion or cough\$).ti,ab.
33	(postur\$ adj2 drain\$).ti,ab.
34	exp POSITIVE-PRESSURE RESPIRATION/
35	(positive expiratory pressure or PEP or hPEP).ti,ab.
36	exp RESPIRATORY THERAPY/ or exp BREATHING EXERCISES/
37	(forced adj2 expirat\$ adj2 technique\$).ti,ab.
38	(ACBT or FET or clap\$).ti,ab.
39	((breath\$ or thora\$ or relax\$ or respirat\$ or inhal\$) adj3 (exercis\$ or technique\$ or control\$ or therap\$)).ti,ab.
40	autogenic drainage.ti,ab.
41	exp CHEST WALL OSCILLATION/ or exp HIGH-FREQUENCY VENTILATION/ or exp MUCOCILIARY CLEARANCE/
42	(oscillat\$ or vest\$ or HFCWO or acapella or flutter or cornet).ti,ab.
43	exp NONINVASIVE VENTILATION/
44	((non-invasive or noninvasive) adj2 ventilat\$).ti,ab.
45	or/25-44
46	and/20,24,45
47	limit 46 to english language
48	LETTER/
49	EDITORIAL/
50	NEWS/
51	exp HISTORICAL ARTICLE/
52	ANECDOTES AS TOPIC/
53	COMMENT/
54	CASE REPORT/
55	(letter or comment*).ti.
56	or/48-55
57	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
58	56 not 57
59	ANIMALS/ not HUMANS/
60	exp ANIMALS, LABORATORY/
61	exp ANIMAL EXPERIMENTATION/
62	exp MODELS, ANIMAL/
63	exp RODENTIA/
64	(rat or rats or mouse or mice).ti.
65	or/58-64
66	47 not 65

## E.7.2 Medline In-Process & Other Non-Indexed Citations

Last searched on **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations** January 04, 2017 on 5<sup>th</sup> January 2017.

#	Searches
1	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
2	mucov\$.ti,ab.
3	1 or 2
4	((physiotherap\$ or physical therap\$ or massage therap\$) adj3 (chest\$ or thora\$)).ti,ab.
5	((mucoc\$ or mucus or airway\$) adj3 clear\$).ti,ab.
6	(chest adj3 (shak\$ or percussion or clap\$)).ti,ab.
7	(huff\$ or percussion or cough\$).ti,ab.
8	(postur\$ adj2 drain\$).ti,ab.
9	(positive expiratory pressure or PEP or hPEP).ti,ab.
10	(forced adj2 expirat\$ adj2 technique\$).ti,ab.
11	(ACBT or FET or clap\$).ti,ab.
12	((breath\$ or thora\$ or relax\$ or respirat\$ or inhal\$) adj3 (exercis\$ or technique\$ or control\$ or therap\$)).ti,ab.
13	autogenic drainage.ti,ab.
14	(oscillat\$ or vest\$ or HFCWO or acapella or flutter or cornet).ti,ab.
15	((non-invasive or noninvasive) adj2 ventilat\$).ti,ab.
16	or/4-15
17	3 and 16
18	limit 17 to english language

### E.7.3 Database: Cochrane Central Register of Controlled Trials

Last searched on **EBM Reviews - Cochrane Central Register of Controlled Trials**  
November 2016 on 5<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab,kw.
3	mucov\$.ti,ab.
4	or/1-3
5	PHYSICAL THERAPY MODALITIES/ or AIRWAY MANAGEMENT/
6	(PHYSIOTHERAPY or BREATHING EXERCISE or LUNG CLEARANCE).kw.
7	exp AIRWAY OBSTRUCTION/th [Therapy]
8	((physiotherap\$ or physical therap\$ or massage therap\$) adj3 (chest\$ or thora\$)).ti,ab.
9	((mucoc\$ or mucus or airway\$) adj3 clear\$).ti,ab.
10	DRAINAGE, POSTURAL/ or POSTURAL DRAINAGE.kw.
11	PERCUSSION.sh,kw.
12	COUGH/ or COUGHING.kw.
13	(chest adj3 (shak\$ or percussion or clap\$)).ti,ab.
14	(huff\$ or percussion or cough\$).ti,ab.
15	(postur\$ adj2 drain\$).ti,ab.
16	POSITIVE-PRESSURE RESPIRATION/ or POSITIVE END EXPIRATORY PRESSURE.kw.
17	(positive expiratory pressure or PEP or hPEP).ti,ab.
18	RESPIRATORY THERAPY/ or BREATHING EXERCISES/
19	(RESPIRATION CONTROL or RELAXATION TRAINING).kw.
20	FORCED EXPIRATION.kw.
21	(forced adj2 expirat\$ adj2 technique\$).ti,ab.

#	Searches
22	(ACBT or FET or clap\$).ti,ab.
23	((breath\$ or thora\$ or relax\$ or respirat\$ or inhal\$) adj3 (exercis\$ or technique\$ or control\$ or therap\$)).ti,ab.
24	autogenic drainage.ti,ab.
25	CHEST WALL OSCILLATION/ or HIGH-FREQUENCY VENTILATION/ or MUCOCILIARY CLEARANCE/
26	(OSCILLATION or CHEST WALL OSCILLATION or HIGH FREQUENCY VENTILATION).kw.
27	(oscillat\$ or vest\$ or HFCWO or acapella or flutter or cornet).ti,ab.
28	NONINVASIVE VENTILATION.sh,kw.
29	((non-invasive or noninvasive) adj2 ventilat\$).ti,ab.
30	or/5-29
31	4 and 30

#### E.7.4 Database: Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects

Last searched on **EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to December 30, 2016, **EBM Reviews - Database of Abstracts of Reviews of Effects** 1st Quarter 2015 5<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS.kw.
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,tw,tx.
3	mucov\$.ti,tw,tx.
4	or/1-3
5	(PHYSICAL THERAPY MODALITIES or PHYSIOTHERAPY or BREATHING EXERCISE or AIRWAY MANAGEMENT or AIRWAY OBSTRUCTION or LUNG CLEARANCE).kw.
6	((physiotherap\$ or physical therap\$ or massage therap\$) adj3 (chest\$ or thora\$)).ti,tw,tx.
7	((mucoc\$ or mucus or airway\$) adj3 clear\$).ti,tw,tx.
8	(DRAINAGE, POSTURAL or POSTURAL DRAINAGE or PERCUSSION or COUGH or COUGHING).kw.
9	(chest adj3 (shak\$ or percussion or clap\$)).ti,tw,tx.
10	(huff\$ or percussion or cough\$).ti,tw,tx.
11	(postur\$ adj2 drain\$).ti,tw,tx.
12	(POSITIVE-PRESSURE RESPIRATION or POSITIVE END EXPIRATORY PRESSURE).kw.
13	(positive expiratory pressure or PEP or hPEP).ti,tw,tx.
14	(RESPIRATORY THERAPY or BREATHING EXERCISES or RESPIRATION CONTROL or RELAXATION TRAINING or FORCED EXPIRATION).kw.
15	(forced adj2 expirat\$ adj2 technique\$).ti,tw,tx.
16	(ACBT or FET or clap\$).ti,tw,tx.
17	((breath\$ or thora\$ or relax\$ or respirat\$ or inhal\$) adj3 (exercis\$ or technique\$ or control\$ or therap\$)).ti,tw,tx.
18	autogenic drainage.ti,tw,tx.
19	(CHEST WALL OSCILLATION or HIGH-FREQUENCY VENTILATION or HIGH FREQUENCY VENTILATION or MUCOCILIARY CLEARANCE or OSCILLATION).kw.
20	(oscillat\$ or vest\$ or HFCWO or acapella or flutter or cornet).ti,tw,tx.
21	NONINVASIVE VENTILATION.kw.
22	((non-invasive or noninvasive) adj2 ventilat\$).ti,tw,tx.

#	Searches
23	or/5-22
24	4 and 23

### E.7.5 Database: Health Technology Assessment

Last searched on **EBM Reviews - Health Technology Assessment 4th Quarter 2016** on 5<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,tw.
3	mucov\$.ti,tw.
4	or/1-3
5	exp PHYSICAL THERAPY MODALITIES/ or exp AIRWAY OBSTRUCTION/th [Therapy]
6	((physiotherap\$ or physical therap\$ or massage therap\$) adj3 (chest\$ or thora\$)).ti,tw.
7	((mucoc\$ or mucus or airway\$) adj3 clear\$).ti,tw.
8	exp DRAINAGE, POSTURAL/
9	exp PERCUSSION/
10	exp COUGH/
11	(chest adj3 (shak\$ or percussion or clap\$)).ti,tw.
12	(huff\$ or percussion or cough\$).ti,tw.
13	(postur\$ adj2 drain\$).ti,tw.
14	exp POSITIVE-PRESSURE RESPIRATION/
15	(positive expiratory pressure or PEP or hPEP).ti,tw.
16	exp RESPIRATORY THERAPY/ or exp BREATHING EXERCISES/
17	(forced adj2 expirat\$ adj2 technique\$).ti,tw.
18	(ACBT or FET or clap\$).ti,tw.
19	((breath\$ or thora\$ or relax\$ or respirat\$ or inhal\$) adj3 (exercis\$ or technique\$ or control\$ or therap\$)).ti,tw.
20	autogenic drainage.ti,tw.
21	exp CHEST WALL OSCILLATION/ or exp HIGH-FREQUENCY VENTILATION/ or exp MUCOCILIARY CLEARANCE/
22	(oscillat\$ or vest\$ or HFCWO or acapella or flutter or cornet).ti,tw.
23	exp RESPIRATORY INSUFFICIENCY/
24	((non-invasive or noninvasive) adj2 ventilat\$).ti,tw.
25	or/5-23
26	4 and 25

### E.7.6 Database: Embase

Last searched on **Embase** 1974 to 2017 Week 01 on 4<sup>th</sup> January.

#	Searches
1	SYSTEMATIC REVIEW/
2	META-ANALYSIS/
3	(meta analy* or metanaly* or metaanaly*).ti,ab.
4	((systematic or evidence) adj2 (review* or overview*)).ti,ab.
5	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.

#	Searches
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	((pool* or combined) adj2 (data or trials or studies or results)).ab.
10	cochrane.jw.
11	or/1-10
12	random*.ti,ab.
13	factorial*.ti,ab.
14	(crossover* or cross over*).ti,ab.
15	((doubl* or singl*) adj blind*).ti,ab.
16	(assign* or allocat* or volunteer* or placebo*).ti,ab.
17	CROSSOVER PROCEDURE/
18	SINGLE BLIND PROCEDURE/
19	RANDOMIZED CONTROLLED TRIAL/
20	DOUBLE BLIND PROCEDURE/
21	or/12-20
22	or/11,21
23	exp CYSTIC FIBROSIS/
24	mucov\$.ti,ab.
25	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
26	or/23-25
27	exp PHYSIOTHERAPY/ or exp LUNG CLEARANCE/
28	exp BREATHING EXERCISE/
29	((physiotherap\$ or physical therap\$ or massage therap\$) adj3 (chest\$ or thora\$)).ti,ab.
30	((mucoc\$ or mucus or airway\$) adj3 clear\$).ti,ab.
31	exp POSTURAL DRAINAGE/
32	exp PERCUSSION/
33	exp COUGHING/
34	(chest adj3 (shak\$ or percussion or clap\$)).ti,ab.
35	(huff\$ or percussion or cough\$).ti,ab.
36	(postur\$ adj2 drain\$).ti,ab.
37	exp POSITIVE END EXPIRATORY PRESSURE/
38	exp RESPIRATION CONTROL/ or exp RELAXATION TRAINING/
39	exp FORCED EXPIRATION/
40	(positive expiratory pressure or PEP or hPEP).ti,ab.
41	(forced adj2 expirat\$ adj2 technique\$).ti,ab.
42	(ACBT or FET or clap\$).ti,ab.
43	((breath\$ or thora\$ or relax\$ or respirat\$ or inhal\$) adj3 (exercis\$ or technique\$ or control\$ or therap\$)).ti,ab.
44	autogenic drainage.ti,ab.
45	exp OSCILLATION/ or exp CHEST WALL OSCILLATION/
46	exp HIGH FREQUENCY VENTILATION/
47	(oscillat\$ or vest\$ or HFCWO or acapella or flutter or cornet).ti,ab.
48	exp NONINVASIVE VENTILATION/

#	Searches
49	((non-invasive or noninvasive) adj2 ventilat\$).ti,ab.
50	or/27-49
51	and/22,26,50
52	limit 51 to english language
53	letter.pt. or LETTER/
54	note.pt.
55	editorial.pt.
56	CASE REPORT/ or CASE STUDY/
57	(letter or comment*).ti.
58	or/53-57
59	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
60	58 not 59
61	ANIMAL/ not HUMAN/
62	NONHUMAN/
63	exp ANIMAL EXPERIMENT/
64	exp EXPERIMENTAL ANIMAL/
65	ANIMAL MODEL/
66	exp RODENT/
67	(rat or rats or mouse or mice).ti.
68	or/60-67
69	52 not 68

### E.7.7 Database: PEDro

Last searched on PEDro 11<sup>th</sup> January 2017.

#	Searches
1	In Title and Abstract box – cystic fibrosis
2	In Therapy box – selected respiratory therapy
3	In Body Part box – selected chest
5	Chose - Match all search terms (AND)
6	Did not limit by year, method or score. Imported all results.
7	In Title and Abstract box – cystic fibrosis

### E.7.8 Database: CINAHL

Last searched on CINAHL 1981 to present on 11<sup>th</sup> January 2017.

#	Query
S39	S5 and S38
S38	S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30 or S31 or S32 or S33 or S34 or S35 or S36 or S37
S37	AB ((non-invasive or noninvasive) N2 ventilat*)
S36	TI ((non-invasive or noninvasive) N2 ventilat*)
S35	MH NONINVASIVE PROCEDURES
S34	AB (oscillat* or vest* or HFCWO or acapella or flutter or cornet)
S33	TI (oscillat* or vest* or HFCWO or acapella or flutter or cornet)
S32	MH MUCOCILIARY CLEARANCE

#	Query
S31	MH VENTILATION, HIGH FREQUENCY
S30	MH CHEST PHYSICAL THERAPY
S29	TI autogenic drainage or((mucoc* or mucus or airway*) N3 clear*) OR AB autogenic drainage or((mucoc* or mucus or airway*) N3 clear*)
S28	AB ((breath* or thora* or relax* or respirat* or inhal*) N3 (exercis* or technique* or control* or therap*))
S27	TI ((breath* or thora* or relax* or respirat* or inhal*) N3 (exercis* or technique* or control* or therap*))
S26	AB (ACBT or FET or clap*)
S25	TI (ACBT or FET or clap*)
S24	AB (forced N2 expirat* N2 technique*)
S23	TI (forced N2 expirat* N2 technique*)
S22	MH BREATHING EXERCISES
S21	MH RESPIRATORY THERAPY
S20	AB (positive expiratory pressure or PEP or hPEP)
S19	TI (positive expiratory pressure or PEP or hPEP)
S18	MH POSITIVE PRESSURE VENTILATION
S17	AB (postur* N2 drain*)
S16	TI (postur* N2 drain*)
S15	AB (huff* or percussion or cough*)
S14	TI (huff* or percussion or cough*)
S13	AB (chest N3 (shak* or percussion or clap*))
S12	TI (chest N3 (shak* or percussion or clap*))
S11	MH COUGH
S10	MH PERCUSSION
S9	MH DRAINAGE, POSTURAL
S8	AB ((physiotherap* or physical therap* or massage therap*) N3 (chest* or thora*))
S7	TI ((physiotherap* or physical therap* or massage therap*) N3 (chest* or thora*))
S6	MH (PHYSICAL THERAPY or AIRWAY MANAGEMENT or AIRWAY OBSTRUCTION+/TH)
S5	S1 or S2 or S3 or S4
S4	TI mucov* OR AB mucov*
S3	AB ((cystic or pancrea*) N2 (fibrosis or fibrocystic))
S2	TI ((cystic or pancrea*) N2 (fibrosis or fibrocystic))
S1	MH CYSTIC FIBROSIS

### E.7.9 Database: AMED

Last searched on AMED 1985 to December 2016 on 11<sup>th</sup> January 2017.

#	Searches
1	cystic fibrosis/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	exp physical therapy modalities/
6	airway obstruction/
7	((physiotherap\$ or physical therap\$ or massage therap\$) adj3 (chest\$ or thora\$)).ti,ab.

#	Searches
8	((mucoc\$ or mucus or airway\$) adj3 clear\$).ti,ab.
9	drainage postural/
10	cough/
11	(chest adj3 (shak\$ or percussion or clap\$)).ti,ab.
12	(huff\$ or percussion or cough\$).ti,ab.
13	(postur\$ adj2 drain\$).ti,ab.
14	exp positive pressure respiration/
15	(positive expiratory pressure or PEP or hPEP).ti,ab.
16	exp respiratory therapy/
17	exp breathing exercises/
18	(forced adj2 expirat\$ adj2 technique\$).ti,ab.
19	(ACBT or FET or clap\$).ti,ab.
20	((breath\$ or thora\$ or relax\$ or respirat\$ or inhal\$) adj3 (exercis\$ or technique\$ or control\$ or therap\$)).ti,ab.
21	autogenic drainage.ti,ab.
22	mucociliary clearance/
23	(oscillat\$ or vest\$ or HFCWO or acapella or flutter or cornet).ti,ab.
24	((non-invasive or noninvasive) adj2 ventilat\$).ti,ab.
25	or/5-24
26	4 and 25
27	limit 26 to english language

## E.8 What is the effectiveness of mucoactive or mucolytic agents, including rhDNase, nebulised saline (isotonic and hypertonic) and mannitol?

### E.8.1 Database: Medline

Last searched on **Ovid MEDLINE(R)** 1946 to December Week 1 2016 on 5<sup>th</sup> January 2017.

#	Searches
1	META-ANALYSIS/
2	META-ANALYSIS AS TOPIC/
3	(meta analy* or metanaly* or metaanaly*).ti,ab.
4	((systematic* or evidence*) adj2 (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	or/1-9
11	randomized controlled trial.pt.
12	controlled clinical trial.pt.

#	Searches
13	pragmatic clinical trial.pt.
14	randomi#ed.ab.
15	placebo.ab.
16	randomly.ab.
17	CLINICAL TRIALS AS TOPIC/
18	trial.ti.
19	or/11-18
20	or/10,19
21	CYSTIC FIBROSIS/
22	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
23	mucov\$.ti,ab.
24	or/21-23
25	exp EXPECTORANTS/
26	ACETYLCYSTEINE/
27	CARBOCYSTEINE/
28	DEOXYRIBONUCLEASE I/
29	SALINE SOLUTION, HYPERTONIC/
30	SODIUM CHLORIDE/
31	ISOTONIC SOLUTIONS/
32	exp MANNITOL/
33	(mucoactive? or mucolytic? or expectorant? or mucokinetic? or mucoregulator? or thiol?).mp.
34	(acetylc#steine or nacetylc#steine or carboc#steine or dornase alfa or rhDNase or recombinant human deoxyribonuclease or recombinant human DNase or saline or sodium chloride or mannitol).mp.
35	or/25-34
36	and/24,35
37	limit 36 to english language
38	LETTER/
39	EDITORIAL/
40	NEWS/
41	exp HISTORICAL ARTICLE/
42	ANECDOTES AS TOPIC/
43	COMMENT/
44	CASE REPORT/
45	(letter or comment*).ti.
46	or/38-45
47	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
48	46 not 47
49	ANIMALS/ not HUMANS/
50	exp ANIMALS, LABORATORY/
51	exp ANIMAL EXPERIMENTATION/
52	exp MODELS, ANIMAL/
53	exp RODENTIA/
54	(rat or rats or mouse or mice).ti.
55	or/48-54

#	Searches
56	37 not 55
57	and/20,56

### E.8.2 Medline In-Process & Other Non-Indexed Citations

Last searched on **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations** January 04, 2017 on 5<sup>th</sup> January 2017.

#	Searches
1	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
2	mucov\$.ti,ab.
3	or/1-2
4	(mucoactive? or mucolytic? or expectorant? or mucokinetic? or mucoregulator? or thiol?).mp.
5	(acetyl#steine or nacylc#steine or carboc#steine or dornase alfa or rhDNase or recombinant human deoxyribonuclease or recombinant human DNase or saline or sodium chloride or mannitol).mp.
6	or/4-5
7	and/3,6

### E.8.3 Database: Cochrane Central Register of Controlled Trials

Last searched on **EBM Reviews - Cochrane Central Register of Controlled Trials** November 2016 on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab,kw.
3	mucov\$.ti,ab.
4	or/1-3
5	exp EXPECTORANTS/
6	ACETYLCYSTEINE/
7	CARBOCYSTEINE/
8	DEOXYRIBONUCLEASE I/
9	SALINE SOLUTION, HYPERTONIC/
10	SODIUM CHLORIDE/
11	ISOTONIC SOLUTIONS/
12	exp MANNITOL/
13	(mucoactive? or mucolytic? or expectorant? or mucokinetic? or mucoregulator? or thiol?).mp.
14	(acetyl#steine or nacylc#steine or carboc#steine or dornase alfa or rhDNase or recombinant human deoxyribonuclease or recombinant human DNase or saline or sodium chloride or mannitol).mp.
15	or/5-14
16	and/4,15

### E.8.4 Database: Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects

Last searched on **EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to January 05, 2017, **EBM Reviews - Database of Abstracts of Reviews of Effects** 1st Quarter 2015 on 10<sup>th</sup> January 2017.

#	Searches
1	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).tw,tx,kw.
2	mucov\$.tw,tx.
3	or/1-2
4	(mucoactive? or mucolytic? or expectorant? or mucokinetic? or mucoregulator? or thiol?).mp.
5	(acetylc#steine or nacetylc#steine or carboc#steine or dornase alfa or rhDNase or recombinant human deoxyribonuclease or recombinant human DNase or saline or sodium chloride or mannitol).mp.
6	or/4-5
7	and/3,6

### E.8.5 Database: Health Technology Assessment

Last searched on **EBM Reviews - Health Technology Assessment 4th Quarter 2016** on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).tw.
3	mucov\$.tw.
4	or/1-3
5	exp EXPECTORANTS/
6	ACETYLCYSTEINE/
7	CARBOCYSTEINE/
8	DEOXYRIBONUCLEASE I/
9	SALINE SOLUTION, HYPERTONIC/
10	SODIUM CHLORIDE/
11	ISOTONIC SOLUTIONS/
12	exp MANNITOL/
13	(mucoactive? or mucolytic? or expectorant? or mucokinetic? or mucoregulator? or thiol?).mp.
14	(acetylc#steine or nacetylc#steine or carboc#steine or dornase alfa or rhDNase or recombinant human deoxyribonuclease or recombinant human DNase or saline or sodium chloride or mannitol).mp.
15	or/5-14
16	and/4,15

### E.8.6 Database: Embase

Last searched on **Embase 1974 to 2017 Week 01** on 4<sup>th</sup> January 2017.

#	Searches
1	SYSTEMATIC REVIEW/
2	META-ANALYSIS/
3	(meta analy* or metanaly* or metaanaly*).ti,ab.
4	((systematic or evidence) adj2 (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.

#	Searches
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	((pool* or combined) adj2 (data or trials or studies or results)).ab.
10	cochrane.jw.
11	or/1-10
12	random*.ti,ab.
13	factorial*.ti,ab.
14	(crossover* or cross over*).ti,ab.
15	((doubl* or singl*) adj blind*).ti,ab.
16	(assign* or allocat* or volunteer* or placebo*).ti,ab.
17	CROSSOVER PROCEDURE/
18	SINGLE BLIND PROCEDURE/
19	RANDOMIZED CONTROLLED TRIAL/
20	DOUBLE BLIND PROCEDURE/
21	or/12-20
22	or/11,21
23	CYSTIC FIBROSIS/
24	mucov\$.ti,ab.
25	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
26	or/23-25
27	exp MUCOLYTIC AGENT/
28	ACETYLCYSTEINE/
29	CARBOCISTEINE/
30	DORNASE ALFA/
31	SODIUM CHLORIDE/
32	MANNITOL/
33	(mucoactive? or mucolytic? or expectorant? or mucokinetic? or mucoregulator? or thiol?).mp.
34	(acetylc#steine or nacetylc#steine or carboc#steine or dornase alfa or rHDNase or recombinant human deoxyribonuclease or recombinant human DNase or saline or sodium chloride or mannitol).mp.
35	or/27-34
36	and/26,35
37	limit 36 to english language
38	letter.pt. or LETTER/
39	note.pt.
40	editorial.pt.
41	CASE REPORT/ or CASE STUDY/
42	(letter or comment*).ti.
43	or/38-42
44	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
45	43 not 44
46	ANIMAL/ not HUMAN/
47	NONHUMAN/
48	exp ANIMAL EXPERIMENT/
49	exp EXPERIMENTAL ANIMAL/

#	Searches
50	ANIMAL MODEL/
51	exp RODENT/
52	(rat or rats or mouse or mice).ti.
53	or/45-52
54	37 not 53
55	and/22,54

## E.9 Antimicrobials

**E.9.1 What is the effectiveness of long-term antimicrobial prophylaxis to prevent pulmonary bacterial colonisation with *Staphylococcus aureus* in people with CF?**

**E.9.2 What is the effectiveness of antimicrobial treatment for acute pulmonary infection or those with an exacerbation in children and adults with cystic fibrosis?**

**E.9.3 What is the effectiveness of antimicrobial regimens in suppressing chronic pulmonary infection in children and adults with CF with any of the following pathogens?**

- *Pseudomonas aeruginosa*
- *Burkholderia cepacia* complex
- *Staphylococcus aureus*
- *Aspergillus fumigatus*
- Database: Medline

Last searched on **Ovid MEDLINE(R)** 1946 to December Week 1 2016 on 5<sup>th</sup> January 2017.

#	Searches
1	META-ANALYSIS/
2	META-ANALYSIS AS TOPIC/
3	(meta analy* or metanaly* or metaanaly*).ti,ab.
4	((systematic* or evidence*) adj2 (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	or/1-9
11	randomized controlled trial.pt.
12	controlled clinical trial.pt.
13	pragmatic clinical trial.pt.
14	randomi#ed.ab.
15	placebo.ab.
16	randomly.ab.

#	Searches
17	CLINICAL TRIALS AS TOPIC/
18	trial.ti.
19	or/11-18
20	or/10,19
21	CYSTIC FIBROSIS/
22	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
23	mucov\$.ti,ab.
24	or/21-23
25	exp ANTI-BACTERIAL AGENTS/ or exp ANTIFUNGAL AGENTS/
26	(antibiotic\$ or anti biotic\$ or antimicrob\$ or anti microb\$ or antibacteri\$ or anti bacteri\$ or antimyobacteri\$ or anti myobacteri\$ or antifung\$ or anti fung\$).ti,ab.
27	exp BETA-LACTAMS/ or exp MACROLIDES/ or exp QUINOLONES/ or exp TETRACYCLINES/ or exp TRIAZOLES/ or exp AMINOGLYCOSIDES/ or exp CARBAPENEMS/ or exp SULFONAMIDES/ or exp OXAZOLIDINONES/
28	(penicil?in\$ or co amox#clav or coamox#clav or amox#cil?in or clavulan\$ or flucloxacil?in or floxacil?in or piperacil?in or ticarcil?in or temocil?i\$).mp.
29	(cotrimoxazole or co trimoxazole or trimethoprim or sul??amethoxazole).mp.
30	(beta lactam\$ or betalactam\$ or ce??alospirin\$ or ce??alexin or ce??aclor or ce??radine or ce??tazidime or ce??uroxime or ce??ixime or ce??oxitin or aztreonam or lysine or tazobactam).mp.
31	(tetracycline\$ or doxycycline or minocycline or glycylicycline\$ or tigecycline).mp.
32	(macrolide\$ or az#throm#cin or clarithrom#cin).mp.
33	(rifampicin or rifampin or rifamycin\$).mp.
34	(linzolid or oxazolidinone\$).mp.
35	(fluoroquinolone\$ or quinalone\$ or ciprofloxacin or ciprofloxain or moxifloxacin or clofazimine or phenazine\$).mp.
36	(carbapenem\$ or meropenem or imipenem).mp.
37	(fosfomycin or phosphomycin or phosphonomycin).mp.
38	(aminoglycoside\$ or tobramycin or amikacin or amikin).mp.
39	(polymyxin\$ or colistin or colistimethate or colimycin).mp.
40	(ethambutol or EMB or chloramphenicol).mp.
41	(triazole\$ or itraconazole or voriconazole or posacon#zole or amphotericin or polyene\$).mp.
42	or/25-41
43	24 and 42
44	20 and 43
45	limit 44 to english language
46	LETTER/
47	EDITORIAL/
48	NEWS/
49	exp HISTORICAL ARTICLE/
50	ANECDOTES AS TOPIC/
51	COMMENT/
52	CASE REPORT/
53	(letter or comment*).ti.
54	or/46-53
55	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.

#	Searches
56	54 not 55
57	ANIMALS/ not HUMANS/
58	exp ANIMALS, LABORATORY/
59	exp ANIMAL EXPERIMENTATION/
60	exp MODELS, ANIMAL/
61	exp RODENTIA/
62	(rat or rats or mouse or mice).ti.
63	or/56-62
64	45 not 63

- Database: Medline In-Process & Other Non-Indexed Citations

Last searched on **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations** January 04, 2017 on 5<sup>th</sup> January 2017.

#	Searches
1	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
2	mucov\$.ti,ab.
3	1 or 2
4	(antibiotic\$ or anti biotic\$ or antimicrob\$ or anti microb\$ or antibacteri\$ or anti bacteri\$ or antimyobacteri\$ or anti myobacteri\$ or antifung\$ or anti fung\$).ti,ab.
5	(penicil?in\$ or co amox#clav or coamox#clav or amox#cil?in or clavulan\$ or flucloxacil?in or floxacil?in or piperacil?in or ticarcil?in or temocil?i\$).mp.
6	(cotrimoxazole or co trimoxazole or trimethoprim or sul??amethoxazole).mp.
7	(beta lactam\$ or betalactam\$ or ce??alospirin\$ or ce??alexin or ce??aclor or ce??radine or ce??tazidime or ce??uroxime or ce??ixime or ce??oxitin or aztreonam or lysine or tazobactam).mp.
8	(tetracycline\$ or doxycycline or minocycline or glycylicycline\$ or tigecycline).mp.
9	(macrolide\$ or az#throm#cin or clarithrom#cin).mp.
10	(rifampicin or rifampin or rifamycin\$).mp.
11	(linzolid or oxazolidinone\$).mp.
12	(fluoroquinolone\$ or quinalone\$ or ciprofloxacin or ciprofloxain or moxifloxacin or clofazimine or phenazine\$).mp.
13	(carbapenem\$ or meropenem or imipenem).mp.
14	(fosfomycin or phosphomycin or phosphonomycin).mp.
15	(aminoglycoside\$ or tobramycin or amikacin or amikin).mp.
16	(polymyxin\$ or colistin or colistimethate or colimycin).mp.
17	(ethambutol or EMB or chloramphenicol).mp.
18	(triazole\$ or itraconazole or voriconazole or posacon#zole or amphotericin or polyene\$).mp.
19	or/4-18
20	3 and 19
21	limit 20 to english language

- Database: Cochrane Central Register of Controlled Trials

Last searched on **EBM Reviews - Cochrane Central Register of Controlled Trials** November 2016 on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab,kw.

#	Searches
3	mucov\$.ti,ab.
4	or/1-3
5	ANTI-BACTERIAL AGENTS/ or ANTIFUNGAL AGENTS/
6	(ANTIBIOTIC AGENT or ANTIFUNGAL AGENT).kw.
7	(antibiotic\$ or anti biotic\$ or antimicrob\$ or anti microb\$ or antibacteri\$ or anti bacteri\$ or antimyobacteri\$ or anti myobacteri\$ or antifung\$ or anti fung\$).ti,ab.
8	exp BETA-LACTAMS/ or exp MACROLIDES/ or QUINOLONES/ or TETRACYCLINES/ or TRIAZOLES/ or AMINOGLYCOSIDES/ or CARBAPENEMS/ or SULFONAMIDES/ or OXAZOLIDINONES/
9	(BETA LACTAM or QUINOLONE or TRIAZOLE or SULFONAMIDE or OXAZOLIDINONE DERIVATIVE).kw.
10	(penicil?in\$ or co amox#clav or coamox#clav or amox#cil?in or clavulan\$ or flucloxacil?in or floxacil?in or piperacil?in or ticarcil?in or temocil?i\$).mp.
11	(cotrimoxazole or co trimoxazole or trimethoprim or sul??amethoxazole).mp.
12	(beta lactam\$ or betalactam\$ or ce??alosporin\$ or ce??alexin or ce??aclor or ce??radine or ce??tazidime or ce??uroxime or ce??ixime or ce??oxitin or aztreonam or lysine or tazobactam).mp.
13	(tetracycline\$ or doxycycline or minocycline or glycylicycline\$ or tigecycline).mp.
14	(macrolide\$ or az#throm#cin or clarithrom#cin).mp.
15	(rifampicin or rifampin or rifamycin\$).mp.
16	(linzolid or oxazolidinone\$).mp.
17	(fluoroquinolone\$ or quinalone\$ or ciprofloxacin or ciprofloxain or moxifloxacin or clofazimine or phenazine\$).mp.
18	(carbapenem\$ or meropenem or imipenem).mp.
19	(fosfomycin or phosphomycin or phosphonomycin).mp.
20	(aminoglycoside\$ or tobramycin or amikacin or amikin).mp.
21	(polymyxin\$ or colistin or colistimethate or colimycin).mp.
22	(ethambutol or EMB or chloramphenicol).mp.
23	(triazole\$ or itraconazole or voriconazole or posacon#zole or amphotericin or polyene\$).mp.
24	or/5-23
25	4 and 24

- Database: Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects

Last searched on **EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to January 05, 2017, **EBM Reviews - Database of Abstracts of Reviews of Effects** 1st Quarter 2015 on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS.kw.
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,tw,tx.
3	mucov\$.ti,tw,tx.
4	or/1-3
5	(ANTI-BACTERIAL AGENTS or ANTIFUNGAL AGENTS or ANTIBIOTIC AGENT or ANTIFUNGAL AGENT).kw.
6	(antibiotic\$ or anti biotic\$ or antimicrob\$ or anti microb\$ or antibacteri\$ or anti bacteri\$ or antimyobacteri\$ or anti myobacteri\$ or antifung\$ or anti fung\$).ti,tw,tx.
7	(BETA-LACTAMS or MACROLIDES or QUINOLONES or TETRACYCLINES or TRIAZOLES or AMINOGLYCOSIDES or CARBAPENEMS or SULFONAMIDES or OXAZOLIDINONES or BETA LACTAM or QUINOLONE or TRIAZOLE or

#	Searches
	SULFONAMIDE or OXAZOLIDINONE DERIVATIVE).kw.
8	(penicil?in\$ or co amox#clav or coamox#clav or amox#cil?in or clavulan\$ or flucloxacil?in or floxacil?in or piperacil?in or ticarcil?in or temocil?i\$).mp.
9	(cotrimoxazole or co trimoxazole or trimethoprim or sul??amethoxazole).mp.
10	(beta lactam\$ or betalactam\$ or ce??alosporin\$ or ce??alexin or ce??aclor or ce??radine or ce??tazidime or ce??uroxime or ce??ixime or ce??oxitin or aztreonam or lysine or tazobactam).mp.
11	(tetracycline\$ or doxycycline or minocycline or glycylicycline\$ or tigecycline).mp.
12	(macrolide\$ or az#throm#cin or clarithrom#cin).mp.
13	(rifampicin or rifampin or rifamycin\$).mp.
14	(linzolid or oxazolidinone\$).mp.
15	(fluoroquinolone\$ or quinolone\$ or ciprofloxacin or ciprofloxain or moxifloxacin or clofazimine or phenazine\$).mp.
16	(carbapenem\$ or meropenem or imipenem).mp.
17	(fosfomycin or phosphomycin or phosphonomycin).mp.
18	(aminoglycoside\$ or tobramycin or amikacin or amikin).mp.
19	(polymyxin\$ or colistin or colistimethate or colimycin).mp.
20	(ethambutol or EMB or chloramphenicol).mp.
21	(triazole\$ or itraconazole or voriconazole or posacon#zole or amphotericin or polyene\$).mp.
22	or/5-21
23	4 and 22

- Database: Health Technology Assessment

Last searched on **EBM Reviews - Health Technology Assessment 4th Quarter 2016** on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,tw.
3	mucov\$.ti,tw.
4	or/1-3
5	exp ANTI-BACTERIAL AGENTS/ or exp ANTIFUNGAL AGENTS/
6	(antibiotic\$ or anti biotic\$ or antimicrob\$ or anti microb\$ or antibacteri\$ or anti bacteri\$ or antimyobacteri\$ or anti myobacteri\$ or antifung\$ or anti fung\$).ti,tw.
7	exp BETA-LACTAMS/ or exp MACROLIDES/ or exp QUINOLONES/ or exp TETRACYCLINES/ or exp TRIAZOLES/ or exp AMINOGLYCOSIDES/ or exp CARBAPENEMS/ or exp SULFONAMIDES/ or exp OXAZOLIDINONES/
8	(penicil?in\$ or co amox#clav or coamox#clav or amox#cil?in or clavulan\$ or flucloxacil?in or floxacil?in or piperacil?in or ticarcil?in or temocil?i\$).mp.
9	(cotrimoxazole or co trimoxazole or trimethoprim or sul??amethoxazole).mp.
10	(beta lactam\$ or betalactam\$ or ce??alosporin\$ or ce??alexin or ce??aclor or ce??radine or ce??tazidime or ce??uroxime or ce??ixime or ce??oxitin or aztreonam or lysine or tazobactam).mp.
11	(tetracycline\$ or doxycycline or minocycline or glycylicycline\$ or tigecycline).mp.
12	(macrolide\$ or az#throm#cin or clarithrom#cin).mp.
13	(rifampicin or rifampin or rifamycin\$).mp.
14	(linzolid or oxazolidinone\$).mp.
15	(fluoroquinolone\$ or quinolone\$ or ciprofloxacin or ciprofloxain or moxifloxacin or clofazimine or phenazine\$).mp.

#	Searches
16	(carbapenem\$ or meropenem or imipenem).mp.
17	(fosfomycin or phosphomycin or phosphonomycin).mp.
18	(aminoglycoside\$ or tobramycin or amikacin or amikin).mp.
19	(polymyxin\$ or colistin or colistimethate or colimycin).mp.
20	(ethambutol or EMB or chloramphenicol).mp.
21	(triazole\$ or itraconazole or voriconazole or posacon#zole or amphotericin or polyene\$).mp.
22	or/5-21
23	4 and 22
24	limit 23 to english language

- Database: Embase

Last searched on **Embase** 1974 to 2017 Week 01 on 4<sup>th</sup> January 2017.

#	Searches
1	SYSTEMATIC REVIEW/
2	META-ANALYSIS/
3	(meta analy* or metanaly* or metaanaly*).ti,ab.
4	((systematic or evidence) adj2 (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 psychlit or psychinfo or psychinfo or cinahl or science citation index or bids or cancerlit).ab.
9	((pool* or combined) adj2 (data or trials or studies or results)).ab.
10	cochrane.jw.
11	or/1-10
12	random*.ti,ab.
13	factorial*.ti,ab.
14	(crossover* or cross over*).ti,ab.
15	((doubl* or singl*) adj blind*).ti,ab.
16	(assign* or allocat* or volunteer* or placebo*).ti,ab.
17	CROSSOVER PROCEDURE/
18	SINGLE BLIND PROCEDURE/
19	RANDOMIZED CONTROLLED TRIAL/
20	DOUBLE BLIND PROCEDURE/
21	or/12-20
22	or/11,21
23	exp CYSTIC FIBROSIS/
24	mucov\$.ti,ab.
25	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
26	or/23-25
27	exp ANTIBIOTIC AGENT/ or exp ANTIFUNGAL AGENT/
28	(antibiotic\$ or anti biotic\$ or antimicrob\$ or anti microb\$ or antibacteri\$ or anti bacteri\$ or antimyobacteri\$ or anti myobacteri\$ or antifung\$ or anti fung\$).ti,ab.
29	exp BETA LACTAM/ or exp QUINOLONE/ or exp TRIAZOLE/ or exp SULFONAMIDE/ or

#	Searches
	exp OXAZOLIDINONE DERIVATIVE/
30	(penicil?in\$ or co amox#clav or coamox#clav or amox#cil?in or clavulan\$ or flucloxacil?in or floxacil?in or piperacil?in or ticarcil?in or temocil?i\$).mp.
31	(cotrimoxazole or co trimoxazole or trimethoprim or sul??amethoxazole).mp.
32	(beta lactam\$ or betalactam\$ or ce??alosporin\$ or ce??alexin or ce??aclor or ce??radine or ce??tazidime or ce??uroxime or ce??ixime or ce??oxitin or aztreonam or lysine or tazobactam).mp.
33	(tetracycline\$ or doxycycline or minocycline or glycylicycline\$ or tigecycline).mp.
34	(macrolide\$ or az#throm#cin or clarithrom#cin).mp.
35	(rifampicin or rifampin or rifamycin\$).mp.
36	(linzolid or oxazolidinone\$).mp.
37	(fluoroquinolone\$ or quinolone\$ or ciprofloxacin or ciprofloxain or moxifloxacin or clofazimine or phenazine\$).mp.
38	(carbapenem\$ or meropenem or imipenem).mp.
39	(fosfomycin or phosphomycin or phosphonomycin).mp.
40	(aminoglycoside\$ or tobramycin or amikacin or amikin).mp.
41	(polymyxin\$ or colistin or colistimethate or colimycin).mp.
42	(ethambutol or EMB or chloramphenicol).mp.
43	(triazole\$ or itraconazole or voriconazole or posaconazole or amphotericin or polyene\$).mp.
44	or/27-43
45	26 and 44
46	22 and 45
47	limit 46 to english language
48	letter.pt. or LETTER/
49	note.pt.
50	editorial.pt.
51	CASE REPORT/ or CASE STUDY/
52	(letter or comment*).ti.
53	or/48-52
54	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
55	53 not 54
56	ANIMAL/ not HUMAN/
57	NONHUMAN/
58	exp ANIMAL EXPERIMENT/
59	exp EXPERIMENTAL ANIMAL/
60	ANIMAL MODEL/
61	exp RODENT/
62	(rat or rats or mouse or mice).ti.
63	or/55-62
64	47 not 63

## E.10 What is the effectiveness of immunomodulatory agents in the management of lung disease, for example corticosteroids, azithromycin?

### E.10.1 Database: Medline

Last searched on **Ovid MEDLINE(R)** 1946 to December Week 1 2016 on 5<sup>th</sup> January 2017.

#	Searches
1	META-ANALYSIS/
2	META-ANALYSIS AS TOPIC/
3	(meta analy* or metanaly* or metaanaly*).ti,ab.
4	((systematic* or evidence*) adj2 (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	or/1-9
11	randomized controlled trial.pt.
12	controlled clinical trial.pt.
13	pragmatic clinical trial.pt.
14	randomi#ed.ab.
15	placebo.ab.
16	randomly.ab.
17	CLINICAL TRIALS AS TOPIC/
18	trial.ti.
19	or/11-18
20	or/10,19
21	CYSTIC FIBROSIS/
22	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
23	mucov\$.ti,ab.
24	or/21-23
25	(immunomodulator\$ or immune modulator\$).ti,ab.
26	exp ADRENAL CORTEX HORMONES/ or exp STEROIDS/
27	(steroid\$ or corticoid\$ or glucocorticoid\$ or corticosteroid\$ or glucocorticosteroid\$).ti,ab.
28	(adrenal adj2 cortex adj2 hormone\$).ti,ab.
29	(beclomet?a#on\$ or bude#onide\$ or flutica#one\$ or methylpredni#olone\$ or predni#olone\$).ti,ab.
30	exp AZITHROMYCIN/
31	az#throm#cin\$.ti,ab.
32	exp ANTI-INFLAMMATORY AGENTS, NON-STEROIDAL/
33	((anti-inflammat\$ or antiinflammat\$) adj3 (non-steroid\$ or nonsteroid\$ or drug\$ or agent\$ or therap\$ or medic\$)).ti,ab.
34	(ibuprofen\$ or nsaid\$).ti,ab.
35	or/25-34

#	Searches
36	and/20,24,35
37	limit 36 to english language
38	LETTER/
39	EDITORIAL/
40	NEWS/
41	exp HISTORICAL ARTICLE/
42	ANECDOTES AS TOPIC/
43	COMMENT/
44	CASE REPORT/
45	(letter or comment*).ti.
46	or/38-45
47	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
48	46 not 47
49	ANIMALS/ not HUMANS/
50	exp ANIMALS, LABORATORY/
51	exp ANIMAL EXPERIMENTATION/
52	exp MODELS, ANIMAL/
53	exp RODENTIA/
54	(rat or rats or mouse or mice).ti.
55	or/48-54
56	37 not 55

### E.10.2 Database: Medline In-Process & Other Non-Indexed Citations

Last searched on **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations** January 04, 2017 on 5<sup>th</sup> January 2017.

#	Searches
1	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
2	mucov\$.ti,ab.
3	1 or 2
4	(immunomodulator\$ or immune modulator\$).ti,ab.
5	(steroid\$ or corticoid\$ or glucocorticoid\$ or corticosteroid\$ or glucocorticosteroid\$).ti,ab.
6	(adrenal adj2 cortex adj2 hormone\$).ti,ab.
7	(beclomet?a#on\$ or bude#onide\$ or flutica#one\$ or methylpredni#olone\$ or predni#olone\$).ti,ab.
8	az#throm#cin\$.ti,ab.
9	((anti-inflammat\$ or antiinflammat\$) adj3 (non-steroid\$ or nonsteroid\$ or drug\$ or agent\$ or therap\$ or medic\$)).ti,ab.
10	(ibuprofen\$ or nsaid\$).ti,ab.
11	or/4-10
12	3 and 11
13	limit 12 to english language

### E.10.3 Database: Cochrane Central Register of Controlled Trials

Last searched on **EBM Reviews - Cochrane Central Register of Controlled Trials** November 2016 on 5<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab,kw.
3	mucov\$.ti,ab.
4	or/1-3
5	(immunomodulator\$ or immune modulator\$).ti,ab.
6	ADRENAL CORTEX HORMONES/ or STEROIDS/
7	CORTICOSTEROID.kw.
8	(steroid\$ or corticoid\$ or glucocorticoid\$ or corticosteroid\$ or glucocorticosteroid\$).ti,ab.
9	(adrenal adj2 cortex adj2 hormone\$).ti,ab.
10	(beclomet?a#on\$ or bude#onide\$ or flutica#one\$ or methylpredni#olone\$ or predni#olone\$).ti,ab.
11	AZITHROMYCIN/ or AZITHROMYCIN.kw.
12	az#throm#cin\$.ti,ab.
13	ANTI-INFLAMMATORY AGENTS, NON-STEROIDAL/ or NONSTEROID ANTIINFLAMMATORY AGENT.kw.
14	((anti-inflammat\$ or antiinflammat\$) adj3 (non-steroid\$ or nonsteroid\$ or drug\$ or agent\$ or therap\$ or medic\$)).ti,ab.
15	(ibuprofen\$ or nsaid\$).ti,ab.
16	or/5-15
17	4 and 16

#### E.10.4 Database: Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects

Last searched on **EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to December 30, 2016, **EBM Reviews - Database of Abstracts of Reviews of Effects** 1st Quarter 2015 on 5<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS.kw.
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,tw,tx.
3	mucov\$.ti,tw,tx.
4	or/1-3
5	(immunomodulator\$ or immune modulator\$).ti,tw,tx.
6	(ADRENAL CORTEX HORMONES or STEROIDS or CORTICOSTEROID).kw.
7	(steroid\$ or corticoid\$ or glucocorticoid\$ or corticosteroid\$ or glucocorticosteroid\$).ti,tw,tx.
8	(adrenal adj2 cortex adj2 hormone\$).ti,tw,tx.
9	(beclomet?a#on\$ or bude#onide\$ or flutica#one\$ or methylpredni#olone\$ or predni#olone\$).ti,tw,tx.
10	AZITHROMYCIN.kw.
11	az#throm#cin\$.ti,tw,tx.
12	(ANTI-INFLAMMATORY AGENTS, NON-STEROIDAL or NONSTEROID ANTIINFLAMMATORY AGENT).kw.
13	((anti-inflammat\$ or antiinflammat\$) adj3 (non-steroid\$ or nonsteroid\$ or drug\$ or agent\$ or therap\$ or medic\$)).ti,tw,tx.
14	(ibuprofen\$ or nsaid\$).ti,tw,tx.
15	or/5-14
16	4 and 15

### E.10.5 Database: Health Technology Assessment

Last searched on **EBM Reviews - Health Technology Assessment 4th Quarter 2016** on 5<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,tw.
3	mucov\$.ti,tw.
4	or/1-3
5	(immunomodulator\$ or immune modulator\$).ti,tw.
6	exp ADRENAL CORTEX HORMONES/ or exp STEROIDS/
7	(steroid\$ or corticoid\$ or glucocorticoid\$ or corticosteroid\$ or glucocorticosteroid\$).ti,tw.
8	(adrenal adj2 cortex adj2 hormone\$).ti,tw.
9	(beclomet#a#on\$ or bude#onide\$ or flutica#one\$ or methylpredni#olone\$ or predni#olone\$).ti,tw.
10	exp AZITHROMYCIN/
11	az#throm#cin\$.ti,tw.
12	exp ANTI-INFLAMMATORY AGENTS, NON-STEROIDAL/
13	((anti-inflammat\$ or antiinflammat\$) adj3 (non-steroid\$ or nonsteroid\$ or drug\$ or agent\$ or therap\$ or medic\$)).ti,tw.
14	(ibuprofen\$ or nsaid\$).ti,tw.
15	or/5-14
16	4 and 15

### E.10.6 Database: Embase

Last searched on **Embase 1974 to 2017 Week 01** on 4<sup>th</sup> January 2017.

#	Searches
1	SYSTEMATIC REVIEW/
2	META-ANALYSIS/
3	(meta analy* or metanaly* or metaanaly*).ti,ab.
4	((systematic or evidence) adj2 (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	((pool* or combined) adj2 (data or trials or studies or results)).ab.
10	cochrane.jw.
11	or/1-10
12	random*.ti,ab.
13	factorial*.ti,ab.
14	(crossover* or cross over*).ti,ab.
15	((doubl* or singl*) adj blind*).ti,ab.
16	(assign* or allocat* or volunteer* or placebo*).ti,ab.
17	CROSSOVER PROCEDURE/
18	SINGLE BLIND PROCEDURE/

#	Searches
19	RANDOMIZED CONTROLLED TRIAL/
20	DOUBLE BLIND PROCEDURE/
21	or/12-20
22	or/11,21
23	exp CYSTIC FIBROSIS/
24	mucov\$.ti,ab.
25	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
26	or/23-25
27	(immunomodulator\$ or immune modulator\$).ti,ab.
28	exp CORTICOSTEROID/
29	(steroid\$ or corticoid\$ or glucocorticoid\$ or corticosteroid\$ or glucocorticosteroid\$).ti,ab.
30	(adrenal adj2 cortex adj2 hormone\$).ti,ab.
31	(beclomet?a#on\$ or bude#onide\$ or flutica#one\$ or methylpredni#olone\$ or predni#olone\$).ti,ab.
32	exp AZITHROMYCIN/
33	az#throm#cin\$.ti,ab.
34	exp NONSTEROID ANTIINFLAMMATORY AGENT/
35	((anti-inflammat\$ or antiinflammat\$) adj3 (non-steroid\$ or nonsteroid\$ or drug\$ or agent\$ or therap\$ or medic\$)).ti,ab.
36	(ibuprofen\$ or nsaid\$).ti,ab.
37	or/27-36
38	and/22,26,37
39	limit 38 to english language
40	letter.pt. or LETTER/
41	note.pt.
42	editorial.pt.
43	CASE REPORT/ or CASE STUDY/
44	(letter or comment*).ti.
45	or/40-44
46	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
47	45 not 46
48	ANIMAL/ not HUMAN/
49	NONHUMAN/
50	exp ANIMAL EXPERIMENT/
51	exp EXPERIMENTAL ANIMAL/
52	ANIMAL MODEL/
53	exp RODENT/
54	(rat or rats or mouse or mice).ti.
55	or/47-54
56	39 not 55

## E.11 What is the clinical and cost effectiveness of nutritional interventions in people with cystic fibrosis?

### E.11.1 Database: Medline

Last searched on **Ovid MEDLINE(R)** 1946 to December Week 1 2016 on 5<sup>th</sup> January 2017.

#	Searches
1	META-ANALYSIS/
2	META-ANALYSIS AS TOPIC/
3	(meta analy* or metanaly* or metaanaly*).ti,ab.
4	((systematic* or evidence*) adj2 (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	or/1-9
11	randomized controlled trial.pt.
12	controlled clinical trial.pt.
13	pragmatic clinical trial.pt.
14	randomi#ed.ab.
15	placebo.ab.
16	randomly.ab.
17	CLINICAL TRIALS AS TOPIC/
18	trial.ti.
19	or/11-18
20	or/10,19
21	OBSERVATIONAL STUDY/
22	(observat\$ adj3 (study or studies)).ti,ab.
23	COHORT STUDIES/
24	(cohort adj3 (study or studies)).ti,ab.
25	(cohort adj3 analy\$).ti,ab.
26	FOLLOW-UP STUDIES/
27	(Follow\$ up adj3 (study or studies)).ti,ab.
28	LONGITUDINAL STUDIES/
29	longitudinal\$.ti,ab.
30	RETROSPECTIVE STUDIES/
31	retrospective\$.ti,ab.
32	CROSS-SECTIONAL STUDIES/
33	cross-sectional\$.ti,ab.
34	CASE-CONTROL STUDIES/
35	case control.ti,ab.
36	or/21-35
37	CYSTIC FIBROSIS/
38	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.

#	Searches
39	mucov\$.ti,ab.
40	37 or 38 or 39
41	exp NUTRITION DISORDERS/
42	exp "FEEDING AND EATING DISORDERS OF CHILDHOOD"/
43	exp "FEEDING AND EATING DISORDERS"/
44	exp NUTRITIONAL STATUS/
45	BODY DYSMORPHIC DISORDERS/
46	exp CHILD NUTRITIONAL PHYSIOLOGICAL PHENOMENA/
47	exp FAILURE TO THRIVE/
48	exp GROWTH DISORDERS/
49	GASTROESOPHAGEAL REFLUX/
50	exp ABDOMINAL PAIN/
51	(malnutrition\$ or malnourish\$ or undernutrition\$ or under nutrition\$ or undernourish\$ or under nourish\$ or overnutrition\$ or over nutrition\$ or overnourish\$ or over nourish\$ or malabsorb\$ or mal?absorb\$).ti,ab.
52	avitaminosis.ti,ab.
53	(underweight? or under weight? or overweight? or over weight? or obes\$).ti,ab.
54	((nutrition\$ or nourish\$ or grow\$ or vitamin? or weight or diet\$ or eat\$) adj3 (disorder? or deficien\$ or poor or status)).ti,ab.
55	(appetite or anorexia or (gord or gerd or acid reflux gastro??esopag\$ reflux or esopag\$ reflux or oesophag\$ reflux) or ((abdomin\$ or stomach or digest\$ or intestin\$ or colon or colic\$) adj3 (pain or discomf\$))).ti,ab.
56	((body dysmorph\$ or body image) adj2 disorder?) or dysmorphophobi?).ti,ab.
57	((fail\$ or falter\$) adj3 (thriv\$ or weight or grow\$)).ti,ab.
58	or/41-57
59	PSYCHOTHERAPY/
60	exp BEHAVIOR THERAPY/
61	COGNITIVE THERAPY/
62	COUNSELING/ or DIRECTIVE COUNSELING/
63	FAMILY THERAPY/
64	ADAPTATION, PSYCHOLOGICAL/
65	(behavi?r\$ or counsel\$ or coach\$ or psychotherap\$ or psycho therap\$ or advis\$ or advi?e\$ or psycholog\$).ti,ab.
66	((behavi\$ or cognit\$) adj3 (technique? or therap\$ or psychotherap\$)).ti,ab.
67	CBT.ti,ab.
68	(mindfulness or relax\$ or meditat\$ or cope? or coping).ti,ab.
69	(psychoeducation\$ or psycho education\$).ti,ab.
70	or/59-69
71	exp NUTRITION THERAPY/
72	exp DIET THERAPY/
73	DIETETICS/
74	((diet\$ or nutrition\$ or eat\$ or feed\$) adj (therap\$ or program\$ or advi?e\$ or advis\$ or support\$ or modif\$ or chang\$)).ti,ab.
75	SNACKS/
76	(snack\$ or fastfood or fast food).ti,ab.
77	exp DIET, HIGH-FAT/
78	DIETARY FATS/

#	Searches
79	ENERGY INTAKE/
80	DIETARY PROTEINS/
81	DIETARY CARBOHYDRATES/
82	VITAMINS/
83	((fat\$ or lipid\$ or energ\$ or calori\$ or oral or nutrition\$ or protein? or carbohydrate? or vitamin\$) adj3 (intake or diet\$ or food\$ or meal?)).ti,ab.
84	or/71-83
85	DIETARY SUPPLEMENTS/
86	FOOD, FORTIFIED/
87	FOOD, FORMULATED/
88	((oral or nutrition\$ or calori\$ or diet\$ or energy or protein) adj2 supplement\$).ti,ab.
89	(supplement\$ adj2 feed\$).ti,ab.
90	prescri\$ feed\$.ti,ab.
91	((food or fed) adj2 (fortifi\$ or formulat\$)).ti,ab.
92	energy drink\$.ti,ab.
93	((oral or nutrition\$ or calori\$) adj3 (enhanc\$ or increas\$)).ti,ab.
94	elemental diet.ti,ab.
95	or/85-94
96	exp ENTERAL NUTRITION/
97	((enteral\$ or enteric\$ or intragastric\$ or intra gastric\$ or nasogastric\$ or naso gastric\$ or intrainestinal\$ or intra intestinal\$ or tube) adj3 (feed\$ or fed)).ti,ab.
98	GASTROSTOMY/
99	JEJUNOSTOMY/
100	INTUBATION, GASTROINTESTINAL/
101	(gastrostom\$ or jejunostom\$ or gastrojejunostom\$ or gastro jejunostom\$).ti,ab.
102	or/96-101
103	FEEDING BEHAVIOR/
104	FOOD HABITS/
105	((eat\$ or feed\$ or food or diet\$) adj (pattern\$ or behavio?r\$ or habit?)).ti,ab.
106	(meal\$ adj3 (manag\$ or timing or regular)).ti,ab.
107	or/103-106
108	exp APPETITE STIMULANTS/
109	CYPROHEPTADINE/
110	MEGESTROL ACETATE/
111	appetite stimulan\$.ti,ab.
112	(cyproheptadine or megace or maygace or megestrol).ti,ab,mp.
113	or/108-112
114	84 or 95 or 102 or 107 or 113
115	40 and 114
116	40 and 58 and 70
117	115 or 116
118	CYSTIC FIBROSIS/dh [DIET THERAPY]
119	117 or 118
120	limit 119 to english language
121	limit 120 to yr="1997 -Current"
122	LETTER/

#	Searches
123	EDITORIAL/
124	NEWS/
125	exp HISTORICAL ARTICLE/
126	ANECDOTES AS TOPIC/
127	COMMENT/
128	CASE REPORT/
129	(letter or comment*).ti.
130	or/122-129
131	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
132	130 not 131
133	ANIMALS/ not HUMANS/
134	exp ANIMALS, LABORATORY/
135	exp ANIMAL EXPERIMENTATION/
136	exp MODELS, ANIMAL/
137	exp RODENTIA/
138	(rat or rats or mouse or mice).ti.
139	or/132-138
140	121 not 139
141	20 and 140
142	36 and 140
143	141 or 142

### E.11.2 Database: Medline In-Process & Other Non-Indexed Citations

Last searched on **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations** January 04, 2017 on 5<sup>th</sup> January 2017.

#	Searches
1	(meta analy* or metanaly* or metaanaly*).ti,ab.
2	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
3	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
4	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
5	(search* adj4 literature).ab.
6	(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.
7	cochrane.jw.
8	randomi#ed.ab.
9	placebo.ab.
10	randomly.ab.
11	trial.ti.
12	or/1-11
13	(observat\$ adj3 (study or studies)).ti,ab.
14	(cohort adj3 (study or studies)).ti,ab.
15	(cohort adj3 analy\$).ti,ab.
16	(Follow\$ up adj3 (study or studies)).ti,ab.
17	longitudinal\$.ti,ab.

#	Searches
18	retrospective\$.ti,ab.
19	cross-sectional\$.ti,ab.
20	case control.ti,ab.
21	or/13-20
22	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
23	mucov\$.ti,ab.
24	or/22-23
25	(malnutrition\$ or malnourish\$ or undernutrition\$ or under nutrition\$ or undernourish\$ or under nourish\$ or overnutrition\$ or over nutrition\$ or overnourish\$ or over nourish\$ or malabsorb\$ or mal?absorb\$).ti,ab.
26	avitaminosis.ti,ab.
27	(underweight? or under weight? or overweight? or over weight? or obes\$).ti,ab.
28	((nutrition\$ or nourish\$ or grow\$ or vitamin? or weight or diet\$ or eat\$) adj3 (disorder? or deficien\$ or poor or status)).ti,ab.
29	(appetite or anorexia or (gord or gerd or acid reflux gastro??esopag\$ reflux or esopag\$ reflux or oesophag\$ reflux) or ((abdomin\$ or stomach or digest\$ or intestin\$ or colon or colic\$) adj3 (pain or discomf\$))).ti,ab.
30	((body dysmorph\$ or body image) adj2 disorder?) or dysmorphophobi?).ti,ab.
31	((fail\$ or falter\$) adj3 (thriv\$ or weight or grow\$)).ti,ab.
32	or/25-31
33	(behavi?r\$ or counsel\$ or coach\$ or psychotherap\$ or psycho therap\$ or advis\$ or advi?e\$ or psycholog\$).ti,ab.
34	((behavi\$ or cognit\$) adj3 (technique? or therap\$ or psychotherap\$)).ti,ab.
35	CBT.ti,ab.
36	(mindfulness or relax\$ or meditat\$ or cope? or coping).ti,ab.
37	(psychoeducation\$ or psycho education\$).ti,ab.
38	or/33-37
39	((diet\$ or nutrition\$ or eat\$ or feed\$) adj (therap\$ or program\$ or advi?e\$ or advis\$ or support\$ or modif\$ or chang\$)).ti,ab.
40	(snack\$ or fastfood or fast food).ti,ab.
41	((fat\$ or lipid\$ or energ\$ or calori\$ or oral or nutrition\$ or protein? or carbohydrate? or vitamin\$) adj3 (intake or diet\$ or food\$ or meal?)).ti,ab.
42	((oral or nutrition\$ or calori\$ or diet\$ or energy or protein) adj2 supplement\$).ti,ab.
43	(supplement\$ adj2 feed\$).ti,ab.
44	prescri\$ feed\$.ti,ab.
45	((food or fed) adj2 (fortifi\$ or formulat\$)).ti,ab.
46	energy drink\$.ti,ab.
47	((oral or nutrition\$ or calori\$) adj3 (enhanc\$ or increas\$)).ti,ab.
48	elemental diet.ti,ab.
49	((enteral\$ or enteric\$ or intragastric\$ or intra gastric\$ or nasogastric\$ or naso gastric\$ or inraintestinal\$ or intra intestinal\$ or tube) adj3 (feed\$ or fed)).ti,ab.
50	(gastrostom\$ or jejunostom\$ or gastrojejunostom\$ or gastro jejunostom\$).ti,ab.
51	((eat\$ or feed\$ or food or diet\$) adj (pattern\$ or behavio?r\$ or habit?)).ti,ab.
52	(meal\$ adj3 (manag\$ or timing or regular)).ti,ab.
53	appetite stimulan\$.ti,ab.
54	(cyproheptadine or megace or maygace or megestrol).ti,ab,mp.
55	or/39-54
56	24 and 32 and 38

#	Searches
57	24 and 55
58	56 or 57
59	12 or 21
60	58 and 59
61	limit 60 to yr="1997 -Current"

### E.11.3 Database: Cochrane Central Register of Controlled Trials

Last searched on **EBM Reviews - Cochrane Central Register of Controlled Trials**  
November 2016 on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab,kw.
3	mucov\$.ti,ab,kw.
4	1 or 2 or 3
5	exp NUTRITION DISORDERS/ or NUTRITION DISORDERS.kw.
6	exp "FEEDING AND EATING DISORDERS OF CHILDHOOD"/
7	exp "FEEDING AND EATING DISORDERS"/
8	(FEEDING DISORDER or MALNUTRITION or PROTEIN CALORIE MALNUTRITION or NUTRITIONAL DEFICIENCY or OVERNUTRITION).kw.
9	(EATING DISORDER or ANOREXIA NERVOSA or FOOD AVERSION or NUTRITIONAL STATUS).kw.
10	exp NUTRITIONAL STATUS/
11	BODY DYSMORPHIC DISORDERS.sh,kw.
12	exp CHILD NUTRITIONAL PHYSIOLOGICAL PHENOMENA/
13	(CHILD NUTRITION or FAILURE TO THRIVE or GROWTH DISORDER or GASTROESOPHAGEAL REFLUX or ABDOMINAL PAIN).kw.
14	exp FAILURE TO THRIVE/
15	exp GROWTH DISORDERS/
16	GASTROESOPHAGEAL REFLUX/
17	exp ABDOMINAL PAIN/
18	(malnutrition\$ or malnourish\$ or undernutrition\$ or under nutrition\$ or undernourish\$ or under nourish\$ or overnutrition\$ or over nutrition\$ or overnourish\$ or over nourish\$ or malabsorb\$ or mal?absorb\$).ti,ab.
19	avitaminosis.ti,ab.
20	(underweight? or under weight? or overweight? or over weight? or obes\$).ti,ab.
21	((nutrition\$ or nourish\$ or grow\$ or vitamin? or weight or diet\$ or eat\$) adj3 (disorder? or deficien\$ or poor or status)).ti,ab.
22	(appetite or anorexia or (gord or gerd or acid reflux gastro??esopag\$ reflux or esopag\$ reflux or oesophag\$ reflux) or ((abdomin\$ or stomach or digest\$ or intestin\$ or colon or colic\$) adj3 (pain or discomf\$))).ti,ab.
23	((((body dysmorph\$ or body image) adj2 disorder?) or dysmorphophobi?).ti,ab.
24	((fail\$ or falter\$) adj3 (thriv\$ or weight or grow\$)).ti,ab.
25	or/5-24
26	PSYCHOTHERAPY.sh,kw.
27	exp BEHAVIOR THERAPY/ or BEHAVIOR THERAPY.kw.
28	COGNITIVE THERAPY.sh,kw.
29	COUNSELING/ or DIRECTIVE COUNSELING/

#	Searches
30	FAMILY THERAPY.sh,kw.
31	ADAPTATION, PSYCHOLOGICAL/
32	(COUNSELING or ADAPTIVE BEHAVIOR or DIRECTIVE COUNSELING).kw.
33	(behavi?r\$ or counsel\$ or coach\$ or psychotherap\$ or psycho therap\$ or advis\$ or advi?e\$ or psycholog\$).ti,ab.
34	((behavi\$ or cognit\$) adj3 (technique? or therap\$ or psychotherap\$)).ti,ab.
35	CBT.ti,ab.
36	(mindfulness or relax\$ or meditat\$ or cope? or coping).ti,ab.
37	(psychoeducation\$ or psycho education\$).ti,ab.
38	or/26-37
39	exp NUTRITION THERAPY/
40	exp DIET THERAPY/
41	DIETETICS/
42	(DIET THERAPY or NUTRITIONAL COUNSELING or DIETETICS).kw.
43	((diet\$ or nutrition\$ or eat\$ or feed\$) adj (therap\$ or program\$ or advi?e\$ or advis\$ or support\$ or modif\$ or chang\$)).ti,ab.
44	SNACKS/ or FAST FOOD.kw.
45	(snack\$ or fastfood or fast food).ti,ab.
46	exp DIET, HIGH-FAT/
47	DIETARY FATS/
48	ENERGY INTAKE/
49	DIETARY PROTEINS/
50	DIETARY CARBOHYDRATES/
51	VITAMINS/
52	(LIPID DIET or FAT INTAKE or CALORIC INTAKE or CARBOHYDRATE DIET or PROTEIN INTAKE).kw.
53	((fat\$ or lipid\$ or energ\$ or calori\$ or oral or nutrition\$ or protein? or carbohydrate? or vitamin\$) adj3 (intake or diet\$ or food\$ or meal?)).ti,ab.
54	or/39-53
55	DIETARY SUPPLEMENTS/ or DIET SUPPLEMENTATION.kw.
56	FOOD, FORTIFIED/ or ELEMENTAL DIET.kw.
57	FOOD, FORMULATED/
58	((oral or nutrition\$ or calori\$ or diet\$ or energy or protein) adj2 supplement\$).ti,ab.
59	(supplement\$ adj2 feed\$).ti,ab.
60	prescri\$ feed\$.ti,ab.
61	((food or fed) adj2 (fortifi\$ or formulat\$)).ti,ab.
62	energy drink\$.ti,ab.
63	((oral or nutrition\$ or calori\$) adj3 (enhanc\$ or increas\$)).ti,ab.
64	elemental diet.ti,ab.
65	or/55-64
66	exp ENTERAL NUTRITION/ or ENTERIC FEEDING.kw.
67	((enteral\$ or enteric\$ or intragastric\$ or intra gastric\$ or nasogastric\$ or naso gastric\$ or intrainestinal\$ or intra intestinal\$ or tube) adj3 (feed\$ or fed)).ti,ab.
68	GASTROSTOMY.sh,kw.
69	JEJUNOSTOMY.sh,kw.
70	INTUBATION, GASTROINTESTINAL/
71	DIGESTIVE TRACT INTUBATION.kw.

#	Searches
72	(gastrostom\$ or jejunostom\$ or gastrojejunostom\$ or gastro jejunostom\$).ti,ab.
73	or/66-72
74	FEEDING BEHAVIOR.sh,kw.
75	FOOD HABITS/
76	((eat\$ or feed\$ or food or diet\$) adj (pattern\$ or behavio?r\$ or habit?)).ti,ab.
77	(meal\$ adj3 (manag\$ or timing or regular)).ti,ab.
78	or/74-77
79	exp APPETITE STIMULANTS/
80	APPETITE STIMULANT.kw.
81	CYPROHEPTADINE.sh,kw.
82	MEGESTROL ACETATE.sh,kw.
83	appetite stimulan\$.ti,ab.
84	(cyproheptadine or megace or maygace or megestrol).ti,ab,mp.
85	or/79-84
86	54 or 65 or 73 or 78 or 85
87	4 and 86
88	4 and 25 and 38
89	87 or 88
90	CYSTIC FIBROSIS/dh [DIET THERAPY]
91	89 or 90
92	limit 91 to yr="1997 -Current"

#### E.11.4 Database: Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects

Last searched on **EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to January 05, 2017, **EBM Reviews - Database of Abstracts of Reviews of Effects** 1st Quarter 2015 on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS.kw.
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab,kw.
3	mucov\$.ti,ab,kw.
4	1 or 2 or 3
5	NUTRITION DISORDERS.kw.
6	"FEEDING AND EATING DISORDERS OF CHILDHOOD".kw.
7	"FEEDING AND EATING DISORDERS".kw.
8	(FEEDING DISORDER or MALNUTRITION or PROTEIN CALORIE MALNUTRITION or NUTRITIONAL DEFICIENCY or OVERNUTRITION).kw.
9	(EATING DISORDER or ANOREXIA NERVOSA or FOOD AVERSION).kw.
10	NUTRITIONAL STATUS.kw.
11	BODY DYSMORPHIC DISORDERS.kw.
12	CHILD NUTRITIONAL PHYSIOLOGICAL PHENOMENA.kw.
13	CHILD NUTRITION.kw.
14	FAILURE TO THRIVE.kw.
15	GROWTH DISORDERS.kw.
16	GASTROESOPHAGEAL REFLUX.kw.
17	ABDOMINAL PAIN.kw.

#	Searches
18	(malnutrition\$ or malnourish\$ or undernutrition\$ or under nutrition\$ or undernourish\$ or under nourish\$ or overnutrition\$ or over nutrition\$ or overnourish\$ or over nourish\$ or malabsorb\$ or mal?absorb\$).ti,ab.
19	avitaminosis.ti,ab.
20	(underweight? or under weight? or overweight? or over weight? or obes\$).ti,ab.
21	((nutrition\$ or nourish\$ or grow\$ or vitamin? or weight or diet\$ or eat\$) adj3 (disorder? or deficien\$ or poor or status)).ti,ab.
22	(appetite or anorexia or (gord or gerd or acid reflux gastro??esopag\$ reflux or esopag\$ reflux or oesophag\$ reflux) or ((abdomin\$ or stomach or digest\$ or intestin\$ or colon or colic\$) adj3 (pain or discomf\$))).ti,ab.
23	((body dysmorph\$ or body image) adj2 disorder?) or dysmorphophobi?).ti,ab.
24	((fail\$ or falter\$) adj3 (thriv\$ or weight or grow\$)).ti,ab.
25	or/5-24
26	PSYCHOTHERAPY.kw.
27	BEHAVIOR THERAPY.kw.
28	COGNITIVE THERAPY.kw.
29	(COUNSELING or DIRECTIVE COUNSELING).kw.
30	FAMILY THERAPY.kw.
31	ADAPTATION, PSYCHOLOGICAL.kw.
32	ADAPTIVE BEHAVIOR.kw.
33	(behavi?r\$ or counsel\$ or coach\$ or psychotherap\$ or psycho therap\$ or advis\$ or advi?e\$ or psycholog\$).ti,ab.
34	((behavi\$ or cognit\$) adj3 (technique? or therap\$ or psychotherap\$)).ti,ab.
35	CBT.ti,ab.
36	(mindfulness or relax\$ or meditat\$ or cope? or coping).ti,ab.
37	(psychoeducation\$ or psycho education\$).ti,ab.
38	or/26-37
39	NUTRITION THERAPY.kw.
40	DIET THERAPY.kw.
41	DIETETICS.kw.
42	NUTRITIONAL COUNSELING.kw.
43	((diet\$ or nutrition\$ or eat\$ or feed\$) adj (therap\$ or program\$ or advi?e\$ or advis\$ or support\$ or modif\$ or chang\$)).ti,ab.
44	SNACKS.kw.
45	(snack\$ or fastfood or fast food).ti,ab.
46	DIET, HIGH-FAT.kw.
47	DIETARY FATS.kw.
48	ENERGY INTAKE.kw.
49	DIETARY PROTEINS.kw.
50	DIETARY CARBOHYDRATES.kw.
51	VITAMINS.kw.
52	((fat\$ or lipid\$ or energ\$ or calor\$ or oral or nutrition\$ or protein? or carbohydrate? or vitamin\$) adj3 (intake or diet\$ or food\$ or meal?)).ti,ab.
53	or/39-52
54	DIETARY SUPPLEMENTS.kw.
55	FOOD, FORTIFIED.kw.
56	FOOD, FORMULATED.kw.

#	Searches
57	((oral or nutrition\$ or calori\$ or diet\$ or energy or protein) adj2 supplement\$).ti,ab.
58	(supplement\$ adj2 feed\$).ti,ab.
59	prescri\$ feed\$.ti,ab.
60	((food or fed) adj2 (fortifi\$ or formulat\$)).ti,ab.
61	energy drink\$.ti,ab.
62	((oral or nutrition\$ or calori\$) adj3 (enhanc\$ or increas\$)).ti,ab.
63	elemental diet.ti,ab.
64	or/54-63
65	ENTERAL NUTRITION.kw.
66	((enteral\$ or enteric\$ or intragastric\$ or intra gastric\$ or nasogastric\$ or naso gastric\$ or intrainestinal\$ or intra intestinal\$ or tube) adj3 (feed\$ or fed)).ti,ab.
67	GASTROSTOMY.kw.
68	JEJUNOSTOMY.kw.
69	INTUBATION, GASTROINTESTINAL.kw.
70	DIGESTIVE TRACT INTUBATION.kw.
71	(gastrostom\$ or jejunostom\$ or gastrojejunostom\$ or gastro jejunostom\$).ti,ab.
72	or/65-71
73	FEEDING BEHAVIOR,kw.
74	FOOD HABITS.kw.
75	((eat\$ or feed\$ or food or diet\$) adj (pattern\$ or behavio?r\$ or habit?)).ti,ab.
76	(meal\$ adj3 (manag\$ or timing or regular)).ti,ab.
77	or/73-76
78	APPETITE STIMULANT?.kw.
79	(cyproheptadine or megace or maygace or megestrol).ti,ab,mp.
80	CYPROHEPTADINE.kw.
81	MEGESTROL ACETATE.kw.
82	appetite stimulan\$.ti,ab.
83	or/78-82
84	53 or 64 or 72 or 77 or 83
85	4 and 84
86	4 and 25 and 38
87	85 or 86

### E.11.5 Database: Health Technology Assessment

Last searched on **EBM Reviews - Health Technology Assessment 4th Quarter 2016** on 10<sup>th</sup> January 2017

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).mp.
3	mucov\$.mp.
4	1 or 2 or 3
5	exp NUTRITION DISORDERS/
6	exp "FEEDING AND EATING DISORDERS OF CHILDHOOD"/
7	exp "FEEDING AND EATING DISORDERS"/
8	exp NUTRITIONAL STATUS/

#	Searches
9	BODY DYSMORPHIC DISORDERS/
10	exp CHILD NUTRITIONAL PHYSIOLOGICAL PHENOMENA/
11	exp FAILURE TO THRIVE/
12	exp GROWTH DISORDERS/
13	GASTROESOPHAGEAL REFLUX/
14	exp ABDOMINAL PAIN/
15	(malnutrition\$ or malnourish\$ or undernutrition\$ or under nutrition\$ or undernourish\$ or under nourish\$ or overnutrition\$ or over nutrition\$ or overnourish\$ or over nourish\$ or malabsorb\$ or mal?absorb\$).tw.
16	avitaminosis.tw.
17	(underweight? or under weight? or overweight? or over weight? or obes\$).tw.
18	((nutrition\$ or nourish\$ or grow\$ or vitamin? or weight or diet\$ or eat\$) adj3 (disorder? or deficien\$ or poor or status)).tw.
19	(appetite or anorexia or (gord or gerd or acid reflux gastro??esopag\$ reflux or esopag\$ reflux or oesophag\$ reflux) or ((abdomin\$ or stomach or digest\$ or intestin\$ or colon or colic\$) adj3 (pain or discomf\$))).tw.
20	((body dysmorph\$ or body image) adj2 disorder?) or dysmorphophobi?).tw.
21	((fail\$ or falter\$) adj3 (thriv\$ or weight or grow\$)).tw.
22	or/5-21
23	PSYCHOTHERAPY/
24	exp BEHAVIOR THERAPY/
25	COGNITIVE THERAPY/
26	COUNSELING/ or DIRECTIVE COUNSELING/
27	FAMILY THERAPY/
28	ADAPTATION, PSYCHOLOGICAL/
29	(behavi?r\$ or counsel\$ or coach\$ or psychotherap\$ or psycho therap\$ or advis\$ or advi?e\$ or psycholog\$).tw.
30	((behavi\$ or cognit\$) adj3 (technique? or therap\$ or psychotherap\$)).tw.
31	CBT.tw.
32	(mindfulness or relax\$ or meditat\$ or cope? or coping).tw.
33	(psychoeducation\$ or psycho education\$).tw.
34	or/23-33
35	exp NUTRITION THERAPY/
36	exp DIET THERAPY/
37	DIETETICS/
38	((diet\$ or nutrition\$ or eat\$ or feed\$) adj (therap\$ or program\$ or advi?e\$ or advis\$ or support\$ or modif\$ or chang\$)).tw.
39	SNACKS/
40	(snack\$ or fastfood or fast food).tw.
41	exp DIET, HIGH-FAT/
42	DIETARY FATS/
43	ENERGY INTAKE/
44	DIETARY PROTEINS/
45	DIETARY CARBOHYDRATES/
46	VITAMINS/
47	((fat\$ or lipid\$ or energ\$ or calori\$ or oral or nutrition\$ or protein? or carbohydrate? or vitamin\$) adj3 (intake or diet\$ or food\$ or meal?)).tw.

#	Searches
48	or/35-47
49	DIETARY SUPPLEMENTS/
50	FOOD, FORTIFIED/
51	FOOD, FORMULATED/
52	((oral or nutrition\$ or calori\$ or diet\$ or energy or protein) adj2 supplement\$).tw.
53	(supplement\$ adj2 feed\$).tw.
54	prescri\$ feed\$.tw.
55	((food or fed) adj2 (fortifi\$ or formulat\$)).tw.
56	energy drink\$.tw.
57	((oral or nutrition\$ or calori\$) adj3 (enhanc\$ or increas\$)).tw.
58	elemental diet.tw.
59	or/49-58
60	exp ENTERAL NUTRITION/
61	((enteral\$ or enteric\$ or intragastric\$ or intra gastric\$ or nasogastric\$ or naso gastric\$ or intrainestinal\$ or intra intestinal\$ or tube) adj3 (feed\$ or fed)).tw.
62	GASTROSTOMY/
63	JEJUNOSTOMY/
64	INTUBATION, GASTROINTESTINAL/
65	(gastrostom\$ or jejunostom\$ or gastrojejunostom\$ or gastro jejunostom\$).tw.
66	or/60-65
67	FEEDING BEHAVIOR/
68	FOOD HABITS/
69	((eat\$ or feed\$ or food or diet\$) adj (pattern\$ or behavio?r\$ or habit?)).tw.
70	(meal\$ adj3 (manag\$ or timing or regular)).tw.
71	or/67-70
72	exp APPETITE STIMULANTS/
73	CYPROHEPTADINE/
74	MEGESTROL ACETATE/
75	appetite stimulan\$.tw.
76	(cyproheptadine or megace or maygace or megestrol).mp.
77	or/72-76
78	48 or 59 or 66 or 71 or 77
79	4 and 78
80	4 and 22 and 34
81	79 or 80
82	CYSTIC FIBROSIS/dh [DIET THERAPY]
83	81 or 82

### E.11.6 Database: Embase

Last searched on **Embase** 1974 to 2017 Week 01 on 4<sup>th</sup> January 2017.

#	Searches
1	SYSTEMATIC REVIEW/
2	META-ANALYSIS/
3	(meta analy* or metanaly* or metaanaly*).ti,ab.
4	((systematic or evidence) adj2 (review* or overview*)).ti,ab.

#	Searches
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	((pool* or combined) adj2 (data or trials or studies or results)).ab.
10	cochrane.jw.
11	or/1-10
12	random*.ti,ab.
13	factorial*.ti,ab.
14	(crossover* or cross over*).ti,ab.
15	((doubl* or singl*) adj blind*).ti,ab.
16	(assign* or allocat* or volunteer* or placebo*).ti,ab.
17	CROSSOVER PROCEDURE/
18	SINGLE BLIND PROCEDURE/
19	RANDOMIZED CONTROLLED TRIAL/
20	DOUBLE BLIND PROCEDURE/
21	or/12-20
22	or/11,21
23	OBSERVATIONAL STUDY/
24	(observat\$ adj3 (study or studies)).ti,ab.
25	COHORT ANALYSIS/
26	(cohort adj3 (study or studies)).ti,ab.
27	(cohort adj3 analy\$).ti,ab.
28	FOLLOW UP/
29	(follow\$ up adj3 (study or studies)).ti,ab.
30	LONGITUDINAL STUDY/
31	longitudinal\$.ti,ab.
32	RETROSPECTIVE STUDIY/
33	retrospective\$.ti,ab.
34	CROSS-SECTIONAL STUDY/
35	cross-sectional\$.ti,ab.
36	CASE CONTROL STUDY/
37	case control.ti,ab.
38	or/23-37
39	CYSTIC FIBROSIS/
40	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
41	mucov\$.ti,ab.
42	39 or 40 or 41
43	NUTRITION DISORDER/
44	FEEDING DISORDER/
45	MALNUTRITION/
46	PROTEIN CALORIE MALNUTRITION/
47	NUTRITIONAL DEFICIENCY/

#	Searches
48	OVERNUTRITION/
49	EATING DISORDER/ or ANOREXIA NERVOSA/ or FOOD AVERSION/
50	NUTRITIONAL STATUS/
51	BODY DYSMORPHIC DISORDER/
52	CHILD NUTRITION/
53	FAILURE TO THRIVE/
54	GROWTH DISORDER/
55	GASTROESOPHAGEAL REFLUX/
56	ABDOMINAL PAIN/
57	(malnutrition\$ or malnourish\$ or undernutrition\$ or under nutrition\$ or undernourish\$ or under nourish\$ or overnutrition\$ or over nutrition\$ or overnourish\$ or over nourish\$ or malabsorb\$ or mal?absorb\$).ti,ab.
58	avitaminosis.ti,ab.
59	(underweight? or under weight? or overweight? or over weight? or obes\$).ti,ab.
60	((nutrition\$ or nourish\$ or grow\$ or vitamin? or weight or diet\$ or eat\$) adj3 (disorder? or deficien\$ or poor or status)).ti,ab.
61	(appetite or anorexia or (gord or gerd or acid reflux gastro??esopag\$ reflux or esopag\$ reflux or oesophag\$ reflux) or ((abdomin\$ or stomach or digest\$ or intestin\$ or colon or colic\$) adj3 (pain or discomf\$))).ti,ab.
62	((body dysmorph\$ or body image) adj2 disorder?) or dysmorphophobi?).ti,ab.
63	((fail\$ or falter\$) adj3 (thriv\$ or weight or grow\$)).ti,ab.
64	or/43-63
65	PSYCHOTHERAPY/
66	BEHAVIOR THERAPY/
67	COGNITIVE THERAPY/
68	COUNSELING/
69	FAMILY THERAPY/
70	ADAPTIVE BEHAVIOR/
71	DIRECTIVE COUNSELING/
72	(behavi?r\$ or counsel\$ or coach\$ or psychotherap\$ or advis\$ or advi?e\$ or psycholog\$).ti,ab.
73	((behavi\$ or cognit\$) adj3 (technique? or therap\$ or psychotherap\$)).ti,ab.
74	CBT.ti,ab.
75	(mindfulness or relax\$ or meditat\$ or cope? or coping).ti,ab.
76	(psychoeducation\$ or psycho education\$).ti,ab.
77	or/65-76
78	DIET THERAPY/
79	NUTRITIONAL COUNSELING/
80	DIETETICS/
81	((diet\$ or nutrition\$ or eat\$ or feed\$) adj (therap\$ or program\$ or advi?e\$ or advis\$ or support\$ or modif\$ or chang\$)).ti,ab.
82	FAST FOOD/
83	(snack\$ or fastfood or fast food).ti,ab.
84	LIPID DIET/
85	FAT INTAKE/
86	CALORIC INTAKE/
87	CARBOHYDRATE DIET/

#	Searches
88	PROTEIN INTAKE/
89	((fat\$ or lipid\$ or energ\$ or calori\$ or oral or nutrition\$ or protein? or carbohydrate? or vitamin\$) adj3 (intake or diet\$ or food\$ or meal?)).ti,ab.
90	or/78-89
91	DIET SUPPLEMENTATION/
92	ELEMENTAL DIET/
93	((oral or nutrition\$ or calori\$ or diet\$ or energy or protein) adj2 supplement\$).ti,ab.
94	(supplement\$ adj2 feed\$).ti,ab.
95	prescri\$ feed\$.ti,ab.
96	((food or fed) adj2 (fortifi\$ or formulat\$)).ti,ab.
97	energy drink\$.ti,ab.
98	((oral or nutrition\$ or calori\$) adj3 (enhanc\$ or increas\$)).ti,ab.
99	or/91-98
100	ENTERIC FEEDING/
101	((enteral\$ or enteric\$ or intragastric\$ or intra gastric\$ or nasogastric\$ or naso gastric\$ or intrainestinal\$ or intra intestinal\$ or tube) adj3 (feed\$ or fed)).ti,ab.
102	GASTROSTOMY/
103	JEJUNOSTOMY/
104	DIGESTIVE TUBE/
105	DIGESTIVE TRACT INTUBATION/
106	(gastrostom\$ or jejunostom\$ or gastrojejunostom\$ or gastro jejunostom\$).ti,ab.
107	or/100-106
108	FEEDING BEHAVIOR/
109	((eat\$ or feed\$ or food or diet\$) adj (pattern\$ or behavio?r\$ or habit?)).ti,ab.
110	(meal\$ adj3 (manag\$ or timing or regular)).ti,ab.
111	or/108-110
112	APPETITE STIMULANT/
113	CYPROHEPTADINE/
114	MEGESTROL ACETATE/
115	appetite stimulan\$.ti,ab.
116	(cyproheptadine or megace or maygace or megestrol).ti,ab,mp.
117	or/112-116
118	90 or 99 or 107 or 111 or 117
119	42 and 118
120	42 and 64 and 77
121	119 or 120
122	limit 121 to english language
123	limit 122 to yr="1997 -Current"
124	letter.pt. or LETTER/
125	note.pt.
126	editorial.pt.
127	CASE REPORT/ or CASE STUDY/
128	(letter or comment*).ti.
129	or/124-128
130	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
131	129 not 130

#	Searches
132	ANIMAL/ not HUMAN/
133	NONHUMAN/
134	exp ANIMAL EXPERIMENT/
135	exp EXPERIMENTAL ANIMAL/
136	ANIMAL MODEL/
137	exp RODENT/
138	(rat or rats or mouse or mice).ti.
139	or/131-138
140	123 not 139
141	22 and 140
142	38 and 140
143	141 or 142

## E.12 In people with cystic fibrosis, what is the effectiveness of enzyme replacement therapy in the treatment of exocrine pancreatic insufficiency?

### E.12.1 Database: Medline

Last searched on **Ovid MEDLINE(R)** 1946 to October Week 3 2016 on 1<sup>st</sup> November 2016.

#	Searches
1	META-ANALYSIS/
2	META-ANALYSIS AS TOPIC/
3	(meta analy* or metanaly* or metaanaly*).ti,ab.
4	((systematic* or evidence*) adj2 (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	or/1-9
11	randomized controlled trial.pt.
12	controlled clinical trial.pt.
13	pragmatic clinical trial.pt.
14	randomi#ed.ab.
15	placebo.ab.
16	randomly.ab.
17	CLINICAL TRIALS AS TOPIC/
18	trial.ti.
19	or/11-18
20	or/10,19
21	CYSTIC FIBROSIS/
22	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.

#	Searches
23	mucov\$.ti,ab.
24	or/21-23
25	exp PANCREATIC EXTRACTS/
26	exp LIPASE/
27	(pancrea\$ adj (enzyme? or extract?) adj3 (therap\$ or treatment? or replacement\$ or supplement\$ or preparation? or formula\$ or product?)).ti,ab.
28	PERT.ti,ab.
29	(lipase or pancreatolipase or pancreatin or panteric or pancrelipase or pan#reon or creon or kreon or pan#rex or nutrizym or pan#rease or liprotamase or pan##trat).mp.
30	or/25-29
31	and/24,30
32	limit 31 to english language
33	LETTER/
34	EDITORIAL/
35	NEWS/
36	exp HISTORICAL ARTICLE/
37	ANECDOTES AS TOPIC/
38	COMMENT/
39	CASE REPORT/
40	(letter or comment* or abstracts).ti.
41	or/33-40
42	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
43	41 not 42
44	ANIMALS/ not HUMANS/
45	exp ANIMALS, LABORATORY/
46	exp ANIMAL EXPERIMENTATION/
47	exp MODELS, ANIMAL/
48	exp RODENTIA/
49	(rat or rats or mouse or mice).ti.
50	or/43-49
51	32 not 50
52	and/20,51

### E.12.2 Database: Medline In-Process & Other Non-Indexed Citations

Last searched on **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations** October 31, 2016 on 1<sup>st</sup> November 2016.

#	Searches
1	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
2	mucov\$.ti,ab.
3	or/1-2
4	(pancrea\$ adj (enzyme? or extract?) adj3 (therap\$ or treatment? or replacement\$ or supplement\$ or preparation? or formula\$ or product?)).ti,ab.
5	PERT.ti,ab.
6	(lipase or pancreatolipase or pancreatin or panteric or pancrelipase or pan#reon or creon or kreon or pan#rex or nutrizym or pan#rease or liprotamase or pan##trat).mp.
7	or/4-6

#	Searches
8	and/3,7

### E.12.3 Database: Cochrane Central Register of Controlled Trials

Last searched on **EBM Reviews - Cochrane Central Register of Controlled Trials** September 2016 on 1<sup>st</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab,kw.
3	Cochrane Cystic Fibrosis Group.gc.
4	mucov\$.ti,ab.
5	or/1-4
6	exp PANCREATIC EXTRACTS/
7	PANCREAS EXTRACT.kw.
8	exp LIPASE/
9	(pancrea\$ adj (enzyme? or extract?)).ti,ab.
10	PERT.ti,ab.
11	(lipase or pancreatolipase or pancreatin or panteric or pancrelipase or pan#reon or creon or kreon or pan#rex or nutrizym or pan#rease or liprotamase or pan##trat).mp.
12	or/6-11
13	and/5,12

### E.12.4 Database: Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects

Last searched on **EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to October 26, 2016, **EBM Reviews - Database of Abstracts of Reviews of Effects** 1st Quarter 2015 on 1<sup>st</sup> December 2015.

#	Searches
1	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).tw,tx,kw.
2	mucov\$.tw,tx.
3	or/1-2
4	(PANCREATIC EXTRACTS or PANCREAS EXTRACT or PANCREAS ENZYME).kw.
5	(pancrea\$ adj (enzyme? or extract?) adj3 (therap\$ or treatment? or replacement\$ or supplement\$ or preparation? or formula\$ or product?)).tw,tx.
6	PERT.tw,tx.
7	(lipase or pancreatolipase or pancreatin or panteric or pancrelipase or pan#reon or creon or kreon or pan#rex or nutrizym or pan#rease or liprotamase or pan##trat).mp.
8	or/4-7
9	and/3,8

### E.12.5 Database: Health Technology Assessment

Last searched on **EBM Reviews - Health Technology Assessment 3<sup>rd</sup> Quarter 2016** on 1<sup>st</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).tw.

#	Searches
3	mucov\$.tw.
4	or/1-3
5	exp PANCREATIC EXTRACTS/
6	exp LIPASE/
7	(pancrea\$ adj (enzyme? or extract?) adj3 (therap\$ or treatment? or replacement\$ or supplement\$ or preparation? or formula\$ or product?)).tw.
8	PERT.tw.
9	(lipase or pancreatolipase or pancreatin or panteric or pancrelipase or pan#reon or creon or kreon or pan#rex or nutrizym or pan#rease or lipotamase or pan##trat).tw,hw.
10	or/5-9
11	and/4,10

### E.12.6 Database: Embase

Last searched on **Embase** 1974 to 2016 Week 44 on 1<sup>st</sup> November 2016.

#	Searches
1	SYSTEMATIC REVIEW/
2	META-ANALYSIS/
3	(meta analy* or metanaly* or metaanaly*).ti,ab.
4	((systematic or evidence) adj2 (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 psychlit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
9	((pool* or combined) adj2 (data or trials or studies or results)).ab.
10	cochrane.jw.
11	or/1-10
12	random*.ti,ab.
13	factorial*.ti,ab.
14	(crossover* or cross over*).ti,ab.
15	((doubl* or singl*) adj blind*).ti,ab.
16	(assign* or allocat* or volunteer* or placebo*).ti,ab.
17	CROSSOVER PROCEDURE/
18	SINGLE BLIND PROCEDURE/
19	RANDOMIZED CONTROLLED TRIAL/
20	DOUBLE BLIND PROCEDURE/
21	or/12-20
22	or/11,21
23	CYSTIC FIBROSIS/
24	mucov\$.ti,ab.
25	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
26	or/23-25
27	PANCREAS EXTRACT/ or PANCREAS ENZYME/
28	TRIACYLGLYCEROL LIPASE/

#	Searches
29	PANCREATIN/
30	PANZYTRAT/
31	PANCRELIPASE/
32	LIPROTAMASE/
33	(pancrea\$ adj (enzyme? or extract?) adj3 (therap\$ or treatment? or replacement\$ or supplement\$ or preparation? or formula\$ or product?)).ti,ab.
34	PERT.ti,ab.
35	(lipase or pancreatolipase or pancreatin or panteric or pancrelipase or pan#reon or creon or kreon or pan#rex or nutrizym or pan#rease or liprotamase or pan##trat).mp.
36	or/27-35
37	and/26,36
38	limit 37 to english language
39	conference abstract.pt.
40	letter.pt. or LETTER/
41	note.pt.
42	editorial.pt.
43	CASE REPORT/ or CASE STUDY/
44	(letter or comment* or abstracts).ti.
45	or/39-44
46	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
47	45 not 46
48	ANIMAL/ not HUMAN/
49	NONHUMAN/
50	exp ANIMAL EXPERIMENT/
51	exp EXPERIMENTAL ANIMAL/
52	ANIMAL MODEL/
53	exp RODENT/
54	(rat or rats or mouse or mice).ti.
55	or/47-54
56	38 not 55
57	and/22,56

## E.13 What are the effective strategies for prevention and treatment of distal ileal obstruction syndrome?

### E.13.1 Database: Medline

Last searched on **Ovid MEDLINE(R)** 1946 to December Week 1 2016 on 5<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	exp INTESTINAL OBSTRUCTION/
6	CONSTIPATION/
7	((ileal or il#um or intestin\$ or gastrointestin\$ or bowel or colon\$) adj3 (obstruct\$ or

#	Searches
	intertia or dysmotil\$ or aton\$ or paraly\$).ti,ab.
8	(ileus or DIOS).ti,ab.
9	(constipat\$ or obstipat\$ or dyschezi\$).ti,ab.
10	or/5-9
11	LAXATIVES/
12	exp CATHARTICS/
13	exp POLYETHYLENE GLYCOLS/
14	LACTULOSE/
15	laxative?.ti,ab.
16	(stool? adj1 soft\$).ti,ab.
17	(cathartic? or purgative? or bowel evacuant? or bowel preparation solution?).ti,ab.
18	(polyethylene glycol? or macrogol? or movicol or laxido or molaxole or klean prep or golytely).mp.
19	(lactulose or duphalac or amivalex or normase or lactugal or laevolac).mp.
20	(senna or sen?kot or sennokot or manevac).mp.
21	(sodium picosul\$ or dulcosan or guttalex or laxober\$ or picolax).mp.
22	(bisacodyl or laxbene or durolax or dulcolax or bicol or laxagetten).mp.
23	FLUID THERAPY/
24	((oral or therap\$) adj3 (rehydrat\$ or hydrat\$ or fluid?)).ti,ab.
25	ENEMA/
26	enema\$.ti,ab.
27	PHOSPHATES/
28	sodium phosphate?.mp.
29	DIATRIZOATE MEGLUMINE/
30	(diatrizoate or meglumin? or gastrogra??in).mp.
31	ACETYLCYSTEINE/
32	(acetylcysteine or nacetylcysteine or acetyl cysteine or nacetyl cysteine).mp.
33	THERAPEUTIC IRRIGATION/
34	((ileal or il#um or intestin\$ or gastrointestin\$ or bowel or colon\$) adj3 (lavage or irrigat\$)).ti,ab.
35	DIGESTIVE SYSTEM SURGICAL PROCEDURES/
36	LAPAROTOMY/
37	ANASTOMOSIS, SURGICAL/
38	ANASTOMOSIS, ROUX-EN-Y/
39	exp ENTEROSTOMY/
40	((ileal or il#um or intestin\$ or gastrointestin\$ or bowel or colon\$) adj3 (surg\$ or resect\$ or anastomosis)).ti,ab.
41	(laparotom\$ or entero?tom\$ or ileo?tom\$).ti,ab.
42	exp PANCREATIC EXTRACTS/
43	exp LIPASE/
44	(pancrea\$ adj (enzyme? or extract?) adj3 (therap\$ or treatment? or replacement\$ or supplement\$ or preparation? or formula\$ or product?)).ti,ab.
45	PERT.ti,ab.
46	(lipase or pancreatolipase or pancreatin or panteric or pancrelipase or pan#reon or creon or kreon or pan#rex or nutrizym or pan#rease or lipotamase or pan##trat).mp.
47	or/11-46
48	4 and 10 and 47

#	Searches
49	exp INTESTINAL OBSTRUCTION/dt, su, th [Drug Therapy, Surgery, Therapy]
50	4 and 49
51	48 or 50
52	limit 51 to english language
53	LETTER/
54	EDITORIAL/
55	NEWS/
56	exp HISTORICAL ARTICLE/
57	ANECDOTES AS TOPIC/
58	COMMENT/
59	CASE REPORT/
60	(letter or comment*).ti.
61	or/53-60
62	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
63	61 not 62
64	ANIMALS/ not HUMANS/
65	exp ANIMALS, LABORATORY/
66	exp ANIMAL EXPERIMENTATION/
67	exp MODELS, ANIMAL/
68	exp RODENTIA/
69	(rat or rats or mouse or mice).ti.
70	or/63-69
71	52 not 70

### E.13.2 Medline In-Process & Other Non-Indexed Citations

Last searched on **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations** January 04, 2017 on 5<sup>th</sup> January 2017.

#	Searches
1	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
2	mucov\$.ti,ab.
3	or/1-2
4	((ileal or il#um or intestin\$ or gastrointestin\$ or bowel or colon\$) adj3 (obstruct\$ or inertia or dysmotil\$ or aton\$ or paraly\$)).ti,ab.
5	(ileus or DIOS).ti,ab.
6	(constipat\$ or obstipat\$ or dyschezi\$).ti,ab.
7	or/4-6
8	laxative?.ti,ab.
9	(stool? adj1 soft\$).ti,ab.
10	(cathartic? or purgative? or bowel evacuant? or bowel preparation solution?).ti,ab.
11	(polyethylene glycol? or macrogol? or movicol or laxido or molaxole or klean prep or golytely).mp.
12	(lactulose or duphalac or amivalex or normase or lactugal or laevolac).mp.
13	(senna or sen?kot or sennokot or manevac).mp.
14	(sodium picosul\$ or dulcosan or guttalex or laxober\$ or picolax).mp.
15	(bisacodyl or laxbene or durolax or dulcolax or bicol or laxagetten).mp.
16	((oral or therap\$) adj3 (rehydrat\$ or hydrat\$ or fluid?)).ti,ab.

#	Searches
17	enema\$.ti,ab.
18	phosphate?.mp.
19	(diatrizoate or meglumin? or gastrogra??in).mp.
20	(acetylcysteine or nacetyl cysteine or acetyl cysteine or nacetyl cysteine).mp.
21	((ileal or il#um or intestin\$ or gastrointestin\$ or bowel or colon\$) adj3 (lavage or irrigat\$)).ti,ab.
22	((ileal or il#um or intestin\$ or gastrointestin\$ or bowel or colon\$) adj3 (surg\$ or resect\$ or anastomosis)).ti,ab.
23	(laparotom\$ or entero?tom\$ or ileo?tom\$).ti,ab.
24	(pancrea\$ adj (enzyme? or extract?) adj3 (therap\$ or treatment? or replacement\$ or supplement\$ or preparation? or formula\$ or product?)).ti,ab.
25	PERT.ti,ab.
26	(lipase or pancreatolipase or pancreatin or panteric or pancrelipase or pan#reon or creon or kreon or pan#rex or nutrizym or pan#rease or liprotamase or pan##trat).mp.
27	or/8-26
28	3 and 7 and 27

### E.13.3 Database: Cochrane Central Register of Controlled Trials

Last searched on **EBM Reviews - Cochrane Central Register of Controlled Trials**  
November 2016 on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab,kw.
3	mucov\$.ti,ab.
4	or/1-3
5	exp INTESTINAL OBSTRUCTION/
6	CONSTIPATION/
7	((ileal or il#um or intestin\$ or gastrointestin\$ or bowel or colon\$) adj3 (obstruct\$ or inertia or dysmotil\$ or aton\$ or paraly\$)).ti,ab,kw.
8	(ileus or DIOS).ti,ab.
9	(constipat\$ or obstipat\$ or dyschezi\$).ti,ab,kw.
10	or/5-9
11	LAXATIVES/
12	exp CATHARTICS/
13	exp POLYETHYLENE GLYCOLS/
14	LACTULOSE/
15	laxative?.ti,ab,kw.
16	(stool? adj1 soft\$).ti,ab.
17	(cathartic? or purgative? or bowel evacuant? or bowel preparation solution?).ti,ab,kw.
18	(polyethylene glycol? or macrogol? or movicol or laxido or molaxole or klean prep or golytely).mp,kw.
19	(lactulose or duphalac or amivalex or normase or lactugal or laevolac).mp,kw.
20	(senna or sen?kot or sennokot or manevac).mp.
21	(sodium picosul\$ or dulcosan or guttalax or laxober\$ or picolax).mp.
22	(bisacodyl or laxbene or durolax or dulcolax or bicol or laxagetten).mp.
23	FLUID THERAPY/
24	((oral or therap\$) adj3 (rehydrat\$ or hydrat\$ or fluid?)).ti,ab,kw.

#	Searches
25	ENEMA/
26	enema\$.ti,ab,kw.
27	PHOSPHATES/
28	phosphate?.mp.
29	DIATRIZOATE MEGLUMINE/
30	(diatrizoate or meglumin? or gastrogra??in).mp,kw.
31	ACETYLCYSTEINE/
32	(acetylcysteine or nacetyl cysteine or acetyl cysteine or nacetyl cysteine).mp,kw.
33	THERAPEUTIC IRRIGATION/
34	((ileal or il#um or intestin\$ or gastrointestin\$ or bowel or colon\$) adj3 (lavage or irrigat\$)).ti,ab,kw.
35	DIGESTIVE SYSTEM SURGICAL PROCEDURES/
36	LAPAROTOMY/
37	ANASTOMOSIS, SURGICAL/
38	ANASTOMOSIS, ROUX-EN-Y/
39	exp ENTEROSTOMY/
40	((ileal or il#um or intestin\$ or gastrointestin\$ or bowel or colon\$) adj3 (surg\$ or resect\$ or anastomosis)).ti,ab,kw.
41	(laparotom\$ or entero?tom\$ or ileo?tom\$).ti,ab,kw.
42	exp PANCREATIC EXTRACTS/
43	exp LIPASE/
44	(pancrea\$ adj (enzyme? or extract?) adj3 (therap\$ or treatment? or replacement\$ or supplement\$ or preparation? or formula\$ or product?)).ti,ab,kw.
45	PERT.ti,ab.
46	(lipase or pancreatolipase or pancreatin or panteric or pancrelipase or pan#reon or creon or kreon or pan#rex or nutrizym or pan#rease or lipotamase or pan##trat).mp,kw.
47	or/11-46
48	4 and 10 and 47
49	exp INTESTINAL OBSTRUCTION/dt, su, th [Drug Therapy, Surgery, Therapy]
50	4 and 49
51	48 or 50

#### E.13.4 Database: Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects

Last searched on **EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to January 05, 2017, **EBM Reviews - Database of Abstracts of Reviews of Effects 1st Quarter 2015** on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS.kw.
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).mp.
3	mucov\$.mp.
4	or/1-3
5	INTESTINAL OBSTRUCTION.kw.
6	CONSTIPATION.kw.
7	((ileal or il#um or intestin\$ or gastrointestin\$ or bowel or colon\$) adj3 (obstruct\$ or inertia or dysmotil\$ or aton\$ or paraly\$)).mp.
8	(ileus or DIOS).mp.

#	Searches
9	(constipat\$ or obstipat\$ or dyschezi\$).mp.
10	or/5-9
11	LAXATIVES.kw.
12	CATHARTICS.kw.
13	POLYETHYLENE GLYCOLS.kw.
14	LACTULOSE.kw.
15	laxative?.mp.
16	(stool? adj1 soft\$).mp.
17	(cathartic? or purgative? or bowel evacuant? or bowel preparation solution?).mp.
18	(polyethylene glycol? or macrogol? or movicol or laxido or molaxole or klean prep or golytely).mp.
19	(lactulose or duphalac or amivalex or normase or lactugal or laevolac).mp.
20	(senna or sen?kot or sennokot or manevac).mp.
21	(sodium picosul\$ or dulcosan or guttalax or laxober\$ or picolax).mp.
22	(bisacodyl or laxbene or durolax or dulcolax or bicol or laxagetten).mp.
23	FLUID THERAPY.kw.
24	((oral or therap\$) adj3 (rehydrat\$ or hydrat\$ or fluid?)).mp.
25	ENEMA.kw.
26	enema\$.mp.
27	PHOSPHATES.kw.
28	phosphate?.mp.
29	DIATRIZOATE MEGLUMINE.kw.
30	(diatrizoate or meglumin? or gastrogra??in).mp.
31	ACETYLCYSTEINE.kw.
32	(acetylcysteine or nacetylcysteine or acetyl cysteine or nacetyl cysteine).mp.
33	THERAPEUTIC IRRIGATION.kw.
34	((ileal or il#um or intestin\$ or gastrointestin\$ or bowel or colon\$) adj3 (lavage or irrigat\$)).mp.
35	DIGESTIVE SYSTEM SURGICAL PROCEDURES.kw.
36	LAPAROTOMY.kw.
37	ANASTOMOSIS, SURGICAL.kw.
38	ANASTOMOSIS, ROUX-EN-Y.kw.
39	ENTEROSTOMY.kw.
40	((ileal or il#um or intestin\$ or gastrointestin\$ or bowel or colon\$) adj3 (surg\$ or resect\$ or anastomosis)).mp.
41	(laparotom\$ or entero?tom\$ or ileo?tom\$).mp.
42	PANCREATIC EXTRACTS.kw.
43	LIPASE.kw.
44	(pancrea\$ adj (enzyme? or extract?) adj3 (therap\$ or treatment? or replacement\$ or supplement\$ or preparation? or formula\$ or product?)).mp.
45	PERT.mp.
46	(lipase or pancreatolipase or pancreatin or panteric or pancrelipase or pan#reon or creon or kreon or pan#rex or nutrizym or pan#rease or liprotamase or pan##trat).mp.
47	or/11-46
48	4 and 10 and 47

### E.13.5 Database: Health Technology Assessment

Last searched on **EBM Reviews - Health Technology Assessment 4th Quarter 2016** on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).tw.
3	mucov\$.tw.
4	or/1-3
5	exp INTESTINAL OBSTRUCTION/
6	CONSTIPATION/
7	((ileal or il#um or intestin\$ or gastrointestin\$ or bowel or colon\$) adj3 (obstruct\$ or inertia or dysmotil\$ or aton\$ or paraly\$)).tw.
8	(ileus or DIOS).tw.
9	(constipat\$ or obstipat\$ or dyschezi\$).tw.
10	or/5-9
11	LAXATIVES/
12	exp CATHARTICS/
13	exp POLYETHYLENE GLYCOLS/
14	LACTULOSE/
15	laxative?.tw.
16	(stool? adj1 soft\$).tw.
17	(cathartic? or purgative? or bowel evacuant? or bowel preparation solution?).tw.
18	(polyethylene glycol? or macrogol? or movicol or laxido or molaxole or klean prep or golytely).mp.
19	(lactulose or duphalac or amivalex or normase or lactugal or laevolac).mp.
20	(senna or sen?kot or sennokot or manevac).mp.
21	(sodium picosul\$ or dulcosan or guttalex or laxober\$ or picolax).mp.
22	(bisacodyl or laxbene or durolax or dulcolax or bicol or laxagetten).mp.
23	FLUID THERAPY/
24	((oral or therap\$) adj3 (rehydrat\$ or hydrat\$ or fluid?)).tw.
25	ENEMA/
26	enema\$.tw.
27	PHOSPHATES/
28	phosphate?.mp.
29	DIATRIZOATE MEGLUMINE/
30	(diatrizoate or meglumin? or gastrogra??in).mp.
31	ACETYLCYSTEINE/
32	(acetylcysteine or nacetylcysteine or acetyl cysteine or nacetyl cysteine).mp.
33	THERAPEUTIC IRRIGATION/
34	((ileal or il#um or intestin\$ or gastrointestin\$ or bowel or colon\$) adj3 (lavage or irrigat\$)).tw.
35	DIGESTIVE SYSTEM SURGICAL PROCEDURES/
36	LAPAROTOMY/
37	ANASTOMOSIS, SURGICAL/
38	ANASTOMOSIS, ROUX-EN-Y/
39	exp ENTEROSTOMY/
40	((ileal or il#um or intestin\$ or gastrointestin\$ or bowel or colon\$) adj3 (surg\$ or resect\$ or

#	Searches
	anastomosis)).tw.
41	(laparotom\$ or entero?tom\$ or ileo?tom\$).tw.
42	exp PANCREATIC EXTRACTS/
43	exp LIPASE/
44	(pancrea\$ adj (enzyme? or extract?) adj3 (therap\$ or treatment? or replacement\$ or supplement\$ or preparation? or formula\$ or product?)).tw.
45	PERT.tw.
46	(lipase or pancreatolipase or pancreatin or panteric or pancrelipase or pan#reon or creon or kreon or pan#rex or nutrizym or pan#rease or liprotamase or pan##trat).mp.
47	or/11-46
48	4 and 10 and 47
49	exp INTESTINAL OBSTRUCTION/dt, su, th [Drug Therapy, Surgery, Therapy]
50	4 and 49
51	48 or 50

### E.13.6 Database: Embase

Last searched on **Embase** 1974 to 2017 Week 01 on 4<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	mucov\$.ti,ab.
3	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
4	or/1-3
5	exp INTESTINE OBSTRUCTION/
6	GASTROINTESTINAL MOTILITY DISORDER/
7	CONSTIPATION/
8	((ileal or il#um or intestin\$ or gastrointestin\$ or bowel or colon\$) adj3 (obstruct\$ or inertia or dysmotil\$ or aton\$ or paraly\$)).ti,ab.
9	(ileus or DIOS).ti,ab.
10	(constipat\$ or obstipat\$ or dyschezi\$).ti,ab.
11	or/5-10
12	exp LAXATIVE/
13	MACROGOL/
14	LACTULOSE/
15	laxative?.ti,ab.
16	(stool? adj1 soft\$).ti,ab.
17	(cathartic? or purgative? or bowel evacuant? or bowel preparation solution?).ti,ab.
18	(polyethylene glycol? or macrogol? or movicol or laxido or molaxole or klean prep or golytely).mp.
19	(lactulose or duphalac or amivalex or normase or lactugal or laevolac).mp.
20	(senna or sen?kot or sennokot or manevac).mp.
21	(sodium picosul\$ or dulcosan or guttalex or laxober\$ or picolax).mp.
22	(bisacodyl or laxbene or durolax or dulcolax or bicol or laxagetten).mp.
23	FLUID THERAPY/
24	REHYDRATION/
25	ORAL REHYDRATION THERAPY/
26	((oral or therap\$) adj3 (rehydrat\$ or hydrat\$ or fluid?)).ti,ab.

#	Searches
27	ENEMA/
28	enema\$.ti,ab.
29	PHOSPHATE/
30	phosphate?.mp.
31	DIATRIZOATE/
32	MEGLUMINE DIATRIZOATE PLUS SODIUM DIATRIZOATE/
33	(diatrizoate or meglumin? or gastrogra??in).mp.
34	ACETYLCYSTEINE/
35	(acetylcysteine or nacetylcysteine or acetyl cysteine or nacetyl cysteine).mp.
36	LAVAGE/
37	exp INTESTINE LAVAGE/
38	((ileal or il#um or intestin\$ or gastrointestin\$ or bowel or colon\$) adj3 (lavage or irrigat\$)).ti,ab.
39	ABDOMINAL SURGERY/
40	GASTROINTESTINAL SURGERY/
41	LAPAROTOMY/
42	ANASTOMOSIS/
43	exp INTESTINE ANASTOMOSIS/
44	exp INTESTINE RESECTION/
45	exp ENTEROSTOMY/
46	((ileal or il#um or intestin\$ or gastrointestin\$ or bowel or colon\$) adj3 (surg\$ or resect\$ or anastomosis)).ti,ab.
47	(laparotom\$ or entero?tom\$ or ileo?tom\$).ti,ab.
48	PANCREAS EXTRACT/
49	PANCREAS ENZYME/
50	TRIACYLGLYCEROL LIPASE/
51	PANCREATIN/
52	PANZYTRAT/
53	PANCRELIPASE/
54	LIPROTAMASE/
55	(pancrea\$ adj (enzyme? or extract?) adj3 (therap\$ or treatment? or replacement\$ or supplement\$ or preparation? or formula\$ or product?)).ti,ab.
56	PERT.ti,ab.
57	(lipase or pancreatolipase or pancreatin or panteric or pancrelipase or pan#reon or creon or kreon or pan#rex or nutrizym or pan#rease or liprotamase or pan##trat).mp.
58	or/12-57
59	4 and 11 and 58
60	exp INTESTINE OBSTRUCTION/dt, su, th [Drug Therapy, Surgery, Therapy]
61	4 and 60
62	59 or 61
63	limit 62 to english language
64	letter.pt. or LETTER/
65	note.pt.
66	editorial.pt.
67	CASE REPORT/ or CASE STUDY/
68	(letter or comment*).ti.

#	Searches
69	or/64-68
70	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
71	69 not 70
72	ANIMAL/ not HUMAN/
73	NONHUMAN/
74	exp ANIMAL EXPERIMENT/
75	exp EXPERIMENTAL ANIMAL/
76	ANIMAL MODEL/
77	exp RODENT/
78	(rat or rats or mouse or mice).ti.
79	or/71-78
80	63 not 79

## E.14 Liver disease

**E.14.1 What is the diagnostic accuracy of tests to detect/ strategies to detect early and late CF liver disease?**

**E.14.2 What is the diagnostic and prognostic value of different strategies to detect CF liver disease and predict progression (including progression to cirrhosis and portal hypertension with (out) oesophageal varices)?**

- Database: Medline

Last searched on **Ovid MEDLINE(R)** 1946 to December Week 1 2016 on 5<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	exp LIVER DISEASES/
6	(liver adj3 (disease? or dysfunction? or abnormal\$ or fail\$ or decompensation)).ab,ti.
7	(hypertension? adj3 portal).ab,ti.
8	((fibros?s or fibrocyst\$ or cirrhos?s) adj3 (liver or hepatic)).ab,ti.
9	hepatomegaly.ti,ab.
10	"ESOPHAGEAL AND GASTRIC VARICES"/
11	((oesophageal or esophageal) adj3 varice?).ti,ab.
12	or/5-11
13	exp PHYSICAL EXAMINATION/
14	(exam? or examin\$).ti,ab.
15	LIVER FUNCTION TESTS/
16	liver function test?.ti,ab.
17	LFT?.ti,ab.
18	(liver enzyme? adj5 (measur\$ or test\$)).ti,ab.
19	ALANINE TRANSAMINASE/
20	alanine transaminase?.ti,ab,nm.
21	alanine aminotransferase.ti,ab,nm.

#	Searches
22	ALT.ti,ab,nm.
23	ASPARTATE AMINOTRANSFERASES/
24	aspartate aminotransferase?.ti,ab,nm.
25	aspartate transaminase?.ti,ab,nm.
26	AST.ti,ab,nm.
27	ALKALINE PHOSPHATASE/
28	alkaline phosphatase?.ti,ab,nm.
29	ALP.ti,ab,nm.
30	GAMMA-GLUTAMYLTRANSFERASE/
31	Gam?a glutamyltransferase?.ti,ab,nm.
32	Gam?a glutamyl transferase?.ti,ab,nm.
33	GMT.ti,ab,nm.
34	gam?a glutamyltranspeptidase?.ti,ab,nm.
35	gam?a glutamyl transpeptidase?.ti,ab,nm.
36	GGT.ti,ab,nm.
37	GLUTATHIONE TRANSFERASE/
38	(glutathione adj2 transferase?).ti,ab,nm.
39	GST.ti,ab,nm.
40	BILIRUBIN/
41	bilirubin.ti,ab,nm.
42	INTERNATIONAL NORMALIZED RATIO/
43	international normali?ed ratio?.ti,ab,nm.
44	INR.ti,ab,nm.
45	ALBUMINS/
46	albumin?.ti,ab,nm.
47	BLOOD PLATELETS/
48	platelet?.ti,ab.
49	exp ULTRASONOGRAPHY/
50	(ultraso\$ or echo\$ or sono\$ or flowmet\$ or doppler\$).ti,ab.
51	uss.ab,ti.
52	ELASTICITY IMAGING TECHNIQUES/
53	elastogra\$.ab,ti.
54	Fibroscan.ab,ti.
55	or/13-54
56	4 and 12 and 55
57	exp LIVER DISEASES/di, us [Diagnosis, Ultrasonography]
58	4 and 57
59	56 or 58
60	limit 59 to english language
61	LETTER/
62	EDITORIAL/
63	NEWS/
64	exp HISTORICAL ARTICLE/
65	ANECDOTES AS TOPIC/
66	COMMENT/

#	Searches
67	CASE REPORT/
68	(letter or comment*).ti.
69	or/61-68
70	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
71	69 not 70
72	ANIMALS/ not HUMANS/
73	exp ANIMALS, LABORATORY/
74	exp ANIMAL EXPERIMENTATION/
75	exp MODELS, ANIMAL/
76	exp RODENTIA/
77	(rat or rats or mouse or mice).ti.
78	or/71-77
79	60 not 78

- Medline In-Process & Other Non-Indexed Citations

Last searched on **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations** January 04, 2017 on 5<sup>th</sup> January 2017.

#	Searches
1	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
2	mucov\$.ti,ab.
3	or/1-2
4	(liver adj3 (disease? or dysfunction? or abnormal\$ or fail\$ or decompensation)).ab,ti.
5	(hypertension? adj3 portal).ab,ti.
6	((fibros?s or fibrocyst\$ or cirrhos?s) adj3 (liver or hepatic)).ab,ti.
7	hepatomegaly.ti,ab.
8	((oesophageal or esophageal) adj3 varice?).ti,ab.
9	or/4-8
10	(exam? or examin\$).ti,ab.
11	liver function test?.ti,ab.
12	LFT?.ti,ab.
13	(liver enzyme? adj5 (measur\$ or test\$)).ti,ab.
14	alanine transaminase?.ti,ab,nm.
15	alanine aminotransferase.ti,ab,nm.
16	ALT.ti,ab,nm.
17	aspartate aminotransferase?.ti,ab,nm.
18	aspartate transaminase?.ti,ab,nm.
19	AST.ti,ab,nm.
20	alkaline phosphatase?.ti,ab,nm.
21	ALP.ti,ab,nm.
22	Gam?a glutamyltransferase?.ti,ab,nm.
23	Gam?a glutamyl transferase?.ti,ab,nm.
24	GMT.ti,ab,nm.
25	gam?a glutamyltranspeptidase?.ti,ab,nm.
26	gam?a glutamyl transpeptidase?.ti,ab,nm.
27	GGT.ti,ab,nm.
28	(glutathione adj2 transferase?).ti,ab,nm.

#	Searches
29	GST.ti,ab,nm.
30	bilirubin.ti,ab,nm.
31	international normali?ed ratio?.ti,ab,nm.
32	INR.ti,ab,nm.
33	albumin?.ti,ab,nm.
34	platelet?.ti,ab.
35	(ultraso\$ or echo\$ or sono\$ or flowmet\$ or doppler\$).ti,ab.
36	uss.ab,ti.
37	elastogra\$.ab,ti.
38	Fibroscan.ab,ti.
39	or/10-38

- Database: Cochrane Central Register of Controlled Trials

Last searched on **EBM Reviews - Cochrane Central Register of Controlled Trials**  
November 2016 on 5<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab,kw.
3	mucov\$.ti,ab,kw.
4	or/1-3
5	exp LIVER DISEASES/
6	(liver adj3 (disease? or dysfunction? or abnormal\$ or fail\$ or decompensation)).ab,ti,kw.
7	(hypertension? adj3 portal).ab,ti,kw.
8	((fibros?s or fibrocyst\$ or cirrhos?s) adj3 (liver or hepatic)).ab,ti,kw.
9	hepatomegaly.ti,ab,kw.
10	"ESOPHAGEAL AND GASTRIC VARICES"/
11	((oesophageal or esophageal) adj3 varice?).ti,ab,kw.
12	or/5-11
13	exp PHYSICAL EXAMINATION/
14	(exam? or examin\$).ti,ab,kw.
15	LIVER FUNCTION TESTS/
16	liver function test?.ti,ab,kw.
17	LFT?.ti,ab,kw.
18	(liver enzyme? adj5 (measur\$ or test\$)).ti,ab,kw.
19	ALANINE TRANSAMINASE/
20	alanine transaminase?.ti,ab,kw.
21	alanine aminotransferase.ti,ab,kw.
22	ALT.ti,ab,kw.
23	ASPARTATE AMINOTRANSFERASES/
24	aspartate aminotransferase?.ti,ab,kw.
25	aspartate transaminase?.ti,ab,kw.
26	AST.ti,ab,kw.
27	ALKALINE PHOSPHATASE/
28	alkaline phosphatase?.ti,ab,kw.
29	ALP.ti,ab,kw.
30	GAMMA-GLUTAMYLTRANSFERASE/

#	Searches
31	Gam?a glutamyltransferase?.ti,ab,kw.
32	Gam?a glutamyl transferase?.ti,ab,kw.
33	GMT.ti,ab,kw.
34	gam?a glutamyltranspeptidase?.ti,ab,kw.
35	gam?a glutamyl transpeptidase?.ti,ab,kw.
36	GGT.ti,ab,kw.
37	GLUTATHIONE TRANSFERASE/
38	(glutathione adj2 transferase?).ti,ab,kw.
39	GST.ti,ab,kw.
40	BILIRUBIN/
41	bilirubin.ti,ab,kw.
42	INTERNATIONAL NORMALIZED RATIO/
43	international normali?ed ratio?.ti,ab,kw.
44	INR.ti,ab,kw.
45	ALBUMINS/
46	albumin?.ti,ab,kw.
47	BLOOD PLATELETS/
48	platelet?.ti,ab,kw.
49	exp ULTRASONOGRAPHY/
50	(ultraso\$ or echo\$ or sono\$ or flowmet\$ or doppler\$).ti,ab,kw.
51	uss.ab,ti,kw.
52	ELASTICITY IMAGING TECHNIQUES/
53	elastogra\$.ab,ti,kw.
54	Fibroscan.ab,ti,kw.
55	or/13-54
56	4 and 12 and 55
57	exp LIVER DISEASES/di, us [Diagnosis, Ultrasonography]
58	4 and 57
59	56 or 58

- Database: Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects

Last searched on **EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to December 30, 2016, **EBM Reviews - Database of Abstracts of Reviews of Effects** 1st Quarter 2015 on 5<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS.kw.
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).tw,tx,kw.
3	mucov\$.tw,tx,kw.
4	or/1-3
5	LIVER DISEASES.kw.
6	(liver adj3 (disease? or dysfunction? or abnormal\$ or fail\$ or decompensation)).tw,tx,kw.
7	(hypertension? adj3 portal).tw,tx,kw.
8	((fibros?s or fibrocyst\$ or cirrhos?s) adj3 (liver or hepatic)).tw,tx,kw.
9	hepatomegaly.tw,tx,kw.
10	ESOPHAGEAL.mp. and GASTRIC VARICES.kw. [mp=ti, ot, ab, tx, kw, ct]

#	Searches
11	((oesophageal or esophageal) adj3 varice?).tw,tx,kw.
12	or/5-11
13	PHYSICAL EXAMINATION.kw.
14	(exam? or examin\$).tw,tx,kw.
15	LIVER FUNCTION TESTS.kw.
16	liver function test?.tw,tx,kw.
17	LFT?.tw,tx,kw.
18	(liver enzyme? adj5 (measur\$ or test\$)).tw,tx,kw.
19	ALANINE TRANSAMINASE.kw.
20	alanine transaminase?.tw,tx,kw.
21	alanine aminotransferase.tw,tx,kw.
22	ALT.tw,tx,kw.
23	ASPARTATE AMINOTRANSFERASES.kw.
24	aspartate aminotransferase?.tw,tx,kw.
25	aspartate transaminase?.tw,tx,kw.
26	AST.tw,tx,kw.
27	ALKALINE PHOSPHATASE.kw.
28	alkaline phosphatase?.tw,tx,kw.
29	ALP.tw,tx,kw.
30	GAMMA-GLUTAMYLTRANSFERASE.kw.
31	Gam?a glutamyltransferase?.tw,tx,kw.
32	Gam?a glutamyl transferase?.tw,tx,kw.
33	GMT.tw,tx,kw.
34	gam?a glutamyltranspeptidase?.tw,tx,kw.
35	gam?a glutamyl transpeptidase?.tw,tx,kw.
36	GGT.tw,tx,kw.
37	GLUTATHIONE TRANSFERASE.kw.
38	(glutathione adj2 transferase?).tw,tx,kw.
39	GST.tw,tx,kw.
40	BILIRUBIN.kw.
41	bilirubin.tw,tx,kw.
42	INTERNATIONAL NORMALIZED RATIO.kw.
43	international normali?ed ratio?.tw,tx,kw.
44	INR.tw,tx,kw.
45	ALBUMINS.kw.
46	albumin?.tw,tx,kw.
47	BLOOD PLATELETS.kw.
48	platelet?.tw,tx,kw.
49	ULTRASONOGRAPHY.kw.
50	(ultraso\$ or echo\$ or sono\$ or flowmet\$ or doppler\$).tw,tx,kw.
51	uss.tw,tx,kw.
52	ELASTICITY IMAGING TECHNIQUES.kw.
53	elastogra\$.tw,tx,kw.
54	Fibroscan.tw,tx,kw.
55	or/13-54

#	Searches
56	4 and 12 and 55

- Database: Health Technology Assessment

Last searched on **EBM Reviews - Health Technology Assessment** 4<sup>th</sup> Quarter 2016 on 5<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).tw.
3	mucov\$.tw.
4	or/1-3
5	exp LIVER DISEASES/
6	(liver adj3 (disease? or dysfunction? or abnormal\$ or fail\$ or decompensation)).tw.
7	(hypertension? adj3 portal).tw.
8	((fibros?s or fibrocyst\$ or cirrhos?s) adj3 (liver or hepatic)).tw.
9	hepatomegaly.tw.
10	"ESOPHAGEAL AND GASTRIC VARICES"/
11	((oesophageal or esophageal) adj3 varice?).tw.
12	or/5-11
13	exp PHYSICAL EXAMINATION/
14	(exam? or examin\$).tw.
15	LIVER FUNCTION TESTS/
16	liver function test?.tw.
17	LFT?.tw.
18	(liver enzyme? adj5 (measur\$ or test\$)).tw.
19	ALANINE TRANSAMINASE/
20	alanine transaminase?.tw.
21	alanine aminotransferase.tw.
22	ALT.tw.
23	ASPARTATE AMINOTRANSFERASES/
24	aspartate aminotransferase?.tw.
25	aspartate transaminase?.tw.
26	AST.tw.
27	ALKALINE PHOSPHATASE/
28	alkaline phosphatase?.tw.
29	ALP.tw.
30	GAMMA-GLUTAMYLTRANSFERASE/
31	Gam?a glutamyltransferase?.tw.
32	Gam?a glutamyl transferase?.tw.
33	GMT.tw.
34	gam?a glutamyltranspeptidase?.tw.
35	gam?a glutamyl transpeptidase?.tw.
36	GGT.tw.
37	GLUTATHIONE TRANSFERASE/
38	(glutathione adj2 transferase?).tw.
39	GST.tw.
40	BILIRUBIN/

#	Searches
41	bilirubin.tw.
42	INTERNATIONAL NORMALIZED RATIO/
43	international normali?ed ratio?.tw.
44	INR.tw.
45	ALBUMINS/
46	albumin?.tw.
47	BLOOD PLATELETS/
48	platelet?.tw.
49	exp ULTRASONOGRAPHY/
50	(ultraso\$ or echo\$ or sono\$ or flowmet\$ or doppler\$).tw.
51	uss.tw.
52	ELASTICITY IMAGING TECHNIQUES/
53	elastogra\$.tw.
54	Fibroscan.tw.
55	or/13-54
56	4 and 12 and 55
57	exp LIVER DISEASES/di, us [Diagnosis, Ultrasonography]
58	4 and 57
59	56 or 58

- Database: Embase

Last searched on **Embase** 1974 to 2017 Week 01 on 4<sup>th</sup> January 2017.

#	Searches
1	*CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	exp *LIVER DISEASE/
6	(liver adj3 (disease? or dysfunction? or abnormal\$ or fail\$ or decompensation)).ab,ti.
7	(hypertension? adj3 portal).ab,ti.
8	((fibros?s or fibrocyst\$ or cirrhos?s) adj3 (liver or hepatic)).ab,ti.
9	hepatomegaly.ti,ab.
10	*ESOPHAGUS VARICES/
11	((oesophageal or esophageal) adj3 varice?).ti,ab.
12	or/5-11
13	*CLINICAL EXAMINATION/
14	exp *PHYSICAL EXAMINATION/
15	(exam? or examin\$).ti,ab.
16	*LIVER FUNCTION TEST/
17	liver function test?.ti,ab.
18	LFT?.ti,ab.
19	(liver enzyme? adj5 (measur\$ or test\$)).ti,ab.
20	*ALANINE AMINOTRANSFERASE/
21	alanine transaminase?.ti,ab,tn.
22	alanine aminotransferase.ti,ab,tn.
23	ALT.ti,ab,tn.

#	Searches
24	*ASPARTATE AMINOTRANSFERASE/
25	aspartate aminotransferase?.ti,ab,tn.
26	aspartate transaminase?.ti,ab,tn.
27	AST.ti,ab,tn.
28	*ALKALINE PHOSPHATASE/
29	alkaline phosphatase?.ti,ab,tn.
30	ALP.ti,ab,tn.
31	*GAMMA GLUTAMYLTRANSFERASE/
32	Gam?a glutamyltransferase?.ti,ab,tn.
33	Gam?a glutamyl transferase?.ti,ab,tn.
34	GMT.ti,ab,tn.
35	gam?a glutamyltranspeptidase?.ti,ab,tn.
36	gam?a glutamyl transpeptidase?.ti,ab,tn.
37	GGT.ti,ab,tn.
38	*GLUTATHIONE TRANSFERASE/
39	(glutathione adj2 transferase?).ti,ab,tn.
40	GST.ti,ab,tn.
41	*BILIRUBIN/
42	bilirubin.ti,ab,tn.
43	*INTERNATIONAL NORMALIZED RATIO/
44	international normali?ed ratio?.ti,ab,tn.
45	INR.ti,ab,tn.
46	*ALBUMINOID/
47	albumin?.ti,ab,tn.
48	*THROMBOCYTE/
49	platelet?.ti,ab.
50	exp *ECHOGRAPHY/
51	*ULTRASOUND/
52	(ultraso\$ or echo\$ or sono\$ or flowmet\$ or doppler\$).ti,ab,dv.
53	uss.ab,ti,dv.
54	elastogra\$.ab,ti,dv.
55	Fibroscan.ab,ti,dv.
56	or/13-55
57	4 and 12 and 56
58	exp *LIVER DISEASE/di [Diagnosis]
59	4 and 58
60	57 or 59
61	limit 60 to english language
62	letter.pt. or LETTER/
63	note.pt.
64	editorial.pt.
65	CASE REPORT/ or CASE STUDY/
66	(letter or comment*).ti.
67	or/62-66
68	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.

#	Searches
69	67 not 68
70	ANIMAL/ not HUMAN/
71	NONHUMAN/
72	exp ANIMAL EXPERIMENT/
73	exp EXPERIMENTAL ANIMAL/
74	ANIMAL MODEL/
75	exp RODENT/
76	(rat or rats or mouse or mice).ti.
77	or/69-76
78	61 not 77

## E.15 What is the effectiveness of ursodeoxycholic acid for preventing liver disease progression in people with cystic fibrosis?

### E.15.1 Database: Medline

Last searched on **Ovid MEDLINE(R)** 1946 to October Week 3 2016 on 1st November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	URSODEOXYCHOLIC ACID/
6	(urso\$ or destolit or ursofalk or ursogal or urdox).mp.
7	UDCA.ti,ab.
8	or/5-7
9	and/4,8
10	limit 9 to english language
11	LETTER/
12	EDITORIAL/
13	NEWS/
14	exp HISTORICAL ARTICLE/
15	ANECDOTES AS TOPIC/
16	COMMENT/
17	CASE REPORT/
18	(letter or comment* or abstracts).ti.
19	or/11-18
20	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
21	19 not 20
22	ANIMALS/ not HUMANS/
23	exp ANIMALS, LABORATORY/
24	exp ANIMAL EXPERIMENTATION/
25	exp MODELS, ANIMAL/
26	exp RODENTIA/

#	Searches
27	(rat or rats or mouse or mice).ti.
28	or/21-27
29	10 not 28

### E.15.2 Database: Medline In-Process & Other Non-Indexed Citations

Last searched on **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations** October 31, 2016 on 1st November 2016.

#	Searches
1	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
2	mucov\$.ti,ab.
3	or/1-2
4	(urso\$ or destolit or ursofalk or ursogal or urdox).mp.
5	UDCA.ti,ab.
6	or/4-5
7	and/3,6

### E.15.3 Database: Cochrane Central Register of Controlled Trials

Last searched on **EBM Reviews - Cochrane Central Register of Controlled Trials** September 2016 on 1<sup>st</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab,kw.
3	mucov\$.ti,ab.
4	or/1-3
5	URSODEOXYCHOLIC ACID/
6	(urso\$ or destolit or ursofalk or ursogal or urdox).mp.
7	UDCA.ti,ab.
8	or/5-6
9	and/4,8

### E.15.4 Database: Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects

Last searched on **EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to October 26, 2016, **EBM Reviews - Database of Abstracts of Reviews of Effects** 1st Quarter 2015 on 1<sup>st</sup> November 2016.

#	Searches
1	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).tw,tx,kw.
2	mucov\$.tw,tx.
3	or/1-2
4	(urso\$ or destolit or ursofalk or ursogal or urdox).mp.
5	UDCA.tw,tx.
6	or/4-5
7	and/3,6

### E.15.5 Database: Health Technology Assessment

Last searched on **EBM Reviews - Health Technology Assessment 3rd Quarter 2016** on 1<sup>st</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).tw.
3	mucov\$.tw.
4	or/1-3
5	URSODEOXYCHOLIC ACID/
6	(urso\$ or destolit or ursofalk or ursogal or urdox).tw,hw.
7	UDCA.tw.
8	or/5-7
9	and/4,8

### E.15.6 Database: Embase

Last searched on **Embase 1974 to 2016 Week 44** on 1<sup>st</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	mucov\$.ti,ab.
3	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
4	or/1-3
5	URSODEOXYCHOLIC ACID/
6	(urso\$ or destolit or ursofalk or ursogal or urdox).mp.
7	UDCA.ti,ab.
8	or/5-7
9	and/4,8
10	limit 9 to english language
11	conference abstract.pt.
12	letter.pt. or LETTER/
13	note.pt.
14	editorial.pt.
15	CASE REPORT/ or CASE STUDY/
16	(letter or comment* or abstracts).ti.
17	or/11-16
18	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
19	17 not 18
20	ANIMAL/ not HUMAN/
21	NONHUMAN/
22	exp ANIMAL EXPERIMENT/
23	exp EXPERIMENTAL ANIMAL/
24	ANIMAL MODEL/
25	exp RODENT/
26	(rat or rats or mouse or mice).ti.
27	or/19-26
28	10 not 27

## E.16 What is the most effective strategy to monitor for the onset of CF-related diabetes (CFRD)?

### E.16.1 Database: Medline

Last searched on **Ovid MEDLINE(R)** 1946 to October Week 3 2016 on 8<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	exp DIABETES MELLITUS/
6	diabet\$.ti,ab.
7	or/5-6
8	and/4,7
9	CFRD.ti,ab.
10	or/8-9
11	exp MASS SCREENING/
12	exp POPULATION SURVEILLANCE/
13	(undiagnos\$ or estimate\$ or suspect\$).ti.
14	(screen\$ or surveill\$ or predict\$ or detect\$).ti.
15	monitor\$.ti,ab.
16	or/11-15
17	and/10,16
18	exp GLYCOSURIA/
19	((glucose or sugar\$) adj2 urine).ti,ab.
20	GLUCOSE TOLERANCE TEST/
21	GLUCOSE INTOLERANCE/di
22	glucose intoleran\$.ti,ab.
23	((impair\$ or abnormal\$) adj glucose tolerance).ti,ab.
24	IGT.ti,ab.
25	(glyc?emi\$ adj2 status).ti,ab.
26	(insulin adj2 (deficien\$ or declin\$ or resist\$ or abnormal\$)).ti,ab.
27	(fast\$ adj2 hyperglyc?emi\$).ti,ab.
28	CFRD FH.ti,ab.
29	BLOOD GLUCOSE/an [Analysis]
30	((random or fast\$ or oral) adj2 blood glucose).ti,ab.
31	((continu\$ or serial) adj2 glucose).ti,ab.
32	"oral glucose tolerance test\$.ti,ab.
33	(glucose adj2 (monitor\$ or self monitor\$)).ti,ab.
34	(OGTT or CGM or CGMS).ti,ab.
35	HEMOGLOBIN A, GLYCOSYLATED/
36	(HbA1c or Hb1c or HGBA1C).ti,ab.
37	((glycated or glycosylated) adj2 (haemoglobin or hemoglobin)).ti,ab.
38	or/18-37
39	and/10,38
40	or/17,39

#	Searches
41	limit 40 to english language
42	LETTER/
43	EDITORIAL/
44	NEWS/
45	exp HISTORICAL ARTICLE/
46	ANECDOTES AS TOPIC/
47	COMMENT/
48	CASE REPORT/
49	(letter or comment*).ti.
50	or/42-49
51	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
52	50 not 51
53	ANIMALS/ not HUMANS/
54	exp ANIMALS, LABORATORY/
55	exp ANIMAL EXPERIMENTATION/
56	exp MODELS, ANIMAL/
57	exp RODENTIA/
58	(rat or rats or mouse or mice).ti.
59	or/52-58
60	41 not 59

## E.16.2 Database: Medline In-Process & Other Non-Indexed Citations

Last searched on **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations**  
November 06, 2016 on 8<sup>th</sup> November 2016.

#	Searches
1	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
2	mucov\$.ti,ab.
3	1 or 2
4	diabet\$.ti,ab.
5	CFRD.ti,ab.
6	3 and 4
7	5 or 6
8	(undiagnos\$ or estimate\$ or suspect\$).ti.
9	(screen\$ or surveill\$ or predict\$ or detect\$).ti.
10	monitor\$.ti,ab.
11	or/8-10
12	7 and 11
13	((glucose or sugar\$) adj2 urine).ti,ab.
14	glucose intoleran\$.ti,ab.
15	((impair\$ or abnormal\$) adj glucose tolerance).ti,ab.
16	IGT.ti,ab.
17	(glyc?emi\$ adj2 status).ti,ab.
18	(insulin adj2 (deficien\$ or declin\$ or resist\$ or abnormal\$)).ti,ab.
19	(fast\$ adj2 hyperglyc?emi\$).ti,ab.
20	CFRD FH.ti,ab.

#	Searches
21	((random or fast\$ or oral) adj2 blood glucose).ti,ab.
22	((continu\$ or serial) adj2 glucose).ti,ab.
23	"oral glucose tolerance test\$.ti,ab.
24	(glucose adj2 (monitor\$ or self monitor\$)).ti,ab.
25	(OGTT or CGM or CGMS).ti,ab.
26	(HbA1c or Hb1c or HGBA1C).ti,ab.
27	((glycated or glycosylated) adj2 (haemoglobin or hemoglobin)).ti,ab.
28	or/13-27
29	7 and 28
30	12 or 29
31	limit 30 to english language

### E.16.3 Database: Cochrane Central Register of Controlled Trials

Last searched on **EBM Reviews - Cochrane Central Register of Controlled Trials**  
October 2016 on 29<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	exp DIABETES MELLITUS/
6	diabet\$.ti,ab.
7	or/5-6
8	and/4,7
9	CFRD.ti,ab.
10	or/8-9
11	exp MASS SCREENING/
12	exp POPULATION SURVEILLANCE/
13	(undiagnos\$ or estimate\$ or suspect\$).ti.
14	(screen\$ or surveill\$ or predict\$ or detect\$).ti.
15	monitor\$.ti,ab.
16	or/11-15
17	and/10,16
18	exp GLYCOSURIA/
19	((glucose or sugar\$) adj2 urine).ti,ab.
20	GLUCOSE TOLERANCE TEST/
21	GLUCOSE INTOLERANCE/di
22	glucose intoleran\$.ti,ab.
23	((impair\$ or abnormal\$) adj glucose tolerance).ti,ab.
24	IGT.ti,ab.
25	(glyc?emi\$ adj2 status).ti,ab.
26	(insulin adj2 (deficien\$ or declin\$ or resist\$ or abnormal\$)).ti,ab.
27	(fast\$ adj2 hyperglyc?emi\$).ti,ab.
28	CFRD FH.ti,ab.
29	BLOOD GLUCOSE/an [Analysis]

#	Searches
30	((random or fast\$ or oral) adj2 blood glucose).ti,ab.
31	((continu\$ or serial) adj2 glucose).ti,ab.
32	"oral glucose tolerance test\$.ti,ab.
33	(glucose adj2 (monitor\$ or self monitor\$)).ti,ab.
34	(OGTT or CGM or CGMS).ti,ab.
35	HEMOGLOBIN A, GLYCOSYLATED/
36	(HbA1c or Hb1c or HGBA1C).ti,ab.
37	((glycated or glycosylated) adj2 (haemoglobin or hemoglobin)).ti,ab.
38	or/18-37
39	and/10,38
40	or/17,39
41	limit 40 to english language

#### E.16.4 Database: Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects

Last searched on **EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to November 02, 2016, **EBM Reviews - Database of Abstracts of Reviews of Effects** 1st Quarter 2015 on 8<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS.kw.
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	DIABETES MELLITUS.kw.
6	diabet\$.ti,ab.
7	or/5-6
8	and/4,7
9	CFRD.ti,ab.
10	or/8-9
11	MASS SCREENING.kw.
12	POPULATION SURVEILLANCE.kw.
13	(undiagnos\$ or estimate\$ or suspect\$.ti.
14	(screen\$ or surveill\$ or predict\$ or detect\$.ti.
15	monitor\$.ti,ab.
16	or/11-15
17	and/10,16
18	GLYCOSURIA.kw.
19	((glucose or sugar\$) adj2 urine).ti,ab.
20	GLUCOSE TOLERANCE TEST.kw.
21	GLUCOSE INTOLERANCE.kw.
22	glucose intoleran\$.ti,ab.
23	((impair\$ or abnormal\$) adj glucose tolerance).ti,ab.
24	IGT.ti,ab.
25	(glyc?emi\$ adj2 status).ti,ab.
26	(insulin adj2 (deficien\$ or declin\$ or resist\$ or abnormal\$)).ti,ab.

#	Searches
27	(fast\$ adj2 hyperglyc?emi\$).ti,ab.
28	CFRD FH.ti,ab.
29	BLOOD GLUCOSE.kw.
30	((random or fast\$ or oral) adj2 blood glucose).ti,ab.
31	((continu\$ or serial) adj2 glucose).ti,ab.
32	"oral glucose tolerance test\$".ti,ab.
33	(glucose adj2 (monitor\$ or self monitor\$)).ti,ab.
34	(OGTT or CGM or CGMS).ti,ab.
35	HEMOGLOBIN A, GLYCOSYLATED.kw.
36	(HbA1c or Hb1c or HGBA1C).ti,ab.
37	((glycated or glycosylated) adj2 (haemoglobin or hemoglobin)).ti,ab.
38	or/18-37
39	and/10,38
40	or/17,39

### E.16.5 Database: Health Technology Assessment

Last searched on **EBM Reviews - Health Technology Assessment 3rd Quarter 2016** on 8<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	exp DIABETES MELLITUS/
6	diabet\$.ti,ab.
7	or/5-6
8	and/4,7
9	CFRD.ti,ab.
10	or/8-9
11	exp MASS SCREENING/
12	exp POPULATION SURVEILLANCE/
13	(undiagnos\$ or estimate\$ or suspect\$).ti.
14	(screen\$ or surveill\$ or predict\$ or detect\$).ti.
15	monitor\$.ti,ab.
16	or/11-15
17	and/10,16
18	exp GLYCOSURIA/
19	((glucose or sugar\$) adj2 urine).ti,ab.
20	GLUCOSE TOLERANCE TEST/
21	GLUCOSE INTOLERANCE/
22	glucose intoleran\$.ti,ab.
23	((impair\$ or abnormal\$) adj glucose tolerance).ti,ab.
24	IGT.ti,ab.
25	(glyc?emi\$ adj2 status).ti,ab.
26	(insulin adj2 (deficien\$ or declin\$ or resist\$ or abnormal\$)).ti,ab.

#	Searches
27	(fast\$ adj2 hyperglyc?emi\$).ti,ab.
28	CFRD FH.ti,ab.
29	BLOOD GLUCOSE/an [Analysis]
30	((random or fast\$ or oral) adj2 blood glucose).ti,ab.
31	((continu\$ or serial) adj2 glucose).ti,ab.
32	"oral glucose tolerance test".ti,ab.
33	(glucose adj2 (monitor\$ or self monitor\$)).ti,ab.
34	(OGTT or CGM or CGMS).ti,ab.
35	HEMOGLOBIN A, GLYCOSYLATED/
36	(HbA1c or Hb1c or HGBA1C).ti,ab.
37	((glycated or glycosylated) adj2 (haemoglobin or hemoglobin)).ti,ab.
38	or/18-37
39	and/10,38
40	or/17,39

### E.16.6 Database: Embase

Last searched on **Embase** 1974 to 2016 Week 44 on 8<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	mucov\$.ti,ab.
3	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
4	or/1-3
5	exp diabetes mellitus/
6	diabet\$.ti,ab.
7	5 or 6
8	4 and 7
9	CFRD.ti,ab.
10	8 or 9
11	exp mass screening/
12	exp health survey/
13	(undiagnos\$ or estimate\$ or suspect\$).ti.
14	(screen\$ or surveill\$ or predict\$ or detect\$).ti.
15	monitor\$.ti,ab.
16	or/11-15
17	10 and 16
18	glucosuria/
19	((glucose or sugar\$) adj2 urine).ti,ab.
20	exp glucose tolerance test/
21	glucose intolerance/di [Diagnosis]
22	glucose intoleran\$.ti,ab.
23	((impair\$ or abnormal\$) adj glucose tolerance).ti,ab.
24	IGT.ti,ab.
25	(glyc?emi\$ adj2 status).ti,ab.
26	(insulin adj2 (deficien\$ or declin\$ or resist\$ or abnormal\$)).ti,ab.
27	(fast\$ adj2 hyperglyc?emi\$).ti,ab.

#	Searches
28	CFRD FH.ti,ab.
29	glucose blood level/
30	((random or fast\$ or oral) adj2 blood glucose).ti,ab.
31	((continu\$ or serial) adj2 glucose).ti,ab.
32	"oral glucose tolerance test\$.ti,ab.
33	(glucose adj2 (monitor\$ or self monitor\$)).ti,ab.
34	(OGTT or CGM or CGMS).ti,ab.
35	glycosylated hemoglobin/
36	(HbA1c or Hb1c or HGBA1C).ti,ab.
37	((glycated or glycosylated) adj2 (haemoglobin or hemoglobin)).ti,ab.
38	or/18-37
39	10 and 38
40	17 or 39
41	limit 40 to english language
42	letter.pt. or LETTER/
43	note.pt.
44	editorial.pt.
45	CASE REPORT/ or CASE STUDY/
46	(letter or comment*).ti.
47	or/42-46
48	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
49	47 not 48
50	ANIMAL/ not HUMAN/
51	NONHUMAN/
52	exp ANIMAL EXPERIMENT/
53	exp EXPERIMENTAL ANIMAL/
54	ANIMAL MODEL/
55	exp RODENT/
56	(rat or rats or mouse or mice).ti.
57	or/49-56
58	41 not 57

## E.17 What is the most effective strategy to monitor for the identification of reduced bone mineral density in people with cystic fibrosis?

### E.17.1 Database: Medline

Last searched on Ovid MEDLINE(R) 1946 to October Week 4 2016 on 8th November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	exp BONE DISEASES, METABOLIC/

#	Searches
6	BONE DENSITY/
7	exp FRACTURES, BONE/
8	exp BONE RESORPTION/
9	exp VITAMIN D DEFICIENCY/
10	(bone? adj2 (dens\$ or mass)).ti,ab.
11	(bone? adj3 (deminerali\$ or de minerali\$ or decalcif\$ or de calcif\$ or fractur\$ or fragil\$ or loss or atroph\$)).ti,ab.
12	(osteoporo\$ or osteop?en\$ or osteoly\$).ti,ab.
13	((fragil\$ or pathologic\$ or spontaneous\$) adj2 fractur\$).ti,ab.
14	((vitamin D or calcium) adj3 deficien\$).ti,ab.
15	or/5-14
16	ABSORPTIOMETRY, PHOTON/
17	((x ray or xray or photon or DPX or dual energy or radiograph\$) adj2 (absorptio\$ or densit\$ or photodensit\$)).ti,ab.
18	(DEXA or DXA).ti,ab.
19	(pQCT or HR pQCT or HRpQCT).ti,ab.
20	peripheral quantitative compute\$ tomogra\$.ti,ab.
21	or/16-20
22	4 and 15 and 21
23	limit 22 to english language
24	LETTER/
25	EDITORIAL/
26	NEWS/
27	exp HISTORICAL ARTICLE/
28	ANECDOTES AS TOPIC/
29	COMMENT/
30	CASE REPORT/
31	(letter or comment*).ti.
32	or/24-31
33	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
34	32 not 33
35	ANIMALS/ not HUMANS/
36	exp ANIMALS, LABORATORY/
37	exp ANIMAL EXPERIMENTATION/
38	exp MODELS, ANIMAL/
39	exp RODENTIA/
40	(rat or rats or mouse or mice).ti.
41	or/34-40
42	27 not 41

### E.17.2 Database: Medline In-Process & Other Non-Indexed Citations

Last searched on Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations November 07, 2016 on 8th November 2016.

#	Searches
1	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
2	mucov\$.ti,ab.

#	Searches
3	1 or 2
4	(bone? adj2 (dens\$ or mass)).ti,ab.
5	(bone? adj3 (deminerali\$ or de minerali\$ or decalcif\$ or de calcif\$ or fractur\$ or fragil\$ or loss or atroph\$)).ti,ab.
6	(osteoporo\$ or osteop?en\$ or osteoly\$).ti,ab.
7	((fragil\$ or pathologic\$ or spontaneous\$) adj2 fractur\$).ti,ab.
8	((vitamin D or calcium) adj3 deficien\$).ti,ab.
9	or/4-8
10	((x ray or xray or photon or DPX or dual energy or radiograph\$) adj2 (absorptio\$ or densit\$ or photodensit\$)).ti,ab.
11	(DEXA or DXA).ti,ab.
12	(pQCT or HR pQCT or HRpQCT).ti,ab.
13	peripheral quantitative compute\$ tomogra\$.ti,ab.
14	or/10-13
15	3 and 9 and 14
16	limit 15 to english language

### E.17.3 Database: Cochrane Central Register of Controlled Trials

Last searched on **EBM Reviews - Cochrane Central Register of Controlled Trials**  
October 2016 on 8<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ab,ti,kw.
3	mucov\$.ab,ti,kw.
4	or/1-3
5	exp Bone Diseases, Metabolic/
6	Bone Density/
7	exp Fractures, Bone/
8	exp Bone Resorption/
9	exp Vitamin D Deficiency/
10	(bone? adj2 (dens\$ or mass)).ti,ab.
11	(bone? adj3 (deminerali\$ or de minerali\$ or decalcif\$ or de calcif\$ or fractur\$ or fragil\$ or loss or atroph\$)).ti,ab.
12	(osteoporo\$ or osteop?en\$ or osteoly\$).ti,ab.
13	((fragil\$ or pathologic\$ or spontaneous\$) adj2 fractur\$).ti,ab.
14	((vitamin D or calcium) adj3 deficien\$).ti,ab.
15	or/5-14
16	ABSORPTIOMETRY, PHOTON/
17	((x ray or xray or photon or DPX or dual energy or radiograph\$) adj2 (absorptio\$ or densit\$ or photodensit\$)).ti,ab.
18	(DEXA or DXA).ti,ab.
19	(pQCT or HR pQCT or HRpQCT).ti,ab.
20	peripheral quantitative computed tomogra\$.ti,ab.
21	or/16-20
22	4 and 15 and 21
23	limit 22 to english language

#### E.17.4 Database: Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects

Last searched on **EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to November 07, 2016, **EBM Reviews - Database of Abstracts of Reviews of Effects 1st Quarter 2015** on 8<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS.kw.
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).mp.
3	mucov\$.mp.
4	or/1-3
5	Bone Diseases, Metabolic.kw.
6	Bone Density.kw.
7	Fractures, Bone.kw.
8	Bone Resorption.kw.
9	Osteolysis.kw.
10	vitamin d deficiency.kw.
11	(bone? adj2 (dens\$ or mass)).mp.
12	(bone? adj3 (deminerali\$ or de minerali\$ or decalcif\$ or de calcif\$ or fractur\$ or fragil\$ or loss or atroph\$)).mp.
13	(osteoporos\$ or osteop?en\$ or osteoly\$).mp.
14	((fragil\$ or pathologic\$ or spontaneous\$) adj2 fractur\$).mp.
15	((vitamin D or calcium) adj3 deficien\$).mp.
16	or/5-15
17	Absorptiometry, Photon.kw.
18	((x ray or xray or photon or DPX or dual energy or radiograph\$) adj2 (absorptio\$ or densit\$ or photodensit\$)).mp.
19	(DEXA or DXA).mp.
20	(pQCT or HR pQCT or HRpQCT).mp.
21	peripheral quantitative computed tomogra\$.mp.
22	or/17-21
23	4 and 16 and 22

#### E.17.5 Database: Health Technology Assessment

Last searched on **EBM Reviews - Health Technology Assessment 4th Quarter 2016** on 8<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).tw.
3	mucov\$.tw.
4	or/1-3
5	exp Bone Diseases, Metabolic/
6	Bone Density/
7	exp Fractures, Bone/
8	exp Bone Resorption/
9	exp Vitamin D Deficiency/
10	(bone? adj2 (dens\$ or mass)).tw.
11	(bone? adj3 (deminerali\$ or de minerali\$ or decalcif\$ or de calcif\$ or fractur\$ or fragil\$ or

#	Searches
	loss or atroph\$).tw.
12	(osteoporos\$ or osteop?en\$ or osteoly\$).tw.
13	((fragil\$ or pathologic\$ or spontaneous\$) adj2 fractur\$).tw.
14	((vitamin D or calcium) adj3 deficien\$).tw.
15	or/5-14
16	ABSORPTIOMETRY, PHOTON/
17	((x ray or xray or photon or DPX or dual energy or radiograph\$) adj2 (absorptio\$ or densit\$ or photodensit\$)).tw.
18	(DEXA or DXA).tw.
19	(pQCT or HR pQCT or HRpQCT).tw.
20	peripheral quantitative compute\$ tomogra\$.tw.
21	or/16-20
22	4 and 15 and 21

### E.17.6 Database: Embase

Last searched on **Embase** 1974 to 2016 Week 45 on 8<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	mucov\$.ti,ab.
3	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
4	or/1-3
5	exp metabolic bone disease/
6	bone density/
7	exp fracture/
8	osteolysis/
9	exp bone demineralization/
10	vitamin D deficiency/
11	bone densitometry/
12	(bone? adj2 (dens\$ or mass)).ti,ab.
13	(bone? adj3 (deminerali\$ or de minerali\$ or decalcif\$ or de calcif\$ or fractur\$ or fragil\$ or loss or atroph\$)).ti,ab.
14	(osteoporos\$ or osteop?en\$ or osteoly\$).ti,ab.
15	((fragil\$ or pathologic\$ or spontaneous\$) adj2 fractur\$).ti,ab.
16	((vitamin D or calcium) adj3 deficien\$).ti,ab.
17	or/5-16
18	photon absorptiometry/
19	dual energy X ray absorptiometry/
20	((x ray or xray or photon or DPX or dual energy or radiograph\$) adj2 (absorptio\$ or densit\$ or photodensit\$)).ti,ab.
21	(DEXA or DXA).ti,ab.
22	high resolution computer tomography/
23	(pQCT or HR pQCT or HRpQCT).ti,ab.
24	peripheral quantitative compute\$ tomogra\$.ti,ab.
25	or/18-24
26	4 and 17 and 25
27	limit 26 to english language

#	Searches
28	letter.pt. or LETTER/
29	note.pt.
30	editorial.pt.
31	CASE REPORT/ or CASE STUDY/
32	(letter or comment*).ti.
33	or/28-32
34	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
35	33 not 34
36	ANIMAL/ not HUMAN/
37	NONHUMAN/
38	exp ANIMAL EXPERIMENT/
39	exp EXPERIMENTAL ANIMAL/
40	ANIMAL MODEL/
41	exp RODENT/
42	(rat or rats or mouse or mice).ti.
43	or/35-42
44	27 not 43

## E.18 What is the effectiveness of programmes of exercise in the management of cystic fibrosis?

### E.18.1 Database: Medline

Last searched on **Ovid MEDLINE(R)** 1946 to December Week 4 2016 on 5<sup>th</sup> January 2017.

#	Searches
1	META-ANALYSIS/
2	META-ANALYSIS AS TOPIC/
3	(meta analy* or metanaly* or metaanaly*).ti,ab.
4	((systematic* or evidence*) adj2 (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	or/1-9
11	randomized controlled trial.pt.
12	controlled clinical trial.pt.
13	pragmatic clinical trial.pt.
14	randomi#ed.ab.
15	placebo.ab.
16	randomly.ab.
17	CLINICAL TRIALS AS TOPIC/
18	trial.ti.

#	Searches
19	or/11-18
20	or/10,19
21	CYSTIC FIBROSIS/
22	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
23	mucov\$.ti,ab.
24	or/21-23
25	exp EXERCISE/
26	exp EXERCISE THERAPY/
27	exp EXERCISE MOVEMENT TECHNIQUES/
28	exp SPORTS/
29	LIFE STYLE/
30	(exercis\$ or sport\$ or fit\$ or activ\$ or life style or lifestyle).ti,ab.
31	(walk\$ or run\$ or jog\$ or swim\$ or football or tennis or basketball or soccer or baseball).ti,ab.
32	(pilates or yoga or stretch\$ exercise\$ or breath\$ exercise?).ti,ab.
33	kinesi?therap\$.ti,ab.
34	((resistan\$ or interval or strength\$ or weight or physical or aerobic or anaerobic or endurance or muscle or isokinetic or dynamic or biometric or cardio\$) adj train\$).ti,ab.
35	(musculoskeletal and (physiotherap\$ or physical therap\$)).ti,ab.
36	or/25-35
37	24 and 36
38	limit 37 to english language
39	LETTER/
40	EDITORIAL/
41	NEWS/
42	exp HISTORICAL ARTICLE/
43	ANECDOTES AS TOPIC/
44	COMMENT/
45	CASE REPORT/
46	(letter or comment*).ti.
47	or/39-46
48	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
49	47 not 48
50	ANIMALS/ not HUMANS/
51	exp ANIMALS, LABORATORY/
52	exp ANIMAL EXPERIMENTATION/
53	exp MODELS, ANIMAL/
54	exp RODENTIA/
55	(rat or rats or mouse or mice).ti.
56	or/49-55
57	38 not 56
58	20 and 57

## E.18.2 Database: Medline In-Process & Other Non-Indexed Citations

Last searched on **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations** January 04, 2017 on 5<sup>th</sup> January 2017.

1	<b>((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.</b>
2	mucov\$.ti,ab.
3	1 or 2
4	(exercis\$ or sport\$ or fit\$ or activ\$ or life style or lifestyle).ti,ab.
5	(walk\$ or run\$ or jog\$ or swim\$ or football or tennis or basketball or soccer or baseball).ti,ab.
6	(pilates or yoga or stretch\$ exercise\$ or breath\$ exercise?).ti,ab.
7	kinesi?therap\$.ti,ab.
8	((resistan\$ or interval or strength\$ or weight or physical or aerobic or anaerobic or endurance or muscle or isokinetic or dynamic or biometric or cardio\$) adj train\$).ti,ab.
9	(musculoskeletal and (physiotherap\$ or physical therap\$)).ti,ab.
10	or/4-9
11	3 and 10

### E.18.3 Database: Cochrane Central Register of Controlled Trials

Last searched on **EBM Reviews - Cochrane Central Register of Controlled Trials** November 2016 on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	<b>((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.</b>
3	mucov\$.ti,ab.
4	or/1-3
5	exp EXERCISE/
6	exp EXERCISE THERAPY/
7	exp EXERCISE MOVEMENT TECHNIQUES/
8	exp SPORTS/
9	LIFE STYLE/
10	(exercis\$ or sport\$ or fit\$ or activ\$ or life style or lifestyle).ti,ab,kw.
11	(walk\$ or run\$ or jog\$ or swim\$ or football or tennis or basketball or soccer or baseball).ti,ab,kw.
12	(pilates or yoga or stretch\$ exercise\$ or breath\$ exercise?).ti,ab,kw.
13	kinesi?therap\$.ti,ab,kw.
14	((resistan\$ or interval or strength\$ or weight or physical or aerobic or anaerobic or endurance or muscle or isokinetic or dynamic or biometric or cardio\$) adj train\$).ti,ab.
15	(musculoskeletal and (physiotherap\$ or physical therap\$)).ti,ab.
16	or/5-15
17	4 and 16
18	limit 17 to english language

### E.18.4 Database: Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects

Last searched on **EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to January 05, 2017, **EBM Reviews - Database of Abstracts of Reviews of Effects 1st Quarter 2015** on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS.kw.
2	<b>((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.</b>

#	Searches
3	mucov\$.ti,ab.
4	or/1-3
5	EXERCISE.kw.
6	EXERCISE THERAPY.kw.
7	EXERCISE MOVEMENT TECHNIQUES.kw.
8	SPORTS.kw.
9	LIFE STYLE.kw.
10	(exercis\$ or sport\$ or fit\$ or activ\$ or life style or lifestyle).ti,ab,kw.
11	(walk\$ or run\$ or jog\$ or swim\$ or football or tennis or basketball or soccer or baseball).ti,ab,kw.
12	(pilates or yoga or stretch\$ exercise\$ or breath\$ exercise?).ti,ab,kw.
13	kinesi?therap\$.ti,ab,kw.
14	((resistan\$ or interval or strength\$ or weight or physical or aerobic or anaerobic or endurance or muscle or isokinetic or dynamic or biometric or cardio\$) adj train\$).ti,ab.
15	(musculoskeletal and (physiotherap\$ or physical therap\$)).ti,ab.
16	or/5-15
17	4 and 16

### E.18.5 Database: Health Technology Assessment

Last searched on EBM Reviews - Health Technology Assessment 4th Quarter 2016 on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).mp.
3	mucov\$.mp.
4	or/1-3
5	exp EXERCISE/
6	exp EXERCISE THERAPY/
7	exp EXERCISE MOVEMENT TECHNIQUES/
8	exp SPORTS/
9	LIFE STYLE/
10	(exercis\$ or sport\$ or fit\$ or activ\$ or life style or lifestyle).ti,tw.
11	(walk\$ or run\$ or jog\$ or swim\$ or football or tennis or basketball or soccer or baseball).ti,tw.
12	(pilates or yoga or stretch\$ exercise\$ or breath\$ exercise?).ti,tw.
13	kinesi?therap\$.ti,tw.
14	((resistan\$ or interval or strength\$ or weight or physical or aerobic or anaerobic or endurance or muscle or isokinetic or dynamic or biometric or cardio\$) adj train\$).ti,tw.
15	(musculoskeletal and (physiotherap\$ or physical therap\$)).ti,tw.
16	or/5-15
17	4 and 16

### E.18.6 Database: Embase

Last searched on **Embase** 1974 to 2017 Week 01 on 4<sup>th</sup> January 2017.

#	Searches
1	SYSTEMATIC REVIEW/

#	Searches
2	META-ANALYSIS/
3	(meta analy* or metanaly* or metaanaly*).ti,ab.
4	((systematic or evidence) adj2 (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	((pool* or combined) adj2 (data or trials or studies or results)).ab.
10	cochrane.jw.
11	or/1-10
12	random*.ti,ab.
13	factorial*.ti,ab.
14	(crossover* or cross over*).ti,ab.
15	((doubl* or singl*) adj blind*).ti,ab.
16	(assign* or allocat* or volunteer* or placebo*).ti,ab.
17	CROSSOVER PROCEDURE/
18	SINGLE BLIND PROCEDURE/
19	RANDOMIZED CONTROLLED TRIAL/
20	DOUBLE BLIND PROCEDURE/
21	or/12-20
22	or/11,21
23	CYSTIC FIBROSIS/
24	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
25	mucov\$.ti,ab.
26	or/23-25
27	EXERCISE/
28	KINESIOTHERAPY/
29	exercise therap\$.ti,ab.
30	exercise movement technique?.ti,ab.
31	SPORT/
32	LIFESTYLE/
33	(exercis\$ or sport\$ or fit\$ or activ\$ or life style or lifestyle).ti. or (exercis\$ or sport\$ or fit\$ or activ\$ or life style or lifestyle).ab. /freq=2
34	(walk\$ or run\$ or jog\$ or swim\$ or football or tennis or basketball or soccer or baseball).ti,ab.
35	(pilates or yoga or stretch\$ exercise\$ or breath\$ exercise?).ti,ab.
36	((resistan\$ or interval or strength\$ or weight or physical or aerobic or anaerobic or endurance or muscle or isokinetic or dynamic or biometric or cardio\$) adj train\$).ti,ab.
37	(musculoskeletal and (physiotherap\$ or physical therap\$)).ti,ab.
38	or/27-37
39	26 and 38
40	limit 39 to english language
41	letter.pt. or LETTER/
42	note.pt.

#	Searches
43	editorial.pt.
44	CASE REPORT/ or CASE STUDY/
45	(letter or comment*).ti.
46	or/41-45
47	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
48	46 not 47
49	ANIMAL/ not HUMAN/
50	NONHUMAN/
51	exp ANIMAL EXPERIMENT/
52	exp EXPERIMENTAL ANIMAL/
53	ANIMAL MODEL/
54	exp RODENT/
55	(rat or rats or mouse or mice).ti.
56	or/48-55
57	40 not 56
58	22 and 57

## E.19 What strategies are effective at identifying people with cystic fibrosis for the presence of a psychological and/or behavioural problem?

### E.19.1 Database: Medline

Last searched on **Ovid MEDLINE(R)** 1946 to October Week 3 2016 on 8<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	MENTAL HEALTH/
6	exp MENTAL DISORDERS/
7	ADAPTATION, PSYCHOLOGICAL/
8	(mental\$ adj2 health?).ab,ti.
9	((Mental\$ or Adjust\$ or Anxiety or Obsessive\$ or Compulsive\$ or Panic\$ or Phobi? or Stress\$ or Dissociative or Eating or food or Binge or Factitious or Impuls\$ or Mood\$ or Affective or Neurotic or Personality or Paranoid or Psychotic or Sexual\$ or Gender or Sleep\$ or Somatoform or Body Dysmorphi? or Conversion) adj3 Disorder?).ab,ti.
10	((Substance? or drug? or Alcohol or Tobacco) adj3 (Disorder? or misus\$ or abus\$)).ab,ti.
11	(Agoraphobi\$ or Anorexi\$ or Bulimi\$ or Schizophreni\$ or Dyssomni\$ or Parasomni\$ or Neurastheni\$).ab,ti.
12	((avoid\$ or restrict\$) adj3 food?).ti,ab.
13	DEPRESSION/
14	depress\$.ab,ti.
15	mood?.ti,ab.
16	ANXIETY/
17	anxiet\$.ti,ab.

#	Searches
18	NEEDLES/
19	needle?.ti,ab.
20	PATIENT COMPLIANCE/
21	MEDICATION ADHERENCE/
22	TREATMENT REFUSAL/
23	((adhere\$ or nonadher\$ or complia\$ or comply\$ or noncomplia\$ or noncomply\$ or cooperat\$ or co-operat\$) adj3 (patient? or medication? or treat\$)).ti,ab.
24	(refus\$ adj3 treat\$).ti,ab.
25	ABSENTEEISM/
26	(School\$ adj3 (refus\$ or absen\$)).ti,ab.
27	truans\$.ti,ab.
28	or/5-27
29	MASS SCREENING/
30	screen\$.ab,ti.
31	exp QUESTIONNAIRES/
32	(questionnaire? or self report\$).ab,ti.
33	(clinical\$ adj3 assess\$).ti,ab.
34	or/29-33
35	4 and 28 and 34
36	(Generalized Anxiety Disorder 7 or Generalized Anxiety Disorder seven or GAD-7 or Patient Health Questionnaire 2 or Patient Health Questionnaire two or PHQ-2 or Patient Health Questionnaire 9 or Patient Health Questionnaire nine or PHQ-9 or (Hospital Anxiety and Depression Scale?) or HADS or P?ediatric Index of Emotional Distress or PI-ED or Cystic Fibrosis Questionnaire Revised or CFQ-R or Cystic Fibrosis Quality of Life Questionnaire or CFQOL or Centre for Epidemiologic Studies Depression Score or CES-D or Eating Disorders Examination or EDE or Child Eating Disorders Examination or CEDE or Eating Attitudes Test or Child Eating Attitude Test or ChEAT or (Cystic fibrosis eating attitudes and behaviours) or CFEAB).ti,ab.
37	4 and 36
38	MENTAL DISORDERS/di [Diagnosis]
39	MENTAL DISORDERS/ep [Epidemiology]
40	DEPRESSION/di [Diagnosis]
41	DEPRESSION/ep [Epidemiology]
42	((mental\$ health or depress\$) adj5 (Identif\$ or assess\$ or diagnos\$)).ab,ti.
43	or/38-42
44	4 and 43
45	35 or 37 or 44
46	limit 45 to english language
47	LETTER/
48	EDITORIAL/
49	NEWS/
50	exp HISTORICAL ARTICLE/
51	ANECDOTES AS TOPIC/
52	COMMENT/
53	CASE REPORT/
54	(letter or comment*).ti.
55	or/47-54
56	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.

#	Searches
57	55 not 56
58	ANIMALS/ not HUMANS/
59	exp ANIMALS, LABORATORY/
60	exp ANIMAL EXPERIMENTATION/
61	exp MODELS, ANIMAL/
62	exp RODENTIA/

## E.19.2 Database: Medline In-Process & Other Non-Indexed Citations

Last searched on **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations**  
November 02, 2016 on 8<sup>th</sup> November 2016.

#	Searches
1	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
2	mucov\$.ti,ab.
3	or/1-2
4	(mental\$ adj2 health?).ab,ti.
5	((Mental\$ or Adjust\$ or Anxiety or Obsessive\$ or Compulsive\$ or Panic\$ or Phobi? or Stress\$ or Dissociative or Eating or food or Binge or Factitious or Impuls\$ or Mood\$ or Affective or Neurotic or Personality or Paranoid or Psychotic or Sexual\$ or Gender or Sleep\$ or Somatoform or Body Dysmorphi? or Conversion) adj3 Disorder?).ab,ti.
6	((Substance? or drug? or Alcohol or Tobacco) adj3 (Disorder? or misus\$ or abus\$)).ab,ti.
7	(Agoraphobi\$ or Anorexi\$ or Bulimi\$ or Schizophreni\$ or Dyssomni\$ or Parasomni\$ or Neurastheni\$).ab,ti.
8	((avoid\$ or restrict\$) adj3 food?).ti,ab.
9	depress\$.ab,ti.
10	mood?.ti,ab.
11	anxiet\$.ti,ab.
12	needle?.ti,ab.
13	((adhere\$ or nonadher\$ or complia\$ or comply\$ or noncomplia\$ or noncomply\$ or cooperat\$ or co-operat\$) adj3 (patient? or medication? or treat\$)).ti,ab.
14	(refus\$ adj3 treat\$).ti,ab.
15	(School\$ adj3 (refus\$ or absen\$)).ti,ab.
16	truan\$.ti,ab.
17	or/4-16
18	screen\$.ab,ti.
19	(questionnaire? or self report\$).ab,ti.
20	(clinical\$ adj3 assess\$).ti,ab.
21	or/18-20
22	3 and 17 and 21
23	(Generalized Anxiety Disorder 7 or Generalized Anxiety Disorder seven or GAD-7 or Patient Health Questionnaire 2 or Patient Health Questionnaire two or PHQ-2 or Patient Health Questionnaire 9 or Patient Health Questionnaire nine or PHQ-9 or (Hospital Anxiety and Depression Scale?) or HADS or P?ediatric Index of Emotional Distress or PI-ED or Cystic Fibrosis Questionnaire Revised or CFQ-R or Cystic Fibrosis Quality of Life Questionnaire or CFQOL or Centre for Epidemiologic Studies Depression Score or CES-D or Eating Disorders Examination or EDE or Child Eating Disorders Examination or CEDE or Eating Attitudes Test or Child Eating Attitude Test or ChEAT or (Cystic fibrosis eating attitudes and behaviours) or CFEAB).ti,ab.
24	3 and 23

#	Searches
25	((mental\$ health or depress\$) adj5 (Identif\$ or assess\$ or diagnos\$)).ab,ti.
26	3 and 25
27	22 or 24 or 26

### E.19.3 Database: Cochrane Central Register of Controlled Trials

Last searched on **EBM Reviews - Cochrane Central Register of Controlled Trials**  
September 2016 on 8<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab,kw.
4	or/1-3
5	MENTAL HEALTH/
6	exp MENTAL DISORDERS/
7	ADAPTATION, PSYCHOLOGICAL/
8	(mental\$ adj2 health?).ab,ti.
9	((Mental\$ or Adjust\$ or Anxiety or Obsessive\$ or Compulsive\$ or Panic\$ or Phobi? or Stress\$ or Dissociative or Eating or food or Binge or Factitious or Impuls\$ or Mood\$ or Affective or Neurotic or Personality or Paranoid or Psychotic or Sexual\$ or Gender or Sleep\$ or Somatoform or Body Dysmorphi? or Conversion) adj3 Disorder?).ab,ti.
10	((Substance? or drug? or Alcohol or Tobacco) adj3 (Disorder? or misus\$ or abus\$)).ab,ti.
11	(Agoraphobi\$ or Anorexi\$ or Bulimi\$ or Schizophreni\$ or Dyssomni\$ or Parasomni\$ or Neurastheni\$).ab,ti,kw.
12	((avoid\$ or restrict\$) adj3 food?).ti,ab.
13	DEPRESSION/
14	depress\$.ab,ti,kw.
15	mood?.ti,ab,kw.
16	ANXIETY/
17	anxiet\$.ti,ab,kw.
18	NEEDLES/
19	needle?.ti,ab,kw.
20	PATIENT COMPLIANCE/
21	MEDICATION ADHERENCE/
22	TREATMENT REFUSAL/
23	((adhere\$ or nonadher\$ or complia\$ or comply\$ or noncomplia\$ or noncomply\$ or cooperat\$ or co-operat\$) adj3 (patient? or medication? or treat\$)).ti,ab.
24	(refus\$ adj3 treat\$).ti,ab.
25	ABSENTEEISM/
26	(School\$ adj3 (refus\$ or absen\$)).ti,ab.
27	truan\$.ti,ab,kw.
28	or/5-27
29	MASS SCREENING/
30	screen\$.ab,ti,kw.
31	exp QUESTIONNAIRES/
32	(questionnaire? or self report\$).ab,ti,kw.
33	(clinical\$ adj3 assess\$).ti,ab.

#	Searches
34	or/29-33
35	4 and 28 and 34
36	(Generalized Anxiety Disorder 7 or Generalized Anxiety Disorder seven or GAD-7 or Patient Health Questionnaire 2 or Patient Health Questionnaire two or PHQ-2 or Patient Health Questionnaire 9 or Patient Health Questionnaire nine or PHQ-9 or (Hospital Anxiety and Depression Scale?) or HADS or P?ediatric Index of Emotional Distress or PI-ED or Cystic Fibrosis Questionnaire Revised or CFQ-R or Cystic Fibrosis Quality of Life Questionnaire or CFQOL or Centre for Epidemiologic Studies Depression Score or CES-D or Eating Disorders Examination or EDE or Child Eating Disorders Examination or CEDE or Eating Attitudes Test or Child Eating Attitude Test or ChEAT or (Cystic fibrosis eating attitudes and behaviours) or CFEAB).ti,ab.
37	4 and 36
38	MENTAL DISORDERS/di [Diagnosis]
39	MENTAL DISORDERS/ep [Epidemiology]
40	DEPRESSION/di [Diagnosis]
41	DEPRESSION/ep [Epidemiology]
42	((mental\$ health or depress\$) adj5 (Identif\$ or assess\$ or diagnos\$)).ab,ti.
43	or/38-42
44	4 and 43
45	35 or 37 or 44

#### E.19.4 Database: Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects

Last searched on **EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to November 02, 2016, **EBM Reviews - Database of Abstracts of Reviews of Effects** 1st Quarter 2015 on 8<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS.kw.
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	MENTAL HEALTH.kw.
6	MENTAL DISORDERS.kw.
7	ADAPTATION, PSYCHOLOGICAL.kw.
8	(mental\$ adj2 health?).ab,ti.
9	((Mental\$ or Adjust\$ or Anxiety or Obsessive\$ or Compulsive\$ or Panic\$ or Phobi? or Stress\$ or Dissociative or Eating or food or Binge or Factitious or Impuls\$ or Mood\$ or Affective or Neurotic or Personality or Paranoid or Psychotic or Sexual\$ or Gender or Sleep\$ or Somatoform or Body Dysmorphi? or Conversion) adj3 Disorder?).ab,ti.
10	((Substance? or drug? or Alcohol or Tobacco) adj3 (Disorder? or misus\$ or abus\$)).ab,ti.
11	(Agoraphobi\$ or Anorexi\$ or Bulimi\$ or Schizophreni\$ or Dyssomni\$ or Parasomni\$ or Neurastheni\$).ab,ti.
12	((avoid\$ or restrict\$) adj3 food?).ti,ab.
13	DEPRESSION.kw.
14	depress\$.ab,ti.
15	mood?.ti,ab.
16	ANXIETY.kw.
17	anxiety\$.ti,ab.

#	Searches
18	NEEDLES.kw.
19	needle?.ti,ab.
20	PATIENT COMPLIANCE.kw.
21	MEDICATION ADHERENCE.kw.
22	TREATMENT REFUSAL.kw.
23	((adhere\$ or nonadher\$ or complia\$ or comply\$ or noncompli\$ or noncomply\$ or cooperat\$ or co-operat\$) adj3 (patient? or medication? or treat\$)).ti,ab.
24	(refus\$ adj3 treat\$).ti,ab.
25	ABSENTEEISM.kw.
26	(School\$ adj3 (refus\$ or absen\$)).ti,ab.
27	truan\$.ti,ab.
28	or/5-27
29	MASS SCREENING.kw.
30	screen\$.ab,ti.
31	QUESTIONNAIRES.kw.
32	(questionnaire? or self report\$).ab,ti.
33	(clinical\$ adj3 assess\$).ti,ab.
34	or/29-33
35	4 and 28 and 34
36	(Generalized Anxiety Disorder 7 or Generalized Anxiety Disorder seven or GAD-7 or Patient Health Questionnaire 2 or Patient Health Questionnaire two or PHQ-2 or Patient Health Questionnaire 9 or Patient Health Questionnaire nine or PHQ-9 or (Hospital Anxiety and Depression Scale?) or HADS or P?ediatric Index of Emotional Distress or PI-ED or Cystic Fibrosis Questionnaire Revised or CFQ-R or Cystic Fibrosis Quality of Life Questionnaire or CFQOL or Centre for Epidemiologic Studies Depression Score or CES-D or Eating Disorders Examination or EDE or Child Eating Disorders Examination or CEDE or Eating Attitudes Test or Child Eating Attitude Test or ChEAT or (Cystic fibrosis eating attitudes and behaviours) or CFEAB).ti,ab.
37	4 and 36
38	((mental\$ health or depress\$) adj5 (Identif\$ or assess\$ or diagnos\$)).ab,ti.
39	4 and 38
40	35 or 37 or 39

### E.19.5 Database: Health Technology Assessment

Last searched on **EBM Reviews - Health Technology Assessment 3rd Quarter 2016** on 8<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).tw.
3	mucov\$.tw.
4	or/1-3
5	MENTAL HEALTH/
6	exp MENTAL DISORDERS/
7	ADAPTATION, PSYCHOLOGICAL/
8	(mental\$ adj2 health?).tw.
9	((Mental\$ or Adjust\$ or Anxiety or Obsessive\$ or Compulsive\$ or Panic\$ or Phobi? or Stress\$ or Dissociative or Eating or food or Binge or Factitious or Impuls\$ or Mood\$ or Affective or Neurotic or Personality or Paranoid or Psychotic or Sexual\$ or Gender or

#	Searches
	Sleep\$ or Somatoform or Body Dysmorphi? or Conversion) adj3 Disorder?).tw.
10	((Substance? or drug? or Alcohol or Tobacco) adj3 (Disorder? or misus\$ or abus\$)).tw.
11	(Agoraphobi\$ or Anorexi\$ or Bulimi\$ or Schizophreni\$ or Dysssomni\$ or Parasomni\$ or Neurastheni\$).tw.
12	((avoid\$ or restrict\$) adj3 food?).tw.
13	DEPRESSION/
14	depress\$.tw.
15	mood?.tw.
16	ANXIETY/
17	anxiety\$.tw.
18	NEEDLES/
19	needle?.tw.
20	PATIENT COMPLIANCE/
21	MEDICATION ADHERENCE/
22	TREATMENT REFUSAL/
23	((adhere\$ or nonadher\$ or complia\$ or comply\$ or noncomplia\$ or noncomply\$ or cooperat\$ or co-operat\$) adj3 (patient? or medication? or treat\$)).tw.
24	(refus\$ adj3 treat\$).tw.
25	ABSENTEEISM/
26	(School\$ adj3 (refus\$ or absen\$)).tw.
27	truancy\$.tw.
28	or/5-27
29	MASS SCREENING/
30	screen\$.tw.
31	exp QUESTIONNAIRES/
32	(questionnaire? or self report\$).tw.
33	(clinical\$ adj3 assess\$).tw.
34	or/29-33
35	4 and 28 and 34
36	(Generalized Anxiety Disorder 7 or Generalized Anxiety Disorder seven or GAD-7 or Patient Health Questionnaire 2 or Patient Health Questionnaire two or PHQ-2 or Patient Health Questionnaire 9 or Patient Health Questionnaire nine or PHQ-9 or (Hospital Anxiety and Depression Scale?) or HADS or P?ediatric Index of Emotional Distress or PI-ED or Cystic Fibrosis Questionnaire Revised or CFQ-R or Cystic Fibrosis Quality of Life Questionnaire or CFQOL or Centre for Epidemiologic Studies Depression Score or CES-D or Eating Disorders Examination or EDE or Child Eating Disorders Examination or CEDE or Eating Attitudes Test or Child Eating Attitude Test or ChEAT or (Cystic fibrosis eating attitudes and behaviours) or CFEAB).tw.
37	4 and 36
38	MENTAL DISORDERS/di [Diagnosis]
39	MENTAL DISORDERS/ep [Epidemiology]
40	DEPRESSION/di [Diagnosis]
41	DEPRESSION/ep [Epidemiology]
42	((mental\$ health or depress\$) adj5 (Identif\$ or assess\$ or diagnos\$)).tw.
43	or/38-42
44	4 and 43
45	35 or 37 or 44

## E.19.6 Database: Embase

Last searched on **Embase** 1974 to 2016 Week 44 on 8<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	exp *MENTAL HEALTH/
6	exp *MENTAL DISEASE/
7	*ADAPTIVE BEHAVIOR/
8	(mental\$ adj2 health?).ab,ti.
9	((Mental\$ or Adjust\$ or Anxiety or Obsessive\$ or Compulsive\$ or Panic\$ or Phobi? or Stress\$ or Dissociative or Eating or food or Binge or Factitious or Impuls\$ or Mood\$ or Affective or Neurotic or Personality or Paranoid or Psychotic or Sexual\$ or Gender or Sleep\$ or Somatoform or Body Dysmorphi? or Conversion) adj3 Disorder?).ab,ti.
10	((Substance? or drug? or Alcohol or Tobacco) adj3 (Disorder? or misus\$ or abus\$)).ab,ti.
11	(Agoraphobi\$ or Anorexi\$ or Bulimi\$ or Schizophreni\$ or Dyssomni\$ or Parasomni\$ or Neurastheni\$).ab,ti.
12	((avoid\$ or restrict\$) adj3 food?).ti,ab.
13	exp *DEPRESSION/
14	depress\$.ti.
15	depress\$.ab. /freq=2
16	mood?.ti,ab.
17	*ANXIETY/
18	anxiety\$.ti.
19	anxiety\$.ab. /freq=2
20	*NEEDLE/
21	needle?.ti,ab.
22	*PATIENT COMPLIANCE/
23	*MEDICATION COMPLIANCE/
24	*TREATMENT REFUSAL/
25	((adhere\$ or nonadher\$ or complia\$ or comply\$ or noncomplia\$ or noncomply\$ or cooperat\$ or co-operat\$) adj3 (patient? or medication? or treat\$)).ti,ab.
26	(refus\$ adj3 treat\$).ti,ab.
27	*ABSENTEEISM/
28	(School\$ adj3 (refus\$ or absen\$)).ti,ab.
29	truan\$.ti,ab.
30	or/5-29
31	*SCREENING/
32	exp *MASS SCREENING/
33	*SCREENING TEST/
34	screen\$.ab,ti.
35	exp *QUESTIONNAIRES/
36	(questionnaire? or self report\$).ab,ti.
37	(clinical\$ adj3 assess\$).ti,ab.
38	or/31-37

#	Searches
39	4 and 30 and 38
40	(Generalized Anxiety Disorder 7 or Generalized Anxiety Disorder seven or GAD-7 or Patient Health Questionnaire 2 or Patient Health Questionnaire two or PHQ-2 or Patient Health Questionnaire 9 or Patient Health Questionnaire nine or PHQ-9 or HADS or P?ediatric Index of Emotional Distress or PI-ED or Cystic Fibrosis Questionnaire Revised or Cystic Fibrosis Quality of Life Questionnaire or CFQOL or Centre for Epidemiologic Studies Depression Score or CES-D or Eating Disorders Examination or EDE or Child Eating Disorders Examination or CEDE or Eating Attitudes Test or Child Eating Attitude Test or ChEAT or (Cystic fibrosis eating attitudes and behaviours) or CFEAB).ti,ab.
41	4 and 40
42	((Hospital Anxiety and Depression Scale?) or CFQ-R).ti,ab.
43	4 and 30 and 42
44	exp *MENTAL DISEASE/di [Diagnosis]
45	exp *MENTAL DISEASE/ep [Epidemiology]
46	exp *DEPRESSION/di [Diagnosis]
47	exp *DEPRESSION/ep [Epidemiology]
48	((mental\$ health or depress\$) adj5 (Identif\$ or assess\$ or diagnos\$)).ab,ti.
49	or/44-48
50	4 and 49
51	39 or 41 or 43 or 50
52	limit 51 to english language
53	letter.pt. or LETTER/
54	note.pt.
55	editorial.pt.
56	CASE REPORT/ or CASE STUDY/
57	(letter or comment*).ti.
58	or/53-57
59	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
60	58 not 59
61	ANIMAL/ not HUMAN/
62	NONHUMAN/
63	exp ANIMAL EXPERIMENT/
64	exp EXPERIMENTAL ANIMAL/
65	ANIMAL MODEL/
66	exp RODENT/
67	(rat or rats or mouse or mice).ti.
68	or/60-67
69	52 not 68

### E.19.7 Database: PsycINFO

Last searched on **PsycINFO** 1967 to October Week 5 2016 on 8<sup>th</sup> November 2016.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3

#	Searches
5	MENTAL HEALTH/
6	exp MENTAL DISORDERS/
7	EMOTIONAL ADJUSTMENT/
8	(mental\$ adj2 health?).ab,ti.
9	((Mental\$ or Adjust\$ or Anxiety or Obsessive\$ or Compulsive\$ or Panic\$ or Phobi? or Stress\$ or Dissociative or Eating or food or Binge or Factitious or Impuls\$ or Mood\$ or Affective or Neurotic or Personality or Paranoid or Psychotic or Sexual\$ or Gender or Sleep\$ or Somatoform or Body Dysmorphi? or Conversion) adj3 Disorder?).ab,ti.
10	((Substance? or drug? or Alcohol or Tobacco) adj3 (Disorder? or misus\$ or abus\$)).ab,ti.
11	(Agoraphobi\$ or Anorexi\$ or Bulimi\$ or Schizophreni\$ or Dyssomni\$ or Parasomni\$ or Neurastheni\$).ab,ti.
12	((avoid\$ or restrict\$) adj3 food?).ti,ab.
13	"DEPRESSION (EMOTION)"/
14	MAJOR DEPRESSION/
15	depress\$.ab,ti.
16	mood?.ti,ab.
17	ANXIETY/
18	anxiety\$.ti,ab.
19	needle?.ti,ab.
20	TREATMENT COMPLIANCE/
21	TREATMENT REFUSAL/
22	((adhere\$ or nonadher\$ or complia\$ or comply\$ or noncomplia\$ or noncomply\$ or cooperat\$ or co-operat\$) adj3 (patient? or medication? or treat\$)).ti,ab.
23	(refus\$ adj3 treat\$).ti,ab.
24	SCHOOL ATTENDANCE/
25	SCHOOL REFUSAL/
26	(School\$ adj3 (refus\$ or absen\$)).ti,ab.
27	truancy\$.ti,ab.
28	or/5-27
29	SCREENING/ or SCREENING TESTS/
30	screen\$.ab,ti.
31	exp QUESTIONNAIRES/
32	(questionnaire? or self report\$).ab,ti.
33	(clinical\$ adj3 assess\$).ti,ab.
34	or/29-33
35	4 and 28 and 34
36	(Generalized Anxiety Disorder 7 or Generalized Anxiety Disorder seven or GAD-7 or Patient Health Questionnaire 2 or Patient Health Questionnaire two or PHQ-2 or Patient Health Questionnaire 9 or Patient Health Questionnaire nine or PHQ-9 or (Hospital Anxiety and Depression Scale?) or HADS or P?ediatric Index of Emotional Distress or PI-ED or Cystic Fibrosis Questionnaire Revised or CFQ-R or Cystic Fibrosis Quality of Life Questionnaire or CFQOL or Centre for Epidemiologic Studies Depression Score or CES-D or Eating Disorders Examination or EDE or Child Eating Disorders Examination or CEDE or Eating Attitudes Test or Child Eating Attitude Test or ChEAT or (Cystic fibrosis eating attitudes and behaviours) or CFEAB).ti,ab.
37	4 and 36
38	PSYCHOLOGICAL ASSESSMENT/
39	PSYCHIATRIC EVALUATION/

#	Searches
40	PSYCHODIAGNOSIS/
41	((mental\$ health or depress\$) adj5 (Identif\$ or assess\$ or diagnos\$)).ab,ti.
42	or/38-41
43	4 and 42
44	35 or 37 or 43
45	limit 44 to english language
46	limit 45 to ("0100 journal" or "0110 peer-reviewed journal" or "0120 non-peer-reviewed journal" or "0130 peer-reviewed status unknown" or "0500 electronic collection")

## E.20 Cross infection control

**E.20.1 What is the effectiveness of cohorting on the basis of pathogen status versus not cohorting on the basis of pathogen status in reducing transmission of CF pathogens?**

**E.20.2 What is the effectiveness of different models of segregating patient's in reducing transmission of CF pathogens?**

**E.20.3 What is the effectiveness of individual protective equipment in reducing transmission of CF pathogens? 4) What is the effectiveness of the combination of cohorting, segregating and protective equipment in reducing transmission of CF pathogens?**

- Database: Medline

Last searched on **Ovid MEDLINE(R)** 1946 to December Week 1 2016 on 5<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	exp CROSS INFECTION/pc [Prevention & Control]
6	exp INFECTION CONTROL/
7	COMMUNICABLE DISEASE CONTROL/
8	INFECTIOUS DISEASE TRANSMISSION, PATIENT-TO-PROFESSIONAL/pc [Prevention & Control]
9	INFECTIOUS DISEASE TRANSMISSION, PROFESSIONAL-TO-PATIENT/pc [Prevention & Control]
10	DISEASE TRANSMISSION, INFECTIOUS/pc [Prevention & Control]
11	BACTERIAL INFECTIONS/pc, tm [Prevention & Control, Transmission]
12	PSEUDOMONAS INFECTIONS/pc, tm [Prevention & Control, Transmission]
13	BURKHOLDERIA INFECTIONS/pc, tm [Prevention & Control, Transmission]
14	STAPHYLOCOCCAL INFECTIONS/pc, tm [Prevention & Control, Transmission]
15	HAEMOPHILUS INFECTIONS/pc, tm [Prevention & Control, Transmission]
16	MYCOBACTERIUM INFECTIONS, NONTUBERCULOUS/pc, tm [Prevention & Control, Transmission]
17	((infect\$ or crossinfect\$ or crosstransmi\$ or contamina\$ or crosscontamina\$) adj3 (prevent\$ or control\$ or reduc\$)).ti,ab.
18	((nosocomial or hospital acquired) adj3 (disease? or infect\$ or pathogen\$) adj3 (prevent\$

#	Searches
	or control\$ or reduc\$).ti,ab.
19	((disease? or infect\$ or pathogen\$ or bacteri\$) adj3 (transmi\$ or acquir\$ or spread\$) adj3 (prevent\$ or control\$ or reduc\$)).ti,ab.
20	((pseudomon\$ or burkholder\$ or staphylococc\$ or MRSA or h?emophil\$ or mycobacteri\$ or aspergill\$) adj3 (transmi\$ or acquir\$ or spread\$) adj3 (prevent\$ or control\$ or reduc\$)).ti,ab.
21	or/5-20
22	PATIENT ISOLATION/
23	PATIENTS' ROOMS/
24	((patient? or clinic?) adj3 (cohorted or cohorting or isolate or isolating or isolation or segregat\$ or separat\$ or seclu\$ or quarantin\$ or confine or confined or confining)).ti,ab.
25	((patient? or inpatient? or single-patient or clinic?) adj3 (ensuite or bathroom? or playroom? or room? or facility or facilities or waiting)).ti,ab.
26	or/22-25
27	PATIENT ISOLATORS/
28	PERSONAL PROTECTIVE EQUIPMENT/
29	PROTECTIVE DEVICES/
30	PROTECTIVE CLOTHING/
31	GLOVES, PROTECTIVE/
32	EYE PROTECTIVE DEVICES/
33	MASKS/
34	(glove? or mask? or gown? or apron? or glasses or goggles).ti,ab.
35	(protect\$ adj3 (cloth\$ or equip\$)).ti,ab.
36	or/27-35
37	or/21,26,36
38	and/4,37
39	limit 38 to english language
40	LETTER/
41	EDITORIAL/
42	NEWS/
43	exp HISTORICAL ARTICLE/
44	ANECDOTES AS TOPIC/
45	COMMENT/
46	CASE REPORT/
47	(letter or comment*).ti.
48	or/40-47
49	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
50	48 not 49
51	ANIMALS/ not HUMANS/
52	exp ANIMALS, LABORATORY/
53	exp ANIMAL EXPERIMENTATION/
54	exp MODELS, ANIMAL/
55	exp RODENTIA/
56	(rat or rats or mouse or mice).ti.
57	or/50-56
58	39 not 57

- Database: Medline In-Process & Other Non-Indexed Citations

Last searched on **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations** January 04, 2017 on 5<sup>th</sup> January 2017.

#	Searches
1	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
2	mucov\$.ti,ab.
3	or/1-2
4	((infect\$ or crossinfect\$ or crosstranmi\$ or contamina\$ or crosscontamina\$) adj3 (prevent\$ or control\$ or reduc\$)).ti,ab.
5	((nosocomial or hospital acquired) adj3 (disease? or infect\$ or pathogen\$) adj3 (prevent\$ or control\$ or reduc\$)).ti,ab.
6	((disease? or infect\$ or pathogen\$ or bacteri\$) adj3 (transmi\$ or acquir\$ or spread\$) adj3 (prevent\$ or control\$ or reduc\$)).ti,ab.
7	((pseudomon\$ or burkholder\$ or staphylococc\$ or MRSA or h?emophil\$ or mycobacteri\$ or aspergill\$) adj3 (transmi\$ or acquir\$ or spread\$) adj3 (prevent\$ or control\$ or reduc\$)).ti,ab.
8	or/4-7
9	((patient? or clinic?) adj3 (cohorted or cohorting or isolate or isolating or isolation or segregat\$ or separat\$ or seclu\$ or quarantin\$ or confine or confined or confining)).ti,ab.
10	((patient? or inpatient? or single-patient or clinic?) adj3 (ensuite or bathroom? or playroom? or room? or facility or facilities or waiting)).ti,ab.
11	or/9-10
12	(glove? or mask? or gown? or apron? or glasses or goggles).ti,ab.
13	(protect\$ adj3 (cloth\$ or equip\$)).ti,ab.
14	or/12-13
15	or/8,11,14
16	and/3,15

- Database: Cochrane Central Register of Controlled Trials

Last searched on **EBM Reviews - Cochrane Central Register of Controlled Trials** November 2016 on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab,kw.
3	mucov\$.ti,ab.
4	or/1-3
5	exp CROSS INFECTION/pc [Prevention & Control]
6	exp INFECTION CONTROL/
7	COMMUNICABLE DISEASE CONTROL/
8	INFECTIOUS DISEASE TRANSMISSION, PATIENT-TO-PROFESSIONAL/pc [Prevention & Control]
9	INFECTIOUS DISEASE TRANSMISSION, PROFESSIONAL-TO-PATIENT/pc [Prevention & Control]
10	DISEASE TRANSMISSION, INFECTIOUS/pc [Prevention & Control]
11	BACTERIAL INFECTIONS/pc, tm [Prevention & Control, Transmission]
12	PSEUDOMONAS INFECTIONS/pc, tm [Prevention & Control, Transmission]
13	BURKHOLDERIA INFECTIONS/pc, tm [Prevention & Control, Transmission]
14	STAPHYLOCOCCAL INFECTIONS/pc, tm [Prevention & Control, Transmission]
15	HAEMOPHILUS INFECTIONS/pc, tm [Prevention & Control, Transmission]
16	MYCOBACTERIUM INFECTIONS, NONTUBERCULOUS/pc, tm [Prevention & Control, Transmission]

#	Searches
17	((infect\$ or crossinfect\$ or crosstransmi\$ or contamina\$ or crosscontamina\$) adj3 (prevent\$ or control\$ or reduc\$)).ti,ab.
18	((nosocomial or hospital acquired) adj3 (disease? or infect\$ or pathogen\$) adj3 (prevent\$ or control\$ or reduc\$)).ti,ab.
19	((disease? or infect\$ or pathogen\$ or bacteri\$) adj3 (transmi\$ or acquir\$ or spread\$) adj3 (prevent\$ or control\$ or reduc\$)).ti,ab.
20	((pseudomon\$ or burkholder\$ or staphylococc\$ or MRSA or h?emophil\$ or mycobacteri\$ or aspergill\$) adj3 (transmi\$ or acquir\$ or spread\$) adj3 (prevent\$ or control\$ or reduc\$)).ti,ab.
21	or/5-20
22	PATIENT ISOLATION/
23	PATIENTS' ROOMS/
24	((patient? or clinic?) adj3 (cohorted or cohorting or isolate or isolating or isolation or segregat\$ or separat\$ or seclu\$ or quarantin\$ or confine or confined or confining)).ti,ab.
25	((patient? or inpatient? or single-patient or clinic?) adj3 (ensuite or bathroom? or playroom? or room? or facility or facilities or waiting)).ti,ab.
26	or/22-25
27	PATIENT ISOLATORS/
28	PROTECTIVE DEVICES/
29	PROTECTIVE CLOTHING/
30	GLOVES, PROTECTIVE/
31	EYE PROTECTIVE DEVICES/
32	MASKS/
33	(glove? or mask? or gown? or apron? or glasses or goggles).ti,ab.
34	(protect\$ adj3 (cloth\$ or equip\$)).ti,ab.
35	or/27-34
36	or/21,26,35
37	and/4,36

- Database: Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects

Last searched on **EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to January 05, 2017, **EBM Reviews - Database of Abstracts of Reviews of Effects** 1st Quarter 2015 on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS.kw.
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,tw,tx.
4	or/1-3
5	CROSS INFECTION.kw.
6	INFECTION CONTROL.kw.
7	COMMUNICABLE DISEASE CONTROL.kw.
8	INFECTIOUS DISEASE TRANSMISSION, PATIENT-TO-PROFESSIONAL.kw.
9	INFECTIOUS DISEASE TRANSMISSION, PROFESSIONAL-TO-PATIENT.kw.
10	DISEASE TRANSMISSION, INFECTIOUS.kw.
11	BACTERIAL INFECTIONS.kw.
12	PSEUDOMONAS INFECTIONS.kw.
13	BURKHOLDERIA INFECTIONS.kw.

#	Searches
14	STAPHYLOCOCCAL INFECTIONS.kw.
15	HAEMOPHILUS INFECTIONS.kw.
16	MYCOBACTERIUM INFECTIONS, NONTUBERCULOUS.kw.
17	((infect\$ or crossinfect\$ or crosstransmi\$ or contamina\$ or crosscontamina\$) adj3 (prevent\$ or control\$ or reduc\$)).ti,tw,tx.
18	((nosocomial or hospital acquired) adj3 (disease? or infect\$ or pathogen\$) adj3 (prevent\$ or control\$ or reduc\$)).ti,tw,tx.
19	((disease? or infect\$ or pathogen\$ or bacteri\$) adj3 (transmi\$ or acquir\$ or spread\$) adj3 (prevent\$ or control\$ or reduc\$)).ti,tw,tx.
20	((pseudomon\$ or burkholder\$ or staphylococc\$ or MRSA or h?emophil\$ or mycobacteri\$ or aspergill\$) adj3 (transmi\$ or acquir\$ or spread\$) adj3 (prevent\$ or control\$ or reduc\$)).ti,tw,tx.
21	or/5-20
22	PATIENT ISOLATION.kw.
23	PATIENTS' ROOMS.kw.

- Database: Health Technology Assessment

Last searched on **EBM Reviews - Health Technology Assessment 4th Quarter 2016** on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).tw.
3	mucov\$.tw.
4	or/1-3
5	exp CROSS INFECTION/pc [Prevention & Control]
6	exp INFECTION CONTROL/
7	COMMUNICABLE DISEASE CONTROL/
8	DISEASE TRANSMISSION, PATIENT-TO-PROFESSIONAL/
9	DISEASE TRANSMISSION, PROFESSIONAL-TO-PATIENT/
10	DISEASE TRANSMISSION/
11	BACTERIAL INFECTIONS/
12	PSEUDOMONAS INFECTIONS/
13	BURKHOLDERIA INFECTIONS/
14	STAPHYLOCOCCAL INFECTIONS/
15	HAEMOPHILUS INFECTIONS/
16	MYCOBACTERIUM INFECTIONS/
17	((infect\$ or crossinfect\$ or crosstransmi\$ or contamina\$ or crosscontamina\$) adj3 (prevent\$ or control\$ or reduc\$)).tw.
18	((nosocomial or hospital acquired) adj3 (disease? or infect\$ or pathogen\$) adj3 (prevent\$ or control\$ or reduc\$)).tw.
19	((disease? or infect\$ or pathogen\$ or bacteri\$) adj3 (transmi\$ or acquir\$ or spread\$) adj3 (prevent\$ or control\$ or reduc\$)).tw.
20	((pseudomon\$ or burkholder\$ or staphylococc\$ or MRSA or h?emophil\$ or mycobacteri\$ or aspergill\$) adj3 (transmi\$ or acquir\$ or spread\$) adj3 (prevent\$ or control\$ or reduc\$)).tw.
21	or/5-20
22	PATIENT ISOLATION/
23	PATIENTS' ROOMS/

#	Searches
24	((patient? or clinic?) adj3 (cohorted or cohorting or isolate or isolating or isolation or segregat\$ or separat\$ or seclu\$ or quarantin\$ or confine or confined or confining)).tw.
25	((patient? or inpatient? or single-patient or clinic?) adj3 (ensuite or bathroom? or playroom? or room? or facility or facilities or waiting)).tw.
26	or/22-25
27	PATIENT ISOLATORS/
28	PROTECTIVE CLOTHING/
29	PROTECTIVE DEVICES/
30	GLOVES, PROTECTIVE/
31	EYE PROTECTIVE DEVICES/
32	MASKS/
33	(glove? or mask? or gown? or apron? or glasses or goggles).tw.
34	(protect\$ adj3 (cloth\$ or equip\$)).tw.
35	or/27-34
36	or/21,26,35
37	and/4,36

- Database: Embase

Last searched on **Embase** 1974 to 2017 Week 01 on 4<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
3	mucov\$.ti,ab.
4	or/1-3
5	CROSS INFECTION/pc [Prevention]
6	INFECTION CONTROL/
7	INFECTION RISK/
8	HOSPITAL INFECTION/pc [Prevention]
9	DISEASE TRANSMISSION/pc [Prevention]
10	BACTERIAL TRANSMISSION/pc [Prevention]
11	PSEUDOMONAS INFECTION/pc [Prevention]
12	exp BURKHOLDERIA INFECTION/pc [Prevention]
13	exp STAPHYLOCOCCUS INFECTION/pc [Prevention]
14	exp HAEMOPHILUS INFECTION/pc [Prevention]
15	MYCOBACTERIOSIS/pc [Prevention]
16	ASPERGILLOSIS/pc [Prevention]
17	((infect\$ or crossinfect\$ or crosstransi\$ or contamina\$ or crosscontamina\$) adj3 (prevent\$ or control\$ or reduc\$)).ti,ab.
18	((nosocomial or hospital acquired) adj3 (disease? or infect\$ or pathogen\$) adj3 (prevent\$ or control\$ or reduc\$)).ti,ab.
19	((disease? or infect\$ or pathogen\$ or bacteri\$) adj3 (transmi\$ or spread\$ or acquir\$) adj3 (prevent\$ or control\$ or reduc\$)).ti,ab.
20	((pseudomon\$ or burkholder\$ or staphylococc\$ or MRSA or h?emophil\$ or mycobacteri\$ or aspergill\$) adj3 (transmi\$ or spread\$ or acquir\$) adj3 (prevent\$ or control\$ or reduc\$)).ti,ab.
21	or/5-20
22	((patient? or clinic?) adj3 (cohorted or cohorting or isolate or isolating or isolation or segregat\$ or separat\$ or seclu\$ or quarantin\$ or confine or confined or confining)).ti,ab.

#	Searches
23	((patient? or inpatient? or single-patient? or clinic?) adj3 (ensuite or bathroom? or playroom? or room? or facility or facilities or waiting)).ti,ab.
24	or/22-23
25	PATIENT ISOLATOR/
26	PROTECTIVE EQUIPMENT/
27	PROTECTIVE CLOTHING/
28	EYE PROTECTIVE DEVICE/
29	SURGICAL GLOVE/
30	(glove? or mask? or gown? or apron? or glasses or goggles).ti,ab.
31	(protect\$ adj3 (cloth\$ or equip\$)).ti,ab.
32	or/25-31
33	or/21,24,32
34	and/4,33
35	limit 34 to english language
36	letter.pt. or LETTER/
37	note.pt.
38	editorial.pt.
39	CASE REPORT/ or CASE STUDY/
40	(letter or comment*).ti.
41	or/36-40
42	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
43	41 not 42
44	ANIMAL/ not HUMAN/
45	NONHUMAN/
46	exp ANIMAL EXPERIMENT/
47	exp EXPERIMENTAL ANIMAL/
48	ANIMAL MODEL/
49	exp RODENT/
50	(rat or rats or mouse or mice).ti.
51	or/43-50
52	35 not 51

## E.21 Health Economics global search

### E.21.1 Database: Medline

Last searched on Ovid MEDLINE(R) 1946 to December Week 1 2016 on 5<sup>th</sup> January 2017.

#	Searches
1	ECONOMICS/
2	VALUE OF LIFE/
3	exp "COSTS AND COST ANALYSIS"/
4	exp ECONOMICS, HOSPITAL/
5	exp ECONOMICS, MEDICAL/
6	exp RESOURCE ALLOCATION/
7	ECONOMICS, NURSING/
8	ECONOMICS, PHARMACEUTICAL/

#	Searches
9	exp "FEES AND CHARGES"/
10	exp BUDGETS/
11	budget*.ti,ab.
12	cost*.ti,ab.
13	(economic* or pharmaco?economic*).ti,ab.
14	(price* or pricing*).ti,ab.
15	(financ* or fee or fees or expenditure* or saving*).ti,ab.
16	(value adj2 (money or monetary)).ti,ab.
17	resourc* allocat*.ti,ab.
18	(fund or funds or funding* or funded).ti,ab.
19	(ration or rations or rationing* or rationed).ti,ab.
20	ec.fs.
21	or/1-20
22	CYSTIC FIBROSIS/
23	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
24	mucov\$.ti,ab.
25	or/22-24
26	and/21,25
27	limit 26 to english language
28	LETTER/
29	EDITORIAL/
30	NEWS/
31	exp HISTORICAL ARTICLE/
32	ANECDOTES AS TOPIC/
33	COMMENT/
34	CASE REPORT/
35	(letter or comment*).ti.
36	or/28-35
37	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
38	36 not 37
39	ANIMALS/ not HUMANS/
40	exp ANIMALS, LABORATORY/
41	exp ANIMAL EXPERIMENTATION/
42	exp MODELS, ANIMAL/
43	exp RODENTIA/
44	(rat or rats or mouse or mice).ti.
45	or/38-44
46	27 not 45

### E.21.2 Database: Cochrane Central Register of Controlled Trials

Last searched on **EBM Reviews - Cochrane Central Register of Controlled Trials**  
November 2016 on 10<sup>th</sup> January 2017.

#	Searches
1	ECONOMICS/

#	Searches
2	VALUE OF LIFE/
3	exp "COSTS AND COST ANALYSIS"/
4	exp ECONOMICS, HOSPITAL/
5	exp ECONOMICS, MEDICAL/
6	exp RESOURCE ALLOCATION/
7	ECONOMICS, NURSING/
8	ECONOMICS, PHARMACEUTICAL/
9	exp "FEES AND CHARGES"/
10	exp BUDGETS/
11	budget*.ti,ab,kw.
12	cost*.ti,ab,kw.
13	(economic* or pharmaco?economic*).ti,ab,kw.
14	(price* or pricing*).ti,ab,kw.
15	(financ* or fee or fees or expenditure* or saving*).ti,ab,kw.
16	(value adj2 (money or monetary)).ti,ab,kw.
17	resourc* allocat*.ti,ab,kw.
18	(fund or funds or funding* or funded).ti,ab,kw.
19	(ration or rations or rationing* or rationed).ti,ab,kw.
20	ec.fs.
21	or/1-20
22	CYSTIC FIBROSIS/
23	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab,kw.
24	mucov\$.ti,ab,kw.
25	or/22-24
26	and/21,25

### E.21.3 Database: NHS Economic Evaluation Database

Last searched on **EBM Reviews - NHS Economic Evaluation Database 1st Quarter 2015** on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).tw.
3	mucov\$.tw.
4	or/1-3

### E.21.4 Database: Health Technology Assessment

Last searched on **EBM Reviews - Health Technology Assessment 4th Quarter 2016** on 10<sup>th</sup> January 2017.

#	Searches
1	CYSTIC FIBROSIS/
2	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).tw.
3	mucov\$.tw.
4	or/1-3

## E.21.5 Database: Embase

Last searched on **Embase** 1974 to 2017 Week 01 on 4<sup>th</sup> January 2017.

#	Searches
1	HEALTH ECONOMICS/
2	exp ECONOMIC EVALUATION/
3	exp HEALTH CARE COST/
4	exp FEE/
5	BUDGET/
6	FUNDING/
7	RESOURCE ALLOCATION/
8	budget*.ti,ab.
9	cost*.ti,ab.
10	(economic* or pharmaco?economic*).ti,ab.
11	(price* or pricing*).ti,ab.
12	(financ* or fee or fees or expenditure* or saving*).ti,ab.
13	(value adj2 (money or monetary)).ti,ab.
14	resourc* allocat*.ti,ab.
15	(fund or funds or funding* or funded).ti,ab.
16	(ration or rations or rationing* or rationed).ti,ab.
17	or/1-16
18	CYSTIC FIBROSIS/
19	mucov\$.ti,ab.
20	((cystic or pancrea\$) adj2 (fibrosis or fibrocystic)).ti,ab.
21	or/18-20
22	and/17,21
23	limit 22 to english language
24	conference abstract.pt.
25	letter.pt. or LETTER/
26	note.pt.
27	editorial.pt.
28	CASE REPORT/ or CASE STUDY/
29	(letter or comment* or abstracts).ti.
30	or/24-29
31	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
32	30 not 31
33	ANIMAL/ not HUMAN/
34	NONHUMAN/
35	exp ANIMAL EXPERIMENT/
36	exp EXPERIMENTAL ANIMAL/
37	ANIMAL MODEL/
38	exp RODENT/
39	(rat or rats or mouse or mice).ti.
40	or/32-39
41	23 not 40

## **Appendix F: Summary of identified studies (prisma charts)**

## **Appendix G: Evidence tables**

## **Appendix H: Excluded studies**