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?

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Review question for the protocol	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) Definition of stablished lung disease: clinical signs and symptoms and/or radiological signs of lung disease.
Objective	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. 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. 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. This review will compare monitoring strategies or combinations of monitoring tests • to identify response to treatment following an acute pulmonary exacerbation • to compare their effects on prioritised outcomes
Language	English
Study design	• Systematic reviews • Test-and-treat randomised trials (RCTs) • Conference abstracts of RCTs (only if fully published RCTs are not available) • 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. To exclude studies if they do not conduct multivariable adjustment for baseline differences between groups. 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.
Population and directness	Children, young people and adults with defined cystic fibrosis, diagnosed clinically and by sweat test or genetic testing. Population size and indirectness: • No sample size specification. • Studies with indirect populations will not be included
Stratified, subgroup and adjusted analyses	Stratified analysis: groups that will be reviewed and analysed separately: • Children • Adults In the presence of heterogeneity sensitivity analysis will be conducted including and excluding studies with a high risk of bias. To be considered as important confounders if comparative cohort studies are included: • Concurrent treatment with immunomodulatory and/or mucolytic agents.

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	• Age (under 5 years)
Monitoring strategies	Invasive microbiological investigations (such as broncheoalveolar lavage) *and/or* Imaging techniques (such as Chest X-rays or CT scans) + Non-invasive microbiological investigation (such as induced sputum samples, cough swab, and throat swab, nasopharangeal aspiration) *and/or* Lung physiological function tests (such as Spirometry, Lung Clearance Index)
Comparison	Non-invasive microbiological investigation (such as induced sputum samples, cough swab, throat swab, and nasopharangeal aspiration) *and/or* Lung physiological function tests (such as Spirometry, and Lung Clearance Index)
Outcomes	• Lung function ○ Lung Clearance Index (LCI) ○ FEV1 (absolute values litres or % predicted or both) ○ Oxygen saturation • High-resolution computed tomography (CT) appearances using a recognised scoring system (e.g. Brody 2004; Loeve 2009) or Chest X-ray appearances • Time to next exacerbation • Clearance of the organism from the cultures • Inflammatory markers (White cell count , CRP, ESR) • Quality of life (CF-QOL, CFQR) • Nutritional parameters (weight, height, body mass index (BMI))
Importance of outcomes	Critical outcomes for decision making: • Lung function ○ LCI ○ (FEV1) (absolute values or change from start of treatment (post hoc change) (litres or per cent (%) predicted or both)) ○ Oxygen saturation • Time to next exacerbation • Clearance of the organism from the cultures
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): Apply standard exclusions and English language filters. Supplementary search techniques: No supplementary search techniques will be used. See appendix E.6.3 for full strategies
Review strategy	Appraisal of methodological quality: • 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). • The quality of the evidence will be assessed by GRADE for each outcome according to the process described in the NICE guidelines manual (2014). Synthesis of data:

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	• 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 • Final and change scores will be pooled and if any study reports both, the method used in the majority of studies will be analysed. • If studies only report p-values, this information will be plotted in GRADE tables without an assessment of imprecision possible to be made. MIDs • Lung function ○ Lung Clearance Index (LCI): GRADE default ○ FEV1 (absolute values litres or % predicted or both): 2 percentage points ○ Oxygen saturation: 2 percentage points • 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 • Time to next exacerbation: any change will be considered clinically significant • Inflammatory markers = normalisation • Quality of life: CFQoL = 5; CFQ-R = 8.5 • Nutritional parameters (BMI, weight/ height): GRADE default • Clearance of the organism from the cultures: any change will be considered clinically significant Default MIDs: 0.8 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes. Review process: • A list of excluded studies will be provided following weeding. • Evidence tables and an evidence profile will be used to summarise the evidence.
Equalities	• Psychological and behavioural issues are more likely in people with a lower socioeconomic status • Gender- outcomes are worse for women although there is no evidence that this is a consequence of difference in care • 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.
Notes/additional information	None.