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	1. What criteria should be used to determine the need for insulin therapy to achieve optimal patient outcomes? 2. What thresholds of glucose dysregulation are associated with more rapid progression of lung disease?
Objective	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 β-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. 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

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	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. 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.
Language	English
Study design	For review question 1: • Systematic reviews • RCTs (test and treat) • 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). • Prospective or retrospective comparative cohort studies (only if RCTs unavailable or limited data to inform decision making) For review question 2: • Prospective or retrospective cohort studies
Population and directness	Infants, children, young people and adults with defined CF, 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	Groups that will be reviewed and analysed separately: • age (young people vs adults) • clinical signs or risk factor (incidental indication of blood glucose dysregulation) Sensitivity analysis: In the presence of heterogeneity, sensitivity analysis will conducted including and excluding studies with a high risk of bias. State important confounders (when comparative observational studies are included for interventional reviews) • Steroid use • Azole (anti-fungal) • Age • Lung disease severity • Exocrine pancreatic insufficiency • Enteral tube feeding? • Transplant
Screening strategy	For review question 1: Any OGTT vs serial/continuous glucose monitoring diagnosis followed up with treatment For review question 2: Continuous glucose monitoring (different groups according to thresholds)
Outcomes	For review question 1: Ideally specify a time to event outcome • Change in lung function (FEV1, FVC, LCI) • Pulmonary exacerbation • BMI (z-scores for children) • Adverse events: ○ hypoglycaemic episodes (with insulin therapy) • Patient acceptability/ satisfaction (with insulin therapy)

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	For review question 2: Ideally specify a time to event outcome • Change in lung function (FEV1, FVC, LCI) • Pulmonary exacerbation • BMI (z-scores for children) • Adverse events: ○ hypoglycaemic episodes (with insulin therapy) • Patient acceptability/ satisfaction (with insulin therapy)
Importance of outcomes	Critical outcomes for decision making: • Change in lung function (FEV1, FVC, LCI) • BMI (z scores) • Pulmonary exacerbations
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 were used. See appendix E.16 for full strategies
Review strategy	Appraisal of methodological quality: • 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 Manual 2014. • The quality of the evidence for an outcome (i.e. across studies) will be assessed using adapted GRADE approach. Synthesis of data: • 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, change scores will be used in preference over final scores. • 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. • 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. • 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.