G.5 Complications of cystic fibrosis

Review question: What are the non-respiratory complications of cystic fibrosis in infants, children, young people and adults?

Study details	Participants	Methods	Outcomes and results	Comments
Full citation Bell, S. C., Bye, P. T., Cooper, P. J., Martin, A. J., McKay, K. O., Robinson, P. J., Ryan, G. F., Sims, G. C., Cystic fibrosis in Australia, 2009: results from a data registry, Medical Journal of Australia, 195, 396-400, 2011 Country/ies where the study was carried out Australia Study type	Sample size N=2986 Characteristics People with CF Median age: 17.6 years Sex: Females: 48% Inclusion criteria People in the Australian CF Registry for 2009 Exclusion criteria Not reported in relation to outcomes of interest	Details Register/Data source Australian CF Data Registry Definitions / thresholds. Not reported Data collection and measurements. All CF centres in Australia submitted data via a web-based form. Measurement tools not reported in the paper	Results Prevalence of insulin-dependent diabetes (chronic): 0-11 years: 0.5% (5/951) 12-17 years: 13.6% (61/448) ≥18 years: 20.7% (144/697) All age groups: 10.0% (210/2096) Prevalence of insulin-dependent diabetes (intermittent):	Limitations Critical appraisal using Munn et al 2014: Was the sample representative of the target population? Yes Were study participants recruited in an appropriate way? Yes, all people in the registry were included Was the sample size adequate? Yes, >250 as per protocol Were the study subjects and the setting described in detail? Yes Was the data analysis conducted with sufficient coverage of the

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Retrospective cross-sectional study Study dates 2009 data Source of funding Financial support from CFA; state CF organisations; Roche Pharmaceuticals and Solvay Pharmaceuticals.			0-11 years: 0% (0/951) 12-17 years: 1.1% (5/448) ≥18 years: 2.3% (16/697) All age groups: 1.0% (21/2096) All age groups: 1.0% (21) Prevalence of osteopenia: 0-11 years: 0.3% (3/951) 12-17 years: 3.3% (15/448) ≥18 years: 25.0% (174/697) All age groups: 9.2% (192/2096) Prevalence of osteoporosis: 0-11 years: 0.2% (2/951) 12-17 years: 1.3% (6/448) ≥18 years: 9.5% (66/697) All age groups: 3.7% (77/2096) Prevalence of fractures in 2009: 0-11 years: 0% (0/951) 12-17 years: 0.4% (2/448) ≥18 years: 1.1% (8/697) All age groups: 0.5% (10/2096)	identified sample? Yes, >250 people in each subgroup Were objective, standard criteria used for the measurement of the condition? Unclear - not reported Was the condition measured reliably? Unclear - not reported Was there appropriate statistical analysis? Yes - confidence intervals of percentages not provided however this is registry data so they are not needed Are all important confounding factors/subgroups/differences identified and accounted for? Yes, results disaggregated into age subgroups: children, adolescents and adults. Were subpopulations identified using objective criteria? Yes, age cut-offs Overall quality: moderate Other information None
Full citation Chavasse, R. J., Francis, J., Balfour-Lynn, I., Rosenthal, M., Bush, A., Serum vitamin D levels in children with cystic	Sample size N=290 Characteristics People with CF Age: 1-18	Details Register/data source. Data from specialist paediatric CF clinic Definitions/thresholds.	Results Prevalence of vitamin deficiency: 25-OHD < 15 nmol/l: 1% (4/290)	Limitations Critical appraisal using Munn et al 2014: Was the sample representative of the target population? Yes

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fibrosis, Pediatric Pulmonology, 38, 119-22, 2004 Country/ies where the study was carried out UK Study type Retrospective study Study dates Levels of 25-OHD measured between August 1999 and April 2001 Source of funding Not reported	Sex: Males: 45% (131/290) Inclusion criteria All people aged 1–18 years, with confirmed diagnosis of CF under the care of specialist paediatric CF clinic who attended an annual assessment during the study period and had 25-OHD measured on at least one occasion. Exclusion criteria Not reported	The laboratory reference range was 15–100 nmol/l. Authors also took into account that 25 nmol/l is generally regarded as the lower limit of normal. So the cut-off points were < 15 nmol/l and < 25 nmol/l. Measurement. 25-hydroxyvitamin D (25-OHD) was measured by an in-house, competitive protein-binding assay following extraction and chromatography of 25-OHD on silicic acid, performed at Charing Cross Hospital.	25-OHD < 25 nmol/l: 6% (17/290)	Were study participants recruited in an appropriate way? Yes, all people meeting inclusion criteria were included Was the sample size adequate? Yes, N>250 as per protocol Were the study subjects and the setting described in detail? Yes Was the data analysis conducted with sufficient coverage of the identified sample? N/A Were objective, standard criteria used for the measurement of the condition? Yes, both the laboratory reference range (15–100 nmol/l) and what is generally regarded as the lower limit of normal (25 nmol/l) were used to define cut-offs. Was the condition measured reliably? Yes Was there appropriate statistical analysis? Yes, no confidence interval provided however all the people in the clinic fitting inclusion criteria were included Are all important confounding factors/subgroups/differences identified and accounted for? No. Results were not disaggregated between infants, children, young people and adults. Were subpopulations identified using objective criteria? N/A Overall quality: moderate Other information None.

Study details	Participants	Methods	Outcomes and results	Comments
Full citation Heltshe, S. L., Borowitz, D. S., Leung, D. H., Ramsey, B., Mayer-Hamblett, N., Early attained weight and length predict growth faltering better than velocity measures in infants with CF, Journal of Cystic Fibrosis, 13, 723-9, 2014 Country/ies where the study was carried out United States Study type Retrospective study Study dates 1st January 2004 - 31st December 2009 Source of funding CFFT Grant BONUS11K0 and NIH NIDDK Grants R01 DK095738-01, and P30DK089507-01.	Sample size N=1992 infants and children Characteristics Infants and children with CF Age: 0-24 months Sex: Males: 50.6% Inclusion criteria Newborns diagnosed with CF who were born between Jan 1, 2004 and Dec 31, 2008, and entered in the registry before 4 months of age. Exclusion criteria Not reported	Details Data source/register. US CF Foundation National Registry Definitions/thresholds. The following thresholds were chosen as potential early markers of deficits at 24 months Guo et. al. US (Guo-US) velocity standards recommended by the CFF infant care guidelines: Guo-US 50th percentile for weight velocity and length velocity WHO standardized 2.5th, 5th, 10th, and 50th percentiles for weight and length velocity WHO standardized 2.5th, 5th, and 10th percentiles for weight and length for age Measurement. Encounter based weight and length measurements were derived from the registry and were used for calculating weight and length velocity as change in grams and centimeters per unit time, respectively. The velocities were then standardized to the WHO cohort and the Guo-US standards to generate age and sex specific percentiles. All analyses only included observations where a patient's	Results Prevalence of inadequate attained weight or length for age or inadequate weight or length velocity: Age 12 months (N=374): weight for age <10th: 11% weight for age <5th: 8.3% weight for age <2.5th: 3.7% weight velocity (GUO-US) <50th: 48.1% weight velocity (WHO)<50th: 30.5% weight velocity <10th (WHO): 6.4% weight velocity<5th (WHO): 4.5% weight velocity<2.5th (WHO): 3.5% length for age <10th: 26.8% length for age <5th: 17.7% length for age <2.5th: 10.4% length velocity (GUO-US) <50th: 45.7% length velocity <50th (WHO): 38.4% length velocity <10th (WHO): 20.7% length velocity<5th (WHO): 13.4%	Limitations Critical appraisal using Munn et al 2014: Was the sample representative of the target population? Yes Were study participants recruited in an appropriate way? Yes, all people in the registry fitting inclusion criteria were included Was the sample size adequate? Yes, >250 as per protocol Were the study subjects and the setting described in detail? Yes Was the data analysis conducted with sufficient coverage of the identified sample? Yes. >250 people in each age subgroup Were objective, standard criteria used for the measurement of the condition? Yes, WHO and GUO-US standards Was the condition measured reliably? Yes Was there appropriate statistical analysis? No, no numerators provided. No confidence intervals provided for percentages however this is registry data so the CIs are not needed. Are all important confounding factors/subgroups/differences identified and accounted for? Yes, prevalence data are disaggregated by age groups

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		weight or length was recorded at an age no more than ±9 days (30% of a month) from expected age at interval start (0–23 months), and follow-up measures of weight or length recorded at 1 or 2 or 3 months ±6 days later (20% of a month).	length velocity<2.5th (WHO): 13.4% Age 24 months (N=317): weight for age <10th: 6.9% weight for age <5th: 2.8% weight for age <2.5th: 1.9% weight velocity (GUO-US) <50th: 59.3% weight velocity (WHO)<50th: 51.1% weight velocity <10th (WHO): 18.3% weight velocity<5th (WHO): 12.6% weight velocity<2.5th (WHO): 8.2% length for age <10th: 24.9% length for age <5th: 17% length for age <2.5th: 11.4% length velocity (GUO-US) <50th: 57.4% length velocity <50th (WHO): 58.7% length velocity <10th (WHO): 30.3% length velocity<5th (WHO): 24.3% length velocity<2.5th (WHO): 19.9%	Were subpopulations identified using objective criteria? Yes, age cut-offs Overall quality: moderate Other information None.

Study details	Participants	Methods	Outcomes and results	Comments
Full citation Lai, H. J., Shoff, S. M., Classification of malnutrition in cystic fibrosis: implications for evaluating and benchmarking clinical practice performance, American Journal of Clinical Nutrition, 88, 161-6, 2008 Country/ies where the study was carried out United States Study type Retrospective study Study dates 2002 Source of funding Not reported	Sample size N=14702 Characteristics Children, young people and adults with CF Age: <20 years Sex: Not reported Inclusion criteria Age: <20 years Exclusion criteria Missing height or weight or height, weight, or BMI values that deviated >4 SD from the reference mean (the authors specify that these height and weight values likely were outliers resulting from measurement or recording errors, and they were excluded)	Details Register / Data source US CF Foundation Patient Registry Definitions and thresholds 2002 CFF definition of nutritional failure: Age <2 y old: HTp <5th, %IBW <90%, or WHp <10th. For ages 2–20 y: HTp <5th, %IBW <90%, or BMIp <10th Corrected classification of nutritional failure: elimination of %IBW as an indicator of underweight Below BMI goal: Age<2 y old: WHp <50th. Ages 2-20 years: BMIp <50th. Measurements Not reported Analysis Age- and sex-specific HTp, WHp for ages <2 y, and BMIp for ages 2–20 y were calculated in a computerized program in SAS software (SAS Inc, Cary, NC) by using the Centers for Disease Control and Prevention reference values. The %IBW was calculated according to the method defined by Moore et al in a computerized program in SAS, by using the Centers for	Results Prevalence of "nutritional failure" using 2002 CFF definition: HTp<5th or BMIp<10th or %IBW<90): 33.0% Prevalence of "nutritional failure" using corrected classification: HTp<5th or BMIp<10th: 26.8% Prevalence of BMIp<50th: 56.8%	Limitations Critical appraisal using Munn et al 2014: Was the sample representative of the target population? Yes Were study participants recruited in an appropriate way? Yes Was the sample size adequate? Yes, >250 as per protocol Were the study subjects and the setting described in detail? No. Unclear how many infants, children, young people and adults. Was the data analysis conducted with sufficient coverage of the identified sample? N/A Were objective, standard criteria used for the measurement of the condition? Unclear. Unclear why results do not take different definitions for infants into account. Was the condition measured reliably? Unclear. Not reported. Was there appropriate statistical analysis? Yes. No confidence intervals provided for prevalence at the national level however this is registry data so no confidence intervals are needed Are all important confounding factors/subgroups/differences identified and accounted for? No. Data not disaggregated between infant, children, young people and adults.

Study details	Participants	Methods	Outcomes and results	Comments
		Disease Control and Prevention reference values.		Were subpopulations identified using objective criteria? N/A Quality: very low Other information None.
Full citation Lewis, C., Blackman, S. M., Nelson, A., Oberdorfer, E., Wells, D., Dunitz, J., Thomas, W., Moran, A., Diabetes-related mortality in adults with cystic fibrosis. Role of genotype and sex, American Journal of Respiratory & Critical Care Medicine, 191, 194-200, 2015 Country/ies where the study was carried out United States Study type Retrospective study Study dates 2008-2012 Source of funding Supported in part by a grant from Pennsylvania Cystic Fibrosis Incorporated. One author was funded by National Institutes of Health grant T32DK66519. Another author was funded by National Institutes of Health K23DK083551.	Sample size N=462 Characteristics Age: ≥ 20 Sex: Not reported Inclusion criteria People attending the CF clinic between September 16, 2008 and December 31, 2012, who gave informed consent permitting their records to be reviewed for research purposes. Exclusion criteria Not reported	Details Register / Data source. University of Minnesota Cystic Fibrosis Database Definitions and thresholds. Not reported Data collection and measurements. Clinical information was reviewed from the database. Tests used not reported.	Results Prevalence of Cystic Fibrosis Related Diabetes (CFRD): 48% (221/462)	Limitations Critical appraisal using Munn et al 2014: Was the sample representative of the target population? Yes Were study participants recruited in an appropriate way? Yes Was the sample size adequate? Yes, >250 as per protocol Were the study subjects and the setting described in detail? No, but age was reported Was the data analysis conducted with sufficient coverage of the identified sample? N/A Were objective, standard criteria used for the measurement of the condition? Unclear. Not reported Was the condition measured reliably? Unclear. Not reported Was there appropriate statistical analysis? Yes. Confidence interval for the percentage not provided however all the people from the centre were included so confidence intervals are not needed. Are all important confounding factors/subgroups/differences identified and accounted for? Yes, the study focused on adults only so

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				there was no need to disaggregate by age subgroups Were subpopulations identified using objective criteria? N/A Overall quality: Moderate Other information Analyses were performed to build on previous study by Moran et al. (2009), which also used data from the University of Minnesota Cystic Fibrosis database, by adding data from the most recent time period.
Full citation Lucidi, V., Alghisi, F., Raia, V., Russo, B., Valmarana, L., Valmarana, R., Coruzzo, A., Beschi, S., Dester, S., Rinaldi, D., Maglieri, M., Guidotti, M. L., Ravaioli, E., Pesola, M., De Alessandri, A., Padoan, R., Grynzich, L., Ratclif, L., Repetto, T., Ambroni, M., Provenzano, E., Tozzi, A. E., Colombo, C., Growth assessment of paediatric patients with CF comparing different auxologic indicators: A multicentre Italian study, Journal of Pediatric Gastroenterology & Nutrition, 49, 335-42, 2009 Country/ies where the study was carried out Italy	Sample size N=892 Characteristics Age range: 0.1-18 Sex: Males: 50.7% (452/892) Inclusion criteria All people with a confirmed diagnosis of CF younger than 18 years on regular follow-up with one of the 10 CF centres during the period January 2005-December 2006 Exclusion criteria Not reported	Details Setting. 10 Italian CF centres Data collection and measurements. Height and weight were measured (when the patient was in a stable clinical condition) by specifically trained personnel and the values entered in a database that also contained demographic and clinical data of the patients. BMI was also calculated on the basis of weight in kilograms/(height in meters2) ratio. Reproducibility in anthropometric measurement was evaluated by comparing measures obtained with standard instruments in all centres with those obtained with reference instruments in a sample of patients.	Results Prevalence of "nutritional failure" and risk of malnutrition by age group: 0-2 years (n=HAP: n=104; WLP: n=101) HAP<5th: 15.4% HAP 5th-25th: 18.3% WLP<10th: 12.9% WLP10th -25th: 22.7% 2-18 years (n=788) HAP<5th: 11.8% HAP 5th-25th: 29.3% BMIp<15th: 20.9% BMIp 15th-25th: 9.6% BMIp<50th: 54.4% 10-14 years (n=179) HAP<5th: 11.7% BMIp<15th: 20.1% 14-18 years (n=183)	Limitations Critical appraisal using Munn et al 2014: Was the sample representative of the target population? Yes Were study participants recruited in an appropriate way? Yes Was the sample size adequate? Yes, >250 as per protocol Were the study subjects and the setting described in detail? Yes Was the data analysis conducted with sufficient coverage of the identified sample? No - Some age subgroups included less than 250 people Were objective, standard criteria used for the measurement of the condition? Yes Was the condition measured reliably? Yes Was there appropriate statistical analysis? Yes, no confidence

Study details	Participants	Methods	Outcomes and results	Comments
Study type Prospective cross-sectional study Study dates Data from January 2005-December 2006 Source of funding Not reported		Definitions and thresholds. The presence of nutritional failure was defined as: HAP <5th (all ages), WLP <10th (age <2 years), and BMIp <15th (age between 2 and 18 years). Risk of malnutrition: HAP <25th (all ages), WLP <25th (<2 years), BMIp <25th (2-18 years)	HAP<5th: 21.9% BMIp<15th: 27.9% 0-18 years (n=892) HAP<5th: 12.2% HAP 5th-25th: 28%	intervals for percentages however all the people in the centres fitting inclusion criteria were included so no confidence intervals are needed Are all important confounding factors/subgroups/differences identified and accounted for? Yes, age subgroups Were subpopulations identified using objective criteria? Yes, age cut-offs. Overall quality: moderate Other information None.
Full citation Moen, I. E., Nilsson, K., Andersson, A., Fagerland, M. W., Fluge, G., Hollsing, A., Gilljam, M., Mared, L., Pressler, T., Santi, H., Storrosten, O. T., Hjelte, L., Dietary intake and nutritional status in a Scandinavian adult cystic fibrosis-population compared with recommendations, Food and Nutrition Research, 55 (no pagination), 2011 Country/ies where the study was carried out Denmark, Norway and Sweden Study type Prospective cross-sectional study	Sample size N=347 Characteristics Age: 18 years and over Sex: Females: 44% (152/347) Inclusion criteria Confirmed CF diagnosis. Age: at least 18 years of age Exclusion criteria Pregnancy People who had had a lung transplant	Details Setting. 7 of 8 centres in Denmark, Norway and Sweden. Definitions / thresholds. BMI < 19.0 and BMI < 18.5 Data collection and measurements. People were included consecutively in the study. Weight was measured in the morning wearing undergarments. Height was measured with no stockings or shoes and the means of 3 measurements were recorded	Results Prevalence of underweight: BMI<19.0 kg/m2: 18% (62/347) BMI<18.5 kg/m2: 13% (44/347)	Limitations Critical appraisal using Munn et al 2014: Was the sample representative of the target population? Yes Were study participants recruited in an appropriate way? Yes, consecutively if fitting inclusion criteria Was the sample size adequate? Yes, >250 as per protocol Were the study subjects and the setting described in detail? Yes Was the data analysis conducted with sufficient coverage of the identified sample? N/A Were objective, standard criteria used for the measurement of the condition? Yes Was the condition measured reliably? Yes

Study details	Participants	Methods	Outcomes and results	Comments
Study dates September 2003-May 2006 Source of funding This work was supported by Swedish Heart Lung Foundation, Stiftelsen Frimurare-Barnhuset i Stockholm, Karolinska Institutet, Norwegian and Swedish Cystic Fibrosis Associations and by an unrestricted grant from Solvay Pharma				Was there appropriate statistical analysis? Yes, no confidence intervals of percentages however all the people attending the centres and fitting inclusion criteria were included so no confidence intervals needed Are all important confounding factors/subgroups/differences identified and accounted for? Yes, the study population were adults only so there was no need to disaggregate data by age subgroup Were subpopulations identified using objective criteria?N/A Overall quality: High Other information People were defined as having CFRD if they used insulin or oral anti-diabetics. This definition was not relevant for the current systematic review so data on CFRD was not extracted.
Full citation Moran, A., Dunitz, J., Nathan, B., Saeed, A., Holme, B., Thomas, W., Cystic fibrosis-related diabetes: current trends in prevalence, incidence, and mortality, Diabetes Care, 32, 1626-31, 2009 Country/ies where the study was carried out United States	Sample size N=872 Characteristics People with CF followed at the University of Minnesota Age: not reported Sex: not reported Inclusion criteria All patients followed at the University of	Details Register / Data source. Minnesota Cystic Fibrosis Database Definitions / thresholds. CFRD was diagnosed by standard criteria including persistent random glucose levels>200mg/dl (11.1 mmol/l) and persistent fasting glucose levels >126 mg/dl (7.0 mmol/l) or by OGTT. People with a fasting glucose ≥126 mg/dl (7.0 mmol/l) were	Results Diabetes CFRD prevalence at the end of the interval (%): 1992-97: 20% +- 2% 1998-2000: 30% +-2% 2003-2008: 33% +-2% Prevalence of CFRD in September 2008 Children < 11 years: 2% (2/93) (both without fasting hyperglycemia)	Limitations Critical appraisal using Munn et al 2014: Was the sample representative of the target population? Yes Were study participants recruited in an appropriate way? Yes, all people in the database giving informed consent Was the sample size adequate? Yes, >250 as per protocol Were the study subjects and the setting described in detail? Yes

Study details	Participants	Methods	Outcomes and results	Comments
Study type Retrospective study Study dates Prevalence at the end of three consecutive intervals: 1992-1997, 1998-2002, 2003-2008 Source of funding Not reported	Minnesota Cystic Fibrosis Database who gave informed consent permitting their records to be reviewed for research purposes Exclusion criteria Not reported	diagnosed with CFRD with fasting hyperglycemia. People with a fasting glucose 126 mg/dl (7.0 mmol/l) and a 2-h glucose ≥200 mg/dl (11.1 mmol/l) were diagnosed with CFRD without fasting hyperglycemia. Data collection and measurements. Routine annual OGTT screening has been recommended at the University of Minnesota since the early 1990s for patients aged ≥6 years (1.75 g/kg glucose [maximum 75g]). OGTTs are performed when patients are in their usual baseline state of health.	Of 75 adolescents aged 11-17: 19% (14/75) (4 with fasting hyperglycemia) Population aged ≥18: 43% (155/359)* *Percentage calculated by the NGA technical team	Was the data analysis conducted with sufficient coverage of the identified sample? No, there were less than 250 people in the children and young people subgroups Were objective, standard criteria used for the measurement of the condition? Yes Was the condition measured reliably? Yes Was there appropriate statistical analysis? No. No numerator or denominator provided for prevalence calculated at the end of the interval Are all important confounding factors/subgroups/differences identified and accounted for? Yes, age subgroups were provided for 2008. Were subpopulations identified using objective criteria? Yes, age cut-offs. Overall quality: Moderate Other information None.
Full citation Quon,B.S., Mayer-Hamblett,N., Aitken,M.L., Smyth,A.R., Goss,C.H., Risk factors for chronic kidney disease in adults with cystic fibrosis, American Journal of Respiratory and Critical Care Medicine, 184, 1147-1152, 2011	Sample size N=11912 Characteristics Adults with CF Age ≥ 18 Sex: Males: No CKD: 53.2% vs CKD: 45.6% Inclusion criteria Age ≥ 18	Details Register / data source. CF Foundation Registry Definitions and thresholds CKD was defined by eGFR measured less than 60 ml/min/1.73 m2 in two consecutive registry years. Based on National Kidney Foundation KDOQI guidelines, this corresponds to stage 3	Results Renal disease Mean annual prevalence: chronic kidney disease (stage 3 or greater): 2.3% Stage 3 or greater CKD amongst 18-25 years old: 0.6% Stage 3 or greater CKD amongst those older than 55 years old: 19.2%	Limitations Critical appraisal using Munn et al 2014: Was the sample representative of the target population? Yes Were study participants recruited in an appropriate way? Yes Was the sample size adequate? Yes, >250 as per protocol. Were the study subjects and the setting described in detail? Yes

Study details	Participants	Methods	Outcomes and results	Comments
Country/ies where the study was carried out United States Study type Retrospective study Study dates 2001-2008 Source of funding Supported by NIH/NIDDK (P30 DK089507–01). B.S.Q. was supported by a British Columbia Lung Association Fellowship Award.	At least two estimated glomerular filtration rate (eGFR) measurements, not separated by more than 2 years, from January 1, 2001 to December 31, 2008. Exclusion criteria Not reported	CKD severity and is the earliest stage that can be diagnosed using serum creatinine alone. More advanced stages of CKD were defined as follows: stage 4, eGFR less than 30 ml/min/1.73 m2; and stage 5, eGFR less than 15 ml/min/ 1.73 m2 or need for hemodialysis. Measurements. Renal function was estimated using the Cockcroft-Gault formula standardized for body surface area. Data on serum creatinine, age, weight, height, and sex were required for this calculation.	stage 4 or greater CKD: 0.7% stage 5 CKD: 0.6%	Was the data analysis conducted with sufficient coverage of the identified sample? N/A Were objective, standard criteria used for the measurement of the condition? Yes Was the condition measured reliably? Yes Was there appropriate statistical analysis? No. No numerators or denominators. Confidence intervals of percentages not provided however this is registry data. Are all important confounding factors/subgroups/differences identified and accounted for? Yes, age subgroups Were subpopulations identified using objective criteria? Yes, age cut-offs. Overall quality: moderate Other information None.
Full citation Rana, M., Wong-See, D., Katz, T., Gaskin, K., Whitehead, B., Jaffe, A., Coakley, J., Lochhead, A., Fat-soluble vitamin deficiency in children and adolescents with cystic fibrosis, Journal of Clinical Pathology, 67, 605-8, 2014 Country/ies where the study was carried out	Sample size N=530 Characteristics People with CF Age: ≤18 years Sex: Males: 49.1% (260/530)* 301/470 children took fat soluble-vitamin supplementation	Details Register/data source. Data from 3 paediatric centres. The Children's Hospital at Westmead, Sydney, Sydney Children's Hospital, and John Hunter Children's Hospital Newcastle. Definitions/thresholds. Vitamins A and E reference ranges varied in each laboratory due to historical	Results Prevalence of vitamin deficiency Vitamin A deficiency: 2007: 11.17% 2010: 13.13% Vitamin A levels on first vitamin level test in the study period: Abnormal:23.4% (123/526)* Low: 15% (80/526)	Limitations Critical appraisal using Munn et al 2014: Was the sample representative of the target population? Yes Were study participants recruited in an appropriate way? Yes, all people fitting inclusion criteria were included Was the sample size adequate? Yes, >250 as per protocol Were the study subjects and the setting described in detail? Yes

Study details	Participants	Methods	Outcomes and results	Comments
Australia Study type Retrospective audit Study dates 2007-2010 Source of funding Research scholarship received from the Royal College of Pathologists of Australasia.	*Percentage calculated by the NGA technical team Inclusion criteria People aged ≤18 years who lived in New South Wales, Australia and attended any of the following three paediatric CF centres from 2007 to 2010: The Children's Hospital at Westmead (CHW), Sydney, Sydney Children's Hospital (SCH), and John Hunter Children's Hospital (JHCH), Newcastle. Exclusion criteria Not reported	reasons. The reference range at CHW was vitamin A (0.8–2.5 mmol/L), vitamin E (12–36 mmol/L); at JHCH, vitamin A (1.05–2.50 mmol/L), vitamin E (8–30 mmol/L). The reference range for vitamins A and E at SCH varied based on the child's age. 25-OHD was measured by radioimmunoassay (Diasorin, Stillwater, MN, USA). Deficiency of 25-OHD was defined as <50 nmol/L. Measurement. Vitamins A and E levels were performed using protein precipitation with high-performance liquid chromatography (HPLC) and ultraviolet detection (in-house method).	Vitamin D deficiency: 2007: 22.11% 2010: 15.54% 25-OHD vitamin levels on first vitamin level test in the study period: Abnormal: 19.8% 65/328* Low: 19% (63/328) Vitamin E deficiency: 2007: 20.22% 2010: 13.89% Vitamin E levels on first vitamin level test in the study period Abnormal: 38.4% (201/523)* Low: 20% (105/523) Deficiency of one or more fat-soluble vitamins on their first vitamin level test: 45% (240/530) *Percentage calculated by the NGA technical team	Was the data analysis conducted with sufficient coverage of the identified sample? N/A Were objective, standard criteria used for the measurement of the condition? No. The percentages for low vitamin levels at first vitamin test are different from the prevalence of vitamin deficiency in 2007 and it is unclear why. Was the condition measured reliably? No. The range for normal levels of vitamins differs between the laboratories taking part in the study. Was there appropriate statistical analysis? No. No numerators or denominators provided for vitamin deficiency. No confidence intervals provided however all the people attending the centres and fitted inclusion criteria were included so confidence intervals not needed Are all important confounding factors/subgroups/differences identified and accounted for? No, data was not disaggregated between infants, children, young people and adults. Were subpopulations identified using objective criteria? N/A Overall quality: Very low Other information None.
Full citation Somerville, R., Lackson, A., Zhou, S., Fletcher, C.,	Sample size	Details	Results	Limitations

Study details	Participants	Methods	Outcomes and results	Comments
Fitzpatrick, P., Non-pulmonary chronic diseases in adults with cystic fibrosis: analysis of data from the Cystic Fibrosis Registry, Irish Medical Journal, 106, 166-8, 2013 Country/ies where the study was carried out Ireland Study type Retrospective study Study dates All people alive on 31/12/2009. Data recorded from 2001. Source of funding Not reported	N=853 people in the analyis on prevalence of diabetes * N=859 people in the analysis on the prevalence of osteopenia or osteoporosis * * N calculated by the NGA technical team Characteristics Age: not reported Sex: not reported Inclusion criteria All people alive on 31/12/2009 Exclusion criteria Not reported	Register/data source CF Registry of Ireland Definitions/thresholds Authors considered osteopenia or osteoporosis present if documented in the medical notes in the last year. Measurement. Authors did not report what measurements were used for writing the medical notes.	Prevalence of osteopenia or osteoporosis: <18 years: 5.5% (25/454*) ≥18 years: 42.7% (173/405) * Denominator calculated by the NGA technical team	Critical appraisal using Munn et al 2014: Was the sample representative of the target population? Yes Were study participants recruited in an appropriate way? Yes Was the sample size adequate? Yes, > 250 as per protocol. Were the study subjects and the setting described in detail? No. Baseline characteristics were provided for the adult population only. N used in the analysis was not reported and was different from N reported by the authors, however authors did not mention it and did not explain why. Was the data analysis conducted with sufficient coverage of the identified sample? Yes, N of each subgroup was >250 Were objective, standard criteria used for the measurement of the condition? Yes, authors considered osteopenia or osteoporosis present if documented in the medical notes. Was the condition measured reliably? Unclear if different medical personnel would have diagnosed osteopenia or osteoporosis using the same criteria. Was there appropriate statistical analysis? No. No denominator was provided for one age subgroup. Confidence intervals of percentages were not reported however this is

Study details	Participants	Methods	Outcomes and results	Comments
				registry data so the confidence intervals are not needed. Are all important confounding factors/subgroups/differences identified and accounted for? No. Age subgroups were <18 years and ≥18 years. Data for the former group was not disaggregated between infants, children and young people. Were subpopulations identified using objective criteria? Yes, 18 years old seems a reasonable cut-off. Overall quality: Low Other information Prevalence data on diabetes was not extracted from this study because it was based on whether a person was on insulin in the previous year - this definition is likely to underestimate prevalence
Full citation Stephenson, A. L., Mannik, L. A., Walsh, S., Brotherwood, M., Robert, R., Darling, P. B., Nisenbaum, R., Moerman, J., Stanojevic, S., Longitudinal trends in nutritional status and the relation between lung function and BMI in cystic fibrosis: a population-based cohort study, American Journal of	Sample size N= 909 Characteristics People with CF attending the Adult CF Clinic in Toronto Age: Not reported Sex: Not reported Inclusion criteria All people followed at St Michael's Hospital in Toronto from 1	Details Register / Data source. Toronto CF registry Data collection and measurements. Registry data are collected prospectively in all individuals attending the CF clinic in Toronto. Height (cm) and weight (kg) were recorded for each subject at each clinic visit. Height was measured by using a wall stadiometer, and weight was measured by using a calibrated balance beam scale. BMI was	Results Prevalence of underweight, overweight and obesity. Nutritional status of 651 subjects using their last available measurement between January 2000 and December 2011: Underweight: 17% Adequate weight: 60% Overweight: 18% Obese: 3.8%	Limitations Critical appraisal using Munn et al 2014: Was the sample representative of the target population? Yes Were study participants recruited in an appropriate way? Yes Was the sample size adequate? Yes, >250 as per protocol Were the study subjects and the setting described in detail? No. Age not reported for each cohort. Only the most recent cohort was described in detail.

Study details	Participants	Methods	Outcomes and results	Comments
Clinical Nutrition, 97, 872-7, 2013 Country/ies where the study was carried out Canada Study type Retrospective study Study dates People followed at the clinic from 1 January 1985 to 31 December 2011 Source of funding Not reported	January 1985 to 31 December 2011 Confirmed diagnosis of CF Exclusion criteria Data obtained after lung transplantation Data obtained during pregnancy and in the 6 months of postpartum period Individuals older than 70 years	calculated by using weight (in kg)/height (in m2). Definitions. Subjects were classified into 1 of 4 BMI categories on the basis of WHO guidelines: Underweight(<18.5), adequate weight (18.5-24.9), overweight (25.0-29.9) or obese (≥30). Analysis. A random sample of 1000 measurements was taken for each of the 3 time intervals.	Underweight, with 1000 random measurements per time interval method: 1985-1990: 20.6% 1991-1999: 11.6%* 2000-2011: 11.1% Overweight, with 1000 random measurements per time interval method: 1985-1990: 7.0% 1991-1999: 15.8% 2000-2011: 18.4% *Percentage calculated by the NGA technical team	Was the data analysis conducted with sufficient coverage of the identified sample? N/A Were objective, standard criteria used for the measurement of the condition? Yes Was the condition measured reliably? Yes Was there appropriate statistical analysis? No, no numerators provided. No confidence intervals of percentages provided however all the people attending the clinic were included so confidence intervals were not needed. Are all important confounding factors/subgroups/differences identified and accounted for? No, no age subgroups. Were subpopulations identified using objective criteria? N/A Overall quality: Low Other information None.
Full citation Vieni, G., Faraci, S., Collura, M., Lombardo, M., Traverso, G., Cristadoro, S., Termini, L., Lucanto, M. C., Furnari, M. L., Trimarchi, G., Triglia, M. R., Costa, S., Pellegrino, S., Magazzu, G., Stunting is an independent predictor of mortality in patients with cystic	Sample size N=393 Characteristics People with CF, alive and deceased Age: > 6 years (193 "paediatric", 200 "adults" - age cut-off not reported)	Details Register / Data source. Data from Regional Centre in Palermo and Satellite Centre in Messina, Italy Definitions and thresholds. "Stunting": Height percentile <5th; "Wasting": BMI percentile <10th in paediatric patients and BMI<18.5 kg/m2 in adult patients	Results Prevalence of “stunting”: Height percentile <5th: 24.4% Prevalence of “wasting”: Either BMI percentile <10th or BMI < 18.5 kg/m2: 35.3%	Limitations Critical appraisal using Munn et al 2014: Was the sample representative of the target population? Yes Were study participants recruited in an appropriate way? Yes Was the sample size adequate? Yes, >250 as per protocol Were the study subjects and the setting described in detail? No.

Study details	Participants	Methods	Outcomes and results	Comments
fibrosis, Clinical Nutrition, 32, 382-5, 2013 Country/ies where the study was carried out Italy Study type Retrospective study Study dates December 2007 Source of funding None of the authors had sources of support	Sex: Males: Alive: 52.3% vs Deceased: 44.2% Inclusion criteria People with CF who were followed up at the Regional Center in Palermo and at the Satellite Center in Messina with availability of clinical and anthropometric data up to December 2007 Exclusion criteria Not reported	Data collection and measurements. People were classified using the lowest height and weight values in the database. Weight and height in the study group were measured by nurses and dieticians by using precision balances and stadiometers, and CDC growth reference curves were used to obtain centiles from the raw measurements.		Although the number of paediatric and adult patients is given, age cut-off unclear. Was the data analysis conducted with sufficient coverage of the identified sample? N/A Were objective, standard criteria used for the measurement of the condition? Yes Was the condition measured reliably? Yes Was there appropriate statistical analysis? No. No numerators; no confidence intervals for percentages however all the people attending the centres were included so confidence intervals were not needed Are all important confounding factors/subgroups/differences identified and accounted for? No, data are not disaggregated by subgroup. Were subpopulations identified using objective criteria? Yes, age cut-offs. Overall quality: Low. Other information None.
Full citation Watts, K. D., Seshadri, R., Sullivan, C., McColley, S. A., Increased prevalence of risk factors for morbidity and mortality in the US Hispanic CF population,	Sample size N=22714 Characteristics Age: only reported for each ethnic subgroup Inclusion criteria Not reported Exclusion criteria	Details Register / Data source. CFF Patient Registry Definitions and thresholds. Bone and joint complications include arthritis, arthropathy, bone fractures, osteopenia, osteoporosis. Criteria to	Results Prevalence of bone and joint complications: 6.7% (1510/22714)* *Prevalence calculated by the NGA technical team summing up cases in the	Limitations Critical appraisal using Munn et al 2014: Was the sample representative of the target population? Yes Were study participants recruited in an appropriate way? Yes

Study details	Participants	Methods	Outcomes and results	Comments
Pediatric Pulmonology, 44, 594-601, 2009 Country/ies where the study was carried out United States Study type Retrospective study Study dates Data from 2004 Source of funding The work was supported in part by a Cystic Fibrosis Foundation Clinical Fellowship Grant.	Not reported	diagnose these complications not reported.	Hispanic and in the non-Hispanic population	Was the sample size adequate? Yes, > 250 as per protocol Were the study subjects and the setting described in detail? Yes Was the data analysis conducted with sufficient coverage of the identified sample? N/A Were objective, standard criteria used for the measurement of the condition? Unclear, not reported Was the condition measured reliably? Unclear, not reported Was there appropriate statistical analysis? No, no separate data for each complication Are all important confounding factors/subgroups/differences identified and accounted for? No, no age subgroups Were subpopulations identified using objective criteria? N/A Overall quality: very low Other information None.
Full citation Wiedemann, B., Steinkamp, G., Sens, B., Stern, M., German Cystic Fibrosis Quality Assurance, Group, The German cystic fibrosis quality assurance project: clinical features in children and adults, European	Sample size N=4306 people in the registry who gave informed consent N=3448 people included in the analysis on the prevalence of medical complications Characteristics Mean age: 15.7 years	Details Register / data source. CF Quality Assurance Project registry Definitions. Not reported Data collection and measurements. Centres reported data for each person with CF once a year	Results Prevalence of DIOS Children: 3.0% Adults: 3.5% All ages: 3.2% Weight for height < 90% predicted in children and young people: 26.8%	Limitations Critical appraisal using Munn et al 2014: Was the sample representative of the target population? Yes Were study participants recruited in an appropriate way? Yes, participating centres reported data for all people under their care. Was the sample size adequate? Yes, >250 as per protocol

Study details	Participants	Methods	Outcomes and results	Comments
Respiratory Journal, 17, 1187-94, 2001 Country/ies where the study was carried out Germany Study type Retrospective study Study dates Data from 1997 Source of funding This work was supported by Christiane Herzog Stiftung, Mukoviszidose e.V., and Niedersächsischer Verein zur Förderung der Qualität im Gesundheitswesen.	Age range: 0-58 Sex: Males: 53.1% Inclusion criteria People in the registry who gave informed consent Exclusion criteria Not reported	from a routine visit near the person's birthday when the person was in a stable clinical condition. Measurement tools were not reported.		Were the study subjects and the setting described in detail? Yes Was the data analysis conducted with sufficient coverage of the identified sample? Yes, N not reported but the authors specify that 35.8% of the people included in the study were older than 18 years, so the number of people in each age subgroup was >250 Were objective, standard criteria used for the measurement of the condition? Unclear. Not reported. Was the condition measured reliably? Unclear. Not reported Was there appropriate statistical analysis? No, numerator and denominator not provided. Confidence intervals of percentages not provided however this is registry data so confidence intervals were not needed. Are all important confounding factors/subgroups/differences identified and accounted for? No. Data was not disaggregated between children and young people. Were subpopulations identified using objective criteria? Unclear, age cut-offs, however cut-off to defined adults not reported. Overall quality: low Other information None.
Full citation	Sample size	Details	Results	Limitations

Study details	Participants	Methods	Outcomes and results	Comments
Wilcock, M. J., Ruddick, A., Gyi, K. M., Hodson, M. E., Renal diseases in adults with cystic fibrosis: a 40 year single centre experience, Journal of Nephrology, 28, 585-91, 2015 Country/ies where the study was carried out UK Study type Retrospective study Study dates 1969-2009 Source of funding Not reported	N=1532 Characteristics Adult CF department at the Royal Brompton Hospital Age: not reported Sex: not reported Inclusion criteria All people with details recorded in the database relating to 1969-2009, alive and deceased. Exclusion criteria Not reported	Register/Data source Database of adult CF department at the Royal Brompton Hospital. A search of the database from 1969 to 2009 was performed to identify patients with an entry in the ‘‘Renal Disease’’, ‘‘Renal Stones’’ or ‘‘Vasculitis’’ categories. All patients who had ever had a plasma urea greater than 10 mmol/l were also identified. Finally, a review of all entries in the ‘‘Other diseases’’ category was made to identify any remaining renal disease. The clinical notes for these patients were then studied for confirmation and to collect clinical data. Definitions AKI was defined as an acute rise in creatinine above the person's established baseline CKD as an abnormal creatinine level for greater than 3 months nephrotic syndrome as proteinuria (>3g/l), hypoalbuminaemia and peripheral oedema Cases were excluded if: isolated rise in plasma urea which resolved with no other evidence of renal impairment impaired renal function in the last few weeks of life	Prevalence of renal disease. Renal problem: 5.1% (78/1532) Acute kidney injury: 1.1%* (17/1532) (9 cases were presumed to be drug-induced; 2 were due to glomerular disease; others were miscellaneous; 3 cases required dyalisis) Chronic kidney disease: 0.9%* (13/1532) (4 cases were presumed to be drug-induced; the other most common aetiology was primary glomerular disease) Renal stone disease: 2.0% (30/1532) Isolated proteinuria: 0.1%* (2/1532) Isolated haematuria: 0.5%* (8/1532) Nephrotic syndrome: 0.1%* (2/1532) Miscellaneous disease: 0.5%* (8/1532) *Percentage calculated by the NGA technical team	Critical appraisal using Munn et al 2014: Was the sample representative of the target population? Yes Were study participants recruited in an appropriate way? Yes, all the people in the database fitting the inclusion criteria were included Was the sample size adequate? Yes, >250 as per protocol Were the study subjects and the setting described in detail? Study subjects were not described in detail. Only the cases were described in detail. Was the data analysis conducted with sufficient coverage of the identified sample? N/A Were objective, standard criteria used for the measurement of the condition? Yes Was the condition measured reliably? Yes Was there appropriate statistical analysis? No, percentages were not provided for some kinds of renal disease (only numerator and denominator were given). No confidence intervals of percentages provided however all the people attending the centre and fitting inclusion criteria were included so confidence intervals were not needed. Are all important confounding factors/subgroups/differences identified and accounted for? Yes.

Study details	Participants	Methods	Outcomes and results	Comments
		nephrotoxic immunosuppressant therapy before any episode of renal disease		The study focuses on a population from an adult centre so there is no need to disaggregate data by age. Were subpopulations identified using objective criteria? N/A Overall quality: Moderate Other information None.
Full citation Zhang, Z., Lindstrom, M. J., Lai, H. J., Pubertal height velocity and associations with prepubertal and adult heights in cystic fibrosis, Journal of Pediatrics, 163, 376-82, 2013 Country/ies where the study was carried out United States Study type Retrospective study Study dates PHV was calculated in relation to time interval 1994-2008. Registry records from 1986-2008 were used to identify participants. Source of funding Supported by the National Institutes of Health (R01DK072126)	Sample size N=1862 Characteristics People with CF Age: 10-18 years Sex: Males: 52.9% Inclusion criteria People with CF born in 1984-1987. Exclusion criteria People who had died by 2008; people lost to follow-up before age 18; people who had <3 height measurements per year during age 10-18 years.	Details Register/data source. Data retrieved from US CF Foundation Registry Definitions/thresholds. Longitudinal standard for peak height velocity for North American children developed by Tanner and Davies were used to define normal Peak Height Velocity (PHV). PHV was classified either as normal, delayed (PHV age at 2 SD later than average), attenuated (magnitude<5th percentile), or both delayed and attenuated (D&A). Measurement. Growth curve modeling was used to identify Peak Height Velocity (PHV). A semi-parametric shape-invariant model developed by Lindstrom was used. "Conceptually, this method assumes that all individuals of the same sex have a common shape for their	Results Prevalence of the following categories of pubertal peak height velocity (PHV): Normal: 60.3% (1123/1862)* Delayed: 9.4% (175/1862)* Attenuated: 20.8% (387/1862)* D&A: 5.3% (98/1862)* Unknown: 4.2% (79/1862)** *Percentage and denominator provided in the paper, numerator calculated by NGA technical team summing up numbers given for males and females ** Percentage and denominator provided the paper, numerator calculated by NGA technical team subtracting the numerators for the	Limitations Critical appraisal using Munn et al 2014: Was the sample representative of the target population? Yes. The authors specify that the study population did not differ significantly with regards to sex and pre-pubertal height percentile at age 7 from those excluded from the analysis. Were study participants recruited in an appropriate way? Yes, all people in the registry meeting inclusion and exclusion criteria were included. Was the sample size adequate? Yes, > 250 as per protocol. Were the study subjects and the setting described in detail? Yes Was the data analysis conducted with sufficient coverage of the identified sample? N/A Were objective, standard criteria used for the measurement of the condition? Yes Was the condition measured reliably? Yes

Study details	Participants	Methods	Outcomes and results	Comments
		age versus height curve, which is estimated using data from all children by a non-linear mixed effects model with regression spline that has 2 continuous analytical derivatives. Each child's individual height curve is then determined by shifting and scaling this common curve to obtain the best fit for his/her data. Once an individual's height curve is fitted, the calculated first derivatives of this curve are used to determine the HV curve. Using this approach, 4 measurements characterizing pubertal growth for each child are identified: age at take-off, height at take-off, age at PHV, and magnitude of PHV".	other categories from total number	Was there appropriate statistical analysis? Yes, no confidence intervals provided for prevalence data however this is registry data so confidence intervals were not needed Are all important confounding factors/subgroups/differences identified and accounted for? Yes, data for age subgroup 10-18. Were subpopulations identified using objective criteria? N/A Overall quality: high Other information None.
Full citation Zhang, Z., Shoff, S. M., Lai, H. J., Incorporating genetic potential when evaluating stature in children with cystic fibrosis, Journal of Cystic Fibrosis, 9, 135-42, 2010 Country/ies where the study was carried out United States Study type Retrospective study Study dates	Sample size N=3306 Characteristics People with CF Age: 2-18.5 years Sex: Males: 50% (1649/3306) Inclusion criteria Age: >2 years Self-reported parental heights available Exclusion criteria People with parental heights less than 100	Details Registry / Data source CFF Patient Registry Definitions / thresholds. Procedure to calculate CFF target height and range (lower bound method): 1. Average two parental heights to obtain mid-parental height. Calculate the child's target adult height by adding 6.5 cm to mid-parental height for a boy, or subtracting 6.5 cm for a girl. Apply ±10 cm for a boy or ±9 cm for a girl to define the target height range. 2. Plot target height and range	Results Prevalence of: Unadjusted height percentile <5th: 16% Unadjusted height percentile <10th: 26% Himes adjusted height percentile <5th: 18% Himes adjusted height percentile <10th: 31% CFF lower bound method: 24%	Limitations Critical appraisal using Munn et al 2014: Was the sample representative of the target population? Yes Were study participants recruited in an appropriate way? Yes Was the sample size adequate? Yes, > 250 as per protocol Were the study subjects and the setting described in detail? Yes Was the data analysis conducted with sufficient coverage of the identified sample? N/A

Study details	Participants	Methods	Outcomes and results	Comments
Data from 1986-2005 Source of funding This work was supported by NIH grant R01-DK72126.	cm (likely due to inch-centimeter conversion or recording errors) were excluded from analysis.	at age 20 years on the 2000 CDC growth chart and estimate their respective percentiles. 3. Extrapolate the percentiles of target height and range at age 20 to the child's current age. 4. Plot the child's height on the 2000 CDC growth chart; if his/her height percentile is below the target height lower bound, he/she is considered to be below genetic potential. Procedure to calculate Himes adjusted height 1. Calculate mid-parental height. 2. Based on the child's sex, age, height and mid-parent height, find the adjustment value from the reference tables. 3. Apply the adjustment value to the child's height to obtain adjusted height. 4. Plot adjusted height on the 2000 CDC growth chart to obtain adjusted height percentile. Measurements. Not reported Analysis. The most recent height measurement between age 2 to 18.5 years for each patient was used for analysis.		Were objective, standard criteria used for the measurement of the condition? Yes Was the condition measured reliably? No. Self-reported parental heights. Was there appropriate statistical analysis? No. No confidence intervals of percentages. Are all important confounding factors/subgroups/differences identified and accounted for? No, data not disaggregated between children and young people. Were subpopulations identified using objective criteria? N/A Overall quality: Low Other information None.
Full citation Cystic Fibrosis Trust, Cystic Fibrosis Trust, UK Cystic Fibrosis Registry	Sample size 9587 Characteristics	Details Register/data source. UK CF registry Data collection.	Results Prevalence of the following complications: Kidney stones:	Limitations Critical appraisal using Munn et al 2014:

Study details	Participants	Methods	Outcomes and results	Comments
2015 Annual Data Report, 2016 Country/ies where the study was carried out UK Study type Registry report Study dates 2015 Source of funding The UK CF Registry has been sponsored and hosted by the Cystic Fibrosis Trust since 2007.	People with CF Median age: 19 Sex: Males: 53.0% Inclusion criteria Informed consent Complete data Exclusion criteria Not reported	CF care teams at every specialist centre and clinic across the UK filled in forms where they selected what complications (if any) each person with CF had. No definition of complications is provided in the form. Definitions. Detailed criteria for diagnosing complications not reported. Definitions are provided for the general public: Arthritis: "A condition causing pain and inflammation in the joints". Arthropathy: "A condition causing pain in the joints". Cirrhosis: "Chronic liver disease". Nasal polyps: "Small, sac-like growths of inflamed mucus caused by chronic inflammation of the nasal lining". Osteopenia: "A medical condition less severe than osteoporosis, where the mineral content of bone is reduced". Osteoporosis: "A condition where the bones become brittle from loss of tissue". Portal hypertension: "High blood pressure in the portal vein system, which is the blood system of the liver".	Overall: 1.0% (96/9587) <16 years: 0.3% (12/3845) ≥16 years: 1.5% (84/5742)Renal failure: Overall: 0.6% (57/9587) <16 years: 0% (<5) ≥16 years: 1.0% (55/5742) Renal failure: Overall: 0.6% (57/9587) <16 years: 0% (<5) ≥16 years: 1.0% (55/5742) Intestinal obstruction: Overall: 5.6% (539/9587) <16 years: 3.0% (116/3845) ≥16 years: 7.4% (423/5742) Treatment for CFRD: ≥10 years: 28.0% (1982/6970) 10-16 years: 10.0% (134/1624) ≥16 years: 32.2% (1848/5346) Nasal polyps requiring surgery: Overall: 2.3% (221/9587) <16 years: 1.1% (44/3845) ≥16 years: 3.1% (177/5742) Sinus disease Overall: 9.8% (939/9587) <16 years: 1.4% (53/3845)	Was the sample representative of the target population? Yes Were study participants recruited in an appropriate way? Yes, all people fitting inclusion criteria were included Was the sample size adequate? Yes, >250 as per protocol Were the study subjects and the setting described in detail? Yes Was the data analysis conducted with sufficient coverage of the identified sample? Yes. >250 people in each age subgroup Were objective, standard criteria used for the measurement of the condition? Unclear. Criteria used to diagnose complications not reported Was the condition measured reliably? Unclear from the report, although diagnosis of relevant complications of CF would be consistent across the NHS. Was there appropriate statistical analysis? Yes, numerators and denominators provided. No confidence intervals provided for percentages however this is registry data so the confidence intervals are not needed. Are all important confounding factors/subgroups/differences identified and accounted for? No. Prevalence data is disaggregated into 2 age subgroups using 16 as cut-off, however data are not disaggregated by infants, children, young people and adults.

Study details	Participants	Methods	Outcomes and results	Comments
		Sinus disease: "When the sinuses, which are usually filled with air, are typically full of thick sticky mucus". Measurements. Not reported.	≥16 years: 15.4% (886/5742) Arthritis: Overall: 1.6% (158/9587) <16 years: 0.2% (7/3845) ≥16 years: 2.6% (151/5742) Arthropathy: Overall: 5.4% (517/9587) <16 years: 0.5% (18/3845) ≥16 years: 8.7% (499/5742) Osteopenia: Overall: 13.5% (1297/9587) <16 years: 0.9% (36/3845) ≥16 years: 22.0% (1261/5742) Osteoporosis: Overall: 5.3% (511/9587) <16 years: 0% (<5/3845) ≥16 years: 8.8% (507/5742) Bone fracture: Overall: 0.5% (46/9587) <16 years: 0.4% (14/3845) ≥16 years: 0.6% (32/5742) Raised liver enzymes: Overall: 11.6% (1116/9587) <16 years: 6.9% (264/3845) ≥16 years: 14.8% (852/5742)	Were subpopulations identified using objective criteria? Yes, age cut-offs Overall quality: moderate Other information None.

Study details	Participants	Methods	Outcomes and results	Comments
			Liver disease: Overall: 14.3% (1371/9587) <16 years: 8.8% (340/3845) ≥16 years: 18.0% (1031/5742) Cirrhosis with no portal hypertension: Overall: 1.2% (116/9587) <16 years: 0.7% (26/3845) ≥16 years: 1.6% (90/5742) Cirrhosis with portal hypertension: Overall: 1.7% (164/9587) <16 years: 0.7% (26/3845) ≥16 years: 2.4% (138/5742) Meconium ileus: Overall: 15.2% (1458/9587) <16 years: 16.7% (643/3845) ≥16 years: 14.2% (815/5742)	
Full citation Cystic Fibrosis Trust, UK CF Registry, BMI and BMI percentile in relation to the UK, year 2015. , [online; accessed 23 November 2016] Country/ies where the study was carried out	Sample size N=9084 Characteristics Age: 2 to 11: n=2498 12 to 16: n=885 >16: n=5701 Inclusion criteria	Details Register/Data source. UK CF Registry Definitions / thresholds. Please see results section for BMI cut-offs requested by the NGA technical team (and used by the registry team in providing the data)	Results Prevalence of malnutrition or impaired growth Data disaggregated using the cut-offs used in the Cystic Fibrosis Trust consensus document on nutritional management of cystic fibrosis (2016):	Limitations Critical appraisal using Munn et al. 2014: Was the sample representative of the target population? Yes Were study participants recruited in an appropriate way? Yes Was the sample size adequate? Yes, >250 as per protocol

Study details	Participants	Methods	Outcomes and results	Comments
UK Study type Data obtained from the UK CF registry following a data request from the NGA technical team Study dates Data obtained on 23 November 2016 Source of funding The UK CF Registry is sponsored and managed by the Cystic Fibrosis Trust	People with CF in the UK with BMIp (BMI percentile) or BMI data recorded in the CF Registry in the year 2015 Exclusion criteria People not consenting to recording their data in the registry* *Information extracted from the UK Cystic Fibrosis Trust Registry 2015 Annual Data Report - which mentions that the registry is a database of consenting people	Data collection and measurements. CF care teams at every specialist centre and clinic across the UK entered data on weight, height and BMI for the registry.	Age 2-11 BMIp < 25th: 17.3% (432/2498)* BMIp >91st: 10.1% (253/2498)* Age 12-16: BMIp < 25th: 27.5% (243/885)* BMIp >91st: 5.9% (52/885)* Age 2-16: · BMIp < 25th: 20.0% (675/3383)* BMIp >91st: 9.0% (305/3383)* Age >16 years: BMI < 20 kg/m2: 24.5% (1398/5701)* BMI > 25 kg/m2: 22.2% (1266/5701)* *Numbers and percentages calculated by the NGA technical team based on the numbers below Data disaggregated by all cut-offs provided by the registry: Age 2-11: BMIp <2nd: 1.5% (38/2498) BMIp ≥2nd and <25th: 15.8% (394/2498) BMIp ≥25th and <50th: 22.9% (572/2498)	Were the study subjects and the setting described in detail? Yes, details available in the UK Cystic Fibrosis Trust Registry 2015 Annual Data Report Was the data analysis conducted with sufficient coverage of the identified sample? Yes, >250 in each age group Were objective, standard criteria used for the measurement of the condition? Unclear from the UK Cystic Fibrosis Trust Registry 2015 Annual Data Report how weight and height were measured Was the condition measured reliably? Unclear from the UK Cystic Fibrosis Trust Registry 2015 Annual Data Report how weight and height were measured Was there appropriate statistical analysis? Yes, numerators, denominators and percentages were provided; no confidence intervals for percentages however this is registry data so confidence intervals were not needed Are all important confounding factors/subgroups/differences identified and accounted for? Yes, data disaggregated into age subgroups: children; young people until 16; and young people older than 16 + adults. BMI is not recorded for infants so data for infants was not provided Were subpopulations identified using objective criteria? Yes, the 16 years

Study details	Participants	Methods	Outcomes and results	Comments
			BMIp ≥50th and ≤75th: 29.9% (748/2498) BMIp >75th and ≤91st: 19.7% (493/2498) BMIp >91st and ≤98th: 8.1% (203/2498) >98th BMIp: 2.0% (50/2498) Age 12-16 BMIp <2nd: 2.0% (18/885) BMIp ≥2nd and <25th: 25.4% (225/885) BMIp ≥25th and <50th: 28.4% (251/885) BMIp ≥50th and ≤75th: 24.6% (218/885) BMIp >75th and ≤91st: 13.7% (121/885) BMIp >91st and ≤98th: 5.4% (48/885) >98th BMIp: 0.5% (4/885) Age 2-16: BMIp <2nd: 1.7% (56/3383) BMIp ≥2nd and <25th: 18.3% (619/3383) BMIp ≥25th and <50th: 24.3% (823/3383) BMIp ≥50th and ≤75th: 28.6% (966/3383) BMIp >75th and ≤91st: 18.1% (614/3383) BMIp >91st and ≤98th: 7.4% (251/3383)	cut-off was used because BMI percentile is recorded in the registry until age 16, and BMI (kg/m2) is recorded for people older than 16. Overall quality: Moderate. Other information 107 people aged 2-16 did not have a record of BMIp in 2015

Study details	Participants	Methods	Outcomes and results	Comments
			>98th BMIp: 1.6% (54/3383) Age >16 years: BMI < 18.5 kg/m2: 8.1% (459/5701) BMI ≥ 18.5 and ≤20 kg/m2: 16.5% (939/5701) BMI ≥ 20 and ≤25 kg/m2: 53.3% (3037/5701) BMI > 25 kg/m2: 22.2% (1266/5701)	
Full citation Cystic Fibrosis Trust, UK CF Registry, Data on intestinal obstruction disaggregated by history of meconium ileus in relation to the UK, year 2015., [online; accessed 11 January 2017] Country/ies where the study was carried out UK Study type Data provided by the UK CF registry following a data request from the NGA technical team Study dates Data provided on 11 January 2017. Source of funding The UK CF Registry is sponsored and managed	Sample size N=9587 Characteristics People with CF Age <16: 3845 Age≥16: 5742 Males: 53%* *Information extracted from the UK Cystic Fibrosis Trust Registry 2015 Annual Data Report Inclusion criteria People with CF recorded in the UK CF registry during the year 2015. Exclusion criteria People not consenting to recording their data in the registry* *Information extracted from the UK Cystic	Details Register/Data source. UK CF Registry Definitions / thresholds. No definition given for intestinal obstruction or meconium ileus. Data collection and measurements. CF care teams at every specialist centre and clinic across the UK entered data on intestinal obstruction and meconium ileus for people with CF	Results Prevalence of intestinal obstruction. Prevalence of intestinal obstruction in age group <16: Among people with a diagnosis of meconium ileus: 6.4% (41/643)* Among people without diagnosis of meconium ileus: 2.3% (75/3202)* Prevalence of intestinal obstruction in age group ≥16: Among people with a diagnosis of meconium ileus: 13.9% (113/815)* Among people without diagnosis of meconium ileus: 6.3% (310/4927)* *Numbers and percentages calculated by the NGA technical team	Limitations Critical appraisal using Munn et al. 2014: Was the sample representative of the target population? Yes Were study participants recruited in an appropriate way? Yes Was the sample size adequate? Yes, >250 as per protocol Were the study subjects and the setting described in detail? Yes, details available in the UK Cystic Fibrosis Trust Registry 2015 Annual Data Report Was the data analysis conducted with sufficient coverage of the identified sample? Yes, more than >250 people in each age subgroup Were objective, standard criteria used for the measurement of the condition? Unclear from the UK Cystic Fibrosis Trust Registry 2015 Annual Data Report how DIOS and meconium ileus were diagnosed

Study details	Participants	Methods	Outcomes and results	Comments
by the Cystic Fibrosis Trust.	Fibrosis Trust Registry 2015 Annual Data Report - which mentions that the registry is a database of consenting people		based on the following numbers provided by the registry: Age group <16 (n=3845): Diagnosed with meconium ileus and 2015 intestinal obstruction: 41 Diagnosed with meconium ileus only: 602 Diagnosed with 2015 intestinal obstruction only: 75 Age group ≥16 (n=5742): Diagnosed with meconium ileus and 2015 intestinal obstruction: 113 Diagnosed with meconium ileus only: 702 Diagnosed with 2015 intestinal obstruction only: 310	Was the condition measured reliably? Unclear from the UK Cystic Fibrosis Trust Registry 2015 Annual Data Report how DIOS and meconium ileus were diagnosed Was there appropriate statistical analysis? Yes, numerators, denominators and percentages were provided; no confidence intervals for percentages however this is registry data so confidence intervals were not needed Are all important confounding factors/subgroups/differences identified and accounted for? No, prevalence data is disaggregated into 2 age subgroups using 16 as cut-off, however data are not disaggregated by infants, children, young people and adults. Were subpopulations identified using objective criteria? Yes, age cut-off Overall quality: Moderate. Other information