Table 71: Tests 10 & 15. Index test (Ultrasound) versus Clinical and/or biochemical definition† to detect CFLD

Number of studies (Reference)	Study design	N	Risk of bias	Inconsistency	Indirectness	Imprecision	Sensitivity % (95% CI)	Specificity % 95% CI)	Positive likelihood ratio (95% CI)	Negative Likelihood ratio (95% CI)	AUROC	Quality
Test 10. Ultrasound (cut off of Williams score ≥ 4) in a population of adults and children												

Number of studies (Reference)	Study design	N	Risk of bias	Inconsistency	Indirectness	Imprecision	Sensitivity % (95% CI)	Specificity % 95% CI)	Positive likelihood ratio (95% CI)	Negative Likelihood ratio (95% CI)	AUROC	Quality
1 (Fagundes 2004)[a]	Cohort study	70	no serious risk of bias	no serious inconsistency	no serious indirectness	serious imprecision[b]	50.0 (95% CI: 22.0-75.1)*	91.7 (95% CI: 87.0-95.8)*	6.0 (95% CI: 1.70-18.07)*	0.55 (95% CI: 0.26-0.90	Not reported	MODERATE
1(Witters 2009)[c]	Cohort study	66	no serious risk of bias	no serious inconsistency	no serious indirectness	serious imprecision[b]	63.6 (95% CI: 33.6-87.0)*	70.9 (95% CI: 64.9-75.6)*	2.19 (95% CI: 0.96-3.56)*	0.51 (95% CI: 0.17-1.02)*	0.70 (95% CI: 0.51-0.89)	MODERATE
Test 15. Transient elastography using Fibroscan (Age-specific cut-off values at 5.63kPa for <12 years and 6.50kPa for ≥12 years in a population of adults and children												
1 (Witters 2009)[c]	Cohort study	66	no serious risk of bias	no serious inconsistency	no serious indirectness	serious imprecision[b]	63.6 (95% CI: 34.4-86.0)*	87.3 (95% CI: 81.4-91.8)*	5.0 (95% CI: 1.86-10.43)*	0.42 (95% CI: 0.15-0.81)*	0.86 (95% CI: 0.74-0.98)	MODERATE

Abbreviations: AUROC: area under the curve; CFLD: cystic fibrosis liver disease; CI: confidence interval; kPA: kilopascal
†Diagnosis of CFLD was defined using clinical and biochemical criteria.
** Calculated by the NGA technical team from data available in the study report*
a. Diagnosis of CFLD: Abnormal clinical examination: the presence of a palpable spleen and/or hepatomegaly (presence of a palpable liver more than 2.5 cm below the right costal margin of firm consistency). Abnormal biochemistry: a significant and persistent increase, of at least 1.5 times the upper limit of the reference range, of at least 2 of the enzymes aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (AP) or gamma-glutamyl transpeptidase (GGT), for a period of more than 6 months
b. 95% confidence interval for sensitivity was wide (width 20-30 percentage points)
c. The North-American cystic fibrosis foundation (CFF) consensus workgroup definition of CFLD: the presence of either clinical or biochemical liver disease. Clinical liver disease was defined as the presence of hepatomegaly or splenomegaly. Biochemical liver disease was defined as persistently elevated results (3–6 months, 1.5 times age-dependent upper limit of normal) for 2 of these liver tests: AST, ALT, alkaline phosphatase, bilirubin and gamma-GT