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NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Diagnostics Advisory Committee – Wednesday 19 June 2024

Technologies for the assessment of attention deficit hyperactivity disorder (ADHD)

The following documents are made available to the Committee:

1. **Overview**

2. **Organisation submission from:** The National Network of Parent Carer Forums CIC

3. **Updated External Assessment Report (EAR) – prepared by** Bristol TAG, Population Health Sciences, Bristol Medical School, University of Bristol**.** ***Note, this report is an updated version to the one issued to stakeholders on 20 May 2024. The updates are listed on page 3-4 of the report.***

4. Stakeholder comments and EAG response to EAR consultation comments

DAP75 Technologies for the assessment of attention deficit hyperactivity disorder (ADHD)

Assessment Report Overview

Diagnostics advisory committee (DAC)

19th June 2024

Lead team: Nicole Horwitz, Patrick McGinley

External Assessment Group: Bristol TAG

NICE technical team: Jessica Wilcock, Thomas Walker

NICE National Institute for Health and Care Excellence

Technologies for the assessment of attention deficit hyperactivity disorder (ADHD)

The following slides provide an overview of the external assessment group (EAG) report for this topic. Not all these slides will be presented at the committee meeting but the main information in this set of slides will be summarised. We have tried not to repeat information found in other documents and references can be found in the slide notes.

Key documents in this assessment include:

- The final scope - contains the decision problem for the assessment
- The external assessment report (EAR)* - assessment of the included technologies by the EAG. The report has a more detailed executive summary which provides an overview of the EAG's work and links to the relevant sections of the report

* These documents are in the Committee pack and will be published at consultation

Background on ADHD

- ADHD is a behavioural syndrome characterised by a persistent pattern of hyperactivity, impulsivity, and inattention that interfere with daily and occupational functioning.
- ADHD is estimated to affect around 2 to 7% of school-aged children and young people and often persists into adulthood. Studies suggest that around 15% of adults with childhood ADHD will continue to meet the full diagnostic criteria for ADHD, and 65% will continue to show symptoms which impact on their life.
- ADHD can have a significant impact on individuals' academic, social, and occupational functioning. Children with ADHD may struggle in school, have difficulty forming and maintaining relationships, and experience low self-esteem. In adulthood, untreated ADHD can lead to challenges in employment, relationships, and mental health.
- There is a large overlap in symptoms between ADHD and other psychiatric disorders, as well as the prevalence of comorbid conditions including oppositional defiant disorder, mood disorders, and other neurodevelopmental disorders (for example, autism spectrum disorder).

ADHD: attention deficit hyperactivity disorder

Current practice - Diagnosis

NICE guideline NG87 provides recommendations on the diagnosis, treatment and management of ADHD in adults and children.

- Diagnosis of ADHD should only be made, based on:
  - A full clinical and psychosocial assessment of the person, including a discussion about behaviour and symptoms in different settings, **and**
  - A full development and psychiatric history, **and**
  - Observer reports and assessment of a person's mental state.
- Diagnosis of ADHD should not be made solely on the basis of rating scale or observational data, however these can be valuable adjuncts.
- Clinical experts commented that CPTs which measure attention and impulsivity (but not movement associated with hyperactivity) have been available for many years, but their use in ADHD diagnosis is not routine or widespread in practice.

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ADHD: attention deficit hyperactivity disorder, CPT: computerised performance test

Current practice – Treatment

- Treatment for ADHD includes pharmacological and non-pharmacological interventions.

Dose titration

- For people starting or switching medication for ADHD symptoms.
- ADHD symptoms, impairment and adverse effects should be recorded at baseline, and at each dose change, on standard observer rating scales by parents and teachers, and progress reviewed regularly (for example, by weekly telephone contact) with a specialist.
- Doses should be titrated against symptoms and adverse effects until dose optimisation is achieved.

Medication review and monitoring

- NG87 recommends to monitor effectiveness of medication for ADHD and adverse effects at least once a year.

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ADHD: attention deficit hyperactivity disorder

Decision problem

Decision question	Do technologies that combine measures of cognition and motor (physical) activity to: • help aid diagnostic decision-making for people with suspected ADHD, • help evaluate intervention effectiveness for people with ADHD represent a clinically and cost-effective use of NHS resources?
Populations	For use in assisting diagnostic decision-making for: 1. people* referred with suspected ADHD, 2. people* referred with suspected ADHD for whom current assessment methods cannot reach a diagnostic decision For use in evaluating intervention effectiveness: 3. during dose titration for people* with a diagnosis of ADHD 4. for longer term treatment monitoring for people* with a diagnosis of ADHD
Interventions	The following technologies, used as part of an ADHD assessment by a healthcare professional: • EFSim Test • Nesplora Attention Aquarium • Nesplora Kids Aula • QbCheck • QbTest
Comparators	Assessment by a healthcare professional without use of the interventions.
Setting	Secondary care or remote assessment

*Technologies included for assessment differ in terms of which ages they are indicated for use in

ADHD: attention deficit hyperactivity disorder

Technologies under assessment

Technologies which combine measures of cognition and motor activity.

Technology name (manufacturer)	Functionality	Setting	Age (years)
EFSim Test (Peili Vision)	VR performance tasks + motor activity (head, hand, eye movement)	In clinic	8 to 16
Nesplora Attention Aquarium (Giunti Psychometrics)	VR CPT + motor activity (head and hand movement)	In clinic	16 to 90
Nesplora Attention Kids Aula (Giunti Psychometrics)	VR CPT + motor activity (head and hand movement)	In clinic	6 to 16
QbCheck (QbTech)	CPT + motor activity (head movement)	Remote	6 to 60
QbTest (6 to 12 years) (QbTech)	CPT + motor activity (head movement)	In clinic	6 to 12
QbTest (12 to 60 years) (QbTech)	CPT + motor activity (head movement)	In clinic	13 to 60

Technologies are **not** intended to be used as a standalone test, but as a decision support tool for use during diagnostic assessment or evaluation of treatment interventions.

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CPT: computerised performance test; VR: virtual reality

Patient and carer perspectives (1)

Submission received from The National Network of Parent Carer Forums

- The impact of ADHD on children and young people is vast. It extends to their parents/carers, siblings and other family members.
- Difficulties with task focus, organisation skills, time keeping not only impact on education and employment but with simple day to day tasks such as engaging in play, sports and social activities, household tasks, hygiene and self-management, and learning to manage finances.
- Currently long waiting lists are a barrier to access early intervention and a lack of diagnosis can be a barrier for appropriate support.
- It is important that any technologies will enable quicker and more efficient diagnosis to enable access to support.

"For children and young people missing school/college/work [*due to lack of support*] this has other implications and includes mental health and self-esteem. If a child or young person is not able to engage in a meaningful way in their community, this will also impact on the family's overall wellbeing and ability to work."

"Families are impacted on a day-to-day basis. Families are not always able to timely access the right information and support to enable them to better understand and support their child and young person."

ADHD: attention deficit hyperactivity disorder

Patient and carer perspectives (2)

Submission received from The National Network of Parent Carer Forums

- A diagnosis or a greater understanding of need, where an ADHD diagnosis is not provided, allows professionals, families and importantly the child or young person to better understand their strengths and needs and aid them in accessing the right support.
- Clear and accessible information must be provided to children, young people and their families regarding the digital assessment process and the outcome of the assessment clearly explained.
- The digital assessment should not unfairly disadvantage any person and alternative methods of assessment should still be considered where appropriate.

"The ability for the child or young person to be able to identify, understand, manage their needs and to be able to develop and celebrate their strengths, leads to independence and a successful transition to adulthood and being able to reach their full potential."

"Whilst some child and young people, find the assessment process manageable, it has been reported than some children find the process overwhelming."

"Confidence in the process, needs to be managed, especially where assessments are borderline, and a re-assessment is provided. Some families, feel concerned that the new technologies will not allow for a complete understanding if their child and could lead to a diagnosis not being provided."

ADHD: attention deficit hyperactivity disorder

Equality considerations (1)

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others

NICE guideline NG87 highlights groups which may have increased prevalence of ADHD including:

- People born preterm
- Looked-after children and young people
- Children and young people diagnosed with oppositional defiant disorder or conduct disorder
- Children and young people with mood disorders (for example, anxiety and depression)
- People with a close family member diagnosed with ADHD
- People with epilepsy
- People with other neurodevelopmental disorders (for example, autism spectrum disorder, tic disorders, learning disability [intellectual disability] and specific learning difficulties)
- Adults with a mental health condition
- People with a history of substance misuse
- People known to the Youth Justice System or Adult Criminal Justice System
- People with acquired brain injury.

ADHD: attention deficit hyperactivity disorder

Equality considerations (2)

- ADHD is thought to be under-diagnosed in girls and women and in those who may 'mask' their symptoms.
- The tests may not be suitable for use in people with existing learning disabilities, visual impairment, or physical disability.
- Clinical experts noted that diagnosis may be more difficult where observer reports are missing, for example, from those not attending school.
- Technologies being considered for this assessment have different age ranges for which they are indicated for use in.
- Technologies with wearable components may not be suitable for all people, such as those with anxiety and sensory difficulties associated with autism spectrum disorders.
- Technologies may offer additional value to people experiencing problems communicating their symptoms.
- Remote appointments, could have greater benefits for people in more rural or remote settings, and may also allow greater access to care for people who are less able to afford travel to in-person appointments.

ADHD: attention deficit hyperactivity disorder

Clinical effectiveness

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Objectives

During scoping it was highlighted that the tests may be a particularly beneficial addition to decision-making for people who are difficult to diagnose (objective 2).

What is the diagnostic accuracy and clinical-effectiveness of technologies that combine measures of cognition and motor activity

1. **for the diagnosis of ADHD in people referred with suspected ADHD?**
2. **for the diagnosis of ADHD in people referred with suspected ADHD for whom current assessment cannot reach a diagnosis?**
3. **in evaluating medication effectiveness during initial dose titration and treatment decisions for people with a diagnosis of ADHD?**
4. **in evaluating medication effectiveness during long-term treatment monitoring for people with a diagnosis of ADHD?**

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Summary of included diagnostic accuracy studies

Objective 1

For all people referred with suspected ADHD

- 21 diagnostic accuracy studies evaluated technologies in the diagnosis of ADHD
    - Most studies evaluated the accuracy of the technologies in isolation, which is not in line with the intended use*

EAG: Estimates of the accuracy of QbTest evaluated in isolation were generally lower than when evaluated in combination with clinical judgement.

* Technologies are not intended to be used as a standalone test, but a decision support tool for use during diagnostic assessment or evaluation of treatment interventions

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ADHD: attention deficit hyperactivity disorder; CPT: computerised performance test

For further details see section 4.2 of the EAR

Diagnostic accuracy – Test + clinical assessment

Objective 1

Four studies were identified which evaluated the accuracy of a technology in combination with clinical assessment.

All studies evaluated the QbTest.

Author	No pts	Study design	Population	Reference Std	Index Test
Bijlenga (2019)	209	Two-gate Control group: Adults below the symptom severity cutoff	Adults	DSM IV	QbTest + symptom severity self-report scale
Emser (2018)	136	Two-gate Control group: No established or suspected ADHD diagnosis	Children and adults	DSM IV, KSADS and rating scales	QbTest + KiTap and TAP
Groom (2016)	57	Two-gate Control group: ASD group ICD10 Asperger's	Adults	DSM V	QbTest + Conners Adult Rating Scale and Autism Quotient-10
Hollis (2018) AQUA	250	One-gate	Children and adolescents	DSM IV, ICD-10 (via DAWBA)	QbTest + clinical judgement

EAG: Hollis (2018) AQUA trial was the only study to combine the QbTest information with clinical assessment in the same way that it would be used in practice.

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For further details see section 4.2.2 of the EAR

Risk of Bias and applicability

Objective 1

Studies were assessed using the QUADAS-2 tool

☺ Low risk / concern	☹ High risk / concern	? Unclear risk / concern

	Risk of bias					Applicability				Rationale
Author	Pts	Index	Ref std	Pt flow	Overall	Pts	Index	Ref std	Overall	
Bijlenga (2019)	☹	?	☺	☹	☹	☹	☺	☺	☹	Two-gate design. High proportion of drop-outs (25/234).
Emser (2018)	☹	?	☺	☺	☹	☹	?	☺	☹	Two-gate design. No information on threshold for Qb-Test + clinical assessment or on blinding of ref standard.
Groom (2016)	☹	?	☺	☹	☹	☹	?	☺	☹	Two-gate design. No information on blinding of QbTest to case/control status. No detail on threshold. High proportion of drop-outs (5/37 in ADHD group).
Hollis (2018) AQUA	☹	☺	☹	☺	☹	☺	☺	☺	☺	Participants eligible for DTA sub-study if diagnostic decision had been made by 6 months. Ref std diagnosis made using limited data for around 50% participants as either parent or teacher assessment missing.

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EAG: No reliable data on the accuracy of any of the tests used in combination with clinical judgement.

DTA: diagnostic test accuracy, Pts: Patients, Ref std: reference standard

Diagnostic accuracy estimates for QbTest + clinical assessment

Objective 1

Reference	Population	Design	Test	Sensitivity % (95% CI)	Specificity % (95% CI)
Bijlenga 2019	Older adults	Two-gate	QbTest (12-60)	90.7 (83.1, 95.7)	91.1 (84.2, 95.6)
Groom 2016	Adults	Two-gate	QbTest (12-60)	93.8 (79.2, 99.2)	84.0 (63.9, 95.5)
Hollis 2018	Children & Adolescents	One-gate	QbTest (6-12) or QbTest (12-60)	86.0 (72.1, 94.7)	39.5 (25.0, 55.6)
Emser 2018	Children	Two-gate	QbTest (6-12)	80.0 (61.4, 92.3)	76.7 (57.7, 90.1)
Emser 2018	Adults	Two-gate	QbTest (12-60)	81.6 (65.7, 92.3)	76.3 (59.8, 88.6)

EAG: Low specificity in the Hollis (2018) AQUA study may be due to the limited information available for the reference standard that may have resulted in the diagnosis being too stringent - this would have resulted in more false-positive results leading to an underestimate of specificity.

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For further details see section 4.2.2 and Figure 2 of the EAR

Diagnostic accuracy estimates QbTest + clinical assessment versus clinical assessment alone

Objective 1

- Only 1 study compared QbTest combined with standard clinical assessment to clinical assessment alone: the AQUA trial (Hollis et al.; as described on previous slides).

	Sensitivity (95% CI)	Specificity (95% CI)
QbTest results available (QbOpen)	0.86 (0.72 to 0.95)	0.40 (0.25 to 0.56)
QbTest results withheld (QbBlind)	0.96 (0.87 to 1)	0.36 (0.01 to 0.58)
Formal statistical comparison between QbOpen and QbBlind; Odds ratio	0.26 (0.02 to 1.53; p=0.14)	1.16 (0.38 to 3.71; p=0.8)

EAG: Sensitivity was slightly higher in the QbBlind group compared to the QbOpen group, but there was no statistical evidence of a difference between groups.

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For further details see section 4.2.2 of the EAR

Summary of diagnostic process studies

Objective 1

The AQUA trial and 5 implementation studies provided information on the impact of technologies on diagnostic decision-making process measures. All studies evaluated QbTest in children or adolescents.

Author	No pts	Study design	Population	Test	Control
Hollis (2018) AQUA	250	RCT	Children and adolescents	Usual care + QbTest with test results available ("QbOpen") (n=123)	Usual care (with test results withheld ("QbBlind") (n=127)
Hall (2016)	80	Before-after study	Children and adolescents	QbTest + standard ADHD assessment (n=40)	Standard ADHD assessment (n=40)
Vogt (2011)	108	Before-after study	Children and adolescents	QbTest + standard ADHD assessment (n=62)	Standard ADHD assessment (n=46)
Sharma (2022)	40	Before-after study	Children	QbTest + standard ADHD assessment (n=20)	Standard ADHD assessment (n=20)
Humphreys (2018)	Unclear	Before-after study + survey	Children Staff and families	QbTest + standard ADHD assessment	Standard ADHD assessment
McKenzie (2022)	1,098	Before-after study + survey + qualitative study	Children Staff and families	QbTest + standard ADHD assessment	Standard ADHD assessment

EAG: The largest of the implementation studies, McKenzie et al. (FOCUS), was severely impacted by COVID-19.

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For further details see section 4.2.3 of the EAR

Risk of bias in diagnostic process studies Objective 1

- The AQUA trial time-to-event outcomes were judged by the EAG as high risk of bias due to a large proportion of participants censored from the analysis as they dropped out or were discharged from the clinic and so did not have a diagnosis at 6 months. The analysis assumed that participants were uninformatively censored and so had equivalent outcomes to those for whom full follow-up data were available.
- All implementation studies were judged high risk of bias due to study design and there were no adjustments for confounding.

AQUA Outcome	Domain						Rationale
	1	2	3	4	5	Overall	
Diagnostic decision made within 6 mo	☺	☺	☺	☺	☺	☺	Outcome not impacted by censoring/withdrawals
Diagnostic status (ADHD confirmed/ excluded)	☺	☺	☺	☺	☺	☺	
Diagnostic confidence	☺	☺	☺	☺	☺	☺	
Stability of diagnosis	☺	☺	☺	☺	☺	☺	
No. consultations to diagnosis	☺	☺	☹	☺	☺	☹	Large proportion of participants (80/250) were censored from the analysis as they dropped out or were discharged from the clinic and so did not have a diagnosis at 6 months.
Time to diagnosis (clinic appt. minutes)	☺	☺	☹	☺	☺	☹	
No. of clinic appointments until diagnosis	☺	☺	☹	☺	☺	☹	
No. of days to diagnosis	☺	☺	☹	☺	☺	☹	
Cost of clinic appointments	☺	☺	?	☺	☺	?	Unclear how censored individuals contributed to this outcome.

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For further details see section 4.2.3 of the EAR

Low risk | High risk | Unclear

Impact of technologies on diagnostic process (1)

Objective 1

Time to diagnostic decision – Number of appointments until diagnosis

Study	Number of appointments	P value
AQUA	QbTest: 2.69, Control: 2.72, HR 1.44	0.029
AQUA Children subgroup (6 to 12 years)	HR 1.84	0.001
AQUA Adolescent subgroup (12+ years)	HR 0.82	0.618
Hall (2016)	QbTest: 2.18, Control: 3.05, IRR 0.71	0.020
Sharma (2022)	QbTest: 2.4, Control: 2.7	>0.05
Humphreys (2018)	QbTest: 0.24 to 1.04, Control: 3 to 8	NR
McKenzie (2022)	QbTest: 2.85, Control: 3.22	NR

AQUA reported time to diagnostic decision for those with a diagnosis within 6 months of baseline

EAG: The AQUA trial findings were supported by the limited data from the before-after studies which found that following implementation of the QbTest, fewer consultations were required to reach a diagnostic decision.

EAG: [redacted]

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HR: Hazard ratio, IRR: incidence rate ratio (Poisson regression)

For further details see section 4.2.3 of the EAR including Table 10

Impact of technologies on diagnostic process (2)

Objective 1

Impact on clinical decision making

- AQUA reported a **higher proportion of diagnostic decisions** made within 6 months in the QbTest group compared to the standard assessment group (76% vs 60%), OR=2.43 (95% CI 1.34 to 4.39, p=0.003).
- In FOCUS ADHD **fewer children were diagnosed with ADHD** after QbTest was implemented compared to the control period (76% vs 81%). However, this study was impacted by the COVID-19 pandemic. AQUA also reported the ADHD could be ruled out in more cases when using the QbTest (RRR 2.14, 95% CI 1.00 to 4.59, p=0.049).
- AQUA reported **higher clinician confidence** in diagnosis in the QbTest group OR 1.77 (95% CI 1.09 to 2.89, p=0.022).

Outcomes at 1 year follow-up

- At 1-year follow up, Vogt (2011) found no difference in groups for: ADHD diagnosis changed, medication trial, continuing medication, discontinued medication and lost to follow-up.
- Vogt (2011) reported more children (37%) who were initially diagnosed with no ADHD received a revised diagnosis of ADHD at 1year in the control group (7/19). No diagnosis revisions were made in the QbTest group (0/19).

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OR: odds ratio, RRR: relative risk reduction

For further details see section 4.2.3 of the EAR including Table 10

Clinician and patient acceptability

Objective 1

QbTest (n=5)

EAG: Overall, findings were in line with process measures data; clinicians felt it increased confidence in clinical decision making, and both clinicians and families felt it may reduce the time to diagnostic decision.

- Clinicians and families felt that the test helped to improve communication. Although, some families felt that the test results were not properly explained to them and did not help them to understand symptoms or how diagnoses were made.
- Barriers to implementation included staffing, training, and technology requirements. Patients and caregivers highlighted concerns with the length and repetitive content of the test.

QbCheck (n=1)

- Brief questionnaire reported that participants found the technology easy to use.

EFSim (n=2)

- People who used the test viewed it as helpful to understand the child and improve communication with carers.

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For further details see section 4.2.4 of the EAR

Diagnostic accuracy in other technologies

EFSim Test - Single study suggested that accuracy was similar to that of the QbTest, but this was based on limited information from study at high risk of bias and no direct comparisons between tests.

Nesplora Kids – Single study also suggested that accuracy was similar to that of the QbTest, but this was based on limited information study at high risk at high risk of bias and no direct comparisons between tests.

Nesplora Adults – No suitable studies identified.

QbCheck - The single study suggested that this was at least as accurate as the in-person version of the test (QbTest), but this was study was judged at high risk of bias and the EAG warned that results should be interpreted with caution.

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AUC: area under the curve

For further details see section 4.2.2 of the EAR

Outcomes in other populations (1)

Objective 2: people referred with suspected ADHD for whom current assessment cannot reach a diagnosis?

- The EAG did not identify any studies that met inclusion criteria for this objective.

Objective 4: evaluating medication effectiveness **during long-term treatment monitoring for people with a diagnosis of ADHD?**

- The EAG did not identify any studies that met inclusion criteria for this objective.

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For further details see section 4.3 to 4.5 of the EAR

Outcomes in other populations (2)

Objective 3: evaluating medication effectiveness during initial dose titration for people with a diagnosis of ADHD?

- One DTA study was identified (Tallberg 2019). The EAG considered this at high risk of bias because the QbTest formed part of the reference standard which is likely to overestimate the accuracy of the test.
    - The study did not assess the use of the test alongside clinician judgement or compare to clinician judgement alone.
- One RCT feasibility study (QUOTA) was identified, but due to the design and small sample size the EAG concluded it was not possible to draw conclusions regarding clinical effectiveness from this study.
    - Those in the QbTest arm were more likely to have had their medication changed (type or dose of ADHD medication) at the first follow up point (10/18 vs 7/21 in control), but figures were similar at follow-up 2 (7/17 vs 9/19 in control).
- Five studies reported interview or survey data, showing healthcare staff and families mostly valued the role of the test for dose titration, checking medication utility, and improving medication adherence.

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DTA: diagnostic test accuracy; RCT: randomised controlled trial

For further details see section 4.4 of the EAR

Issues for consideration (1)

A. Data availability for the different technologies

- Limited data was available for the EFSim Test, Nesplora Kids, Nesplora Adults, QbCheck.

B. Diagnostic accuracy

- Only 1 study (AQUA) assessed a test used with clinical judgement (the assessment intervention) compared with clinical judgement alone (the assessment comparator).
  - The EAG considered that this provided no evidence of a difference in diagnostic accuracy.
  - EAG raised concerns in its risk of bias assessment of this study.
  - Trial suggests that ADHD could be ruled out in more cases when using the QbTest.

C. Data across age groups

- There was more data from studies evaluating children.
- AQUA enrolled children aged 6 to 17 years referred for their first ADHD assessment.
- Most participants (79%) were aged 6 to 12 years. The 2 groups (6 to 12 and 12 to 17) used different versions of the QbTest.

Issues for consideration (2)

D. Diagnostic process outcomes

- The AQUA trial and before-after implementation studies reported some benefits from using QbTest.
  - All the before-after studies were considered by the EAG to be at high risk of bias.
  - Some of the outcomes from AQUA were considered at high risk of bias while others were not.
  - Data split by age was only available for the number of appointments until diagnosis outcome from AQUA.
    - The 6 to 12 years subgroup showed benefit for QbTest, whereas 12+ years subgroup did not.

E. Subgroups

- Except by age (as stated above), data by subgroups stated in the scope were not reported.
  - This included people with mental health, behavioural or neurodevelopmental conditions.
- Autism has been highlighted as often co-occurring with ADHD and may make diagnosis more difficult.
  - One accuracy study (Groom et al.) reported accuracy of QbTest plus clinical judgement against a control group of people with autism spectrum disorder.
  - AQUA reported 9% of participants had a diagnosis of autism

Cost effectiveness

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Objectives

What is the cost-effectiveness of technologies that combine measures of cognition and motor activity

1. **for the diagnosis of ADHD in people referred with suspected ADHD?**
2. **for the diagnosis of ADHD in people referred with suspected ADHD for whom current assessment cannot reach a diagnosis?**
3. **in evaluating medication effectiveness during initial dose titration and treatment decisions for people with a diagnosis of ADHD?**
4. **in evaluating medication effectiveness during long-term treatment monitoring for people with a diagnosis of ADHD?**

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EAG cost-effectiveness model

- Two studies (the AQUA trial, and a report from the East Midlands AHSN) reported that implementing QbTest was cost saving and cost effective and provided a positive return on investment.
    - The EAG noted that both analysis were not clearly described.
- The EAG did not find any studies reporting cost-effectiveness models of diagnostic tests for the assessment of ADHD, so it developed a de novo decision-analytic model

Assessment strategies for ADHD diagnosis

- **Standard**: All patients receive standard assessment using current methods.
- **QbTestAll (objective 1)**: All patients are offered QbTest, along with standard assessment.
- **QbTestUnclear (objective 2; scenario analyses only):** All patients receive standard assessment, and those patients who do not receive a diagnosis after 2 appointments are offered QbTest.

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ADHD: attention deficit hyperactivity disorder; AHSN: Academic health science network

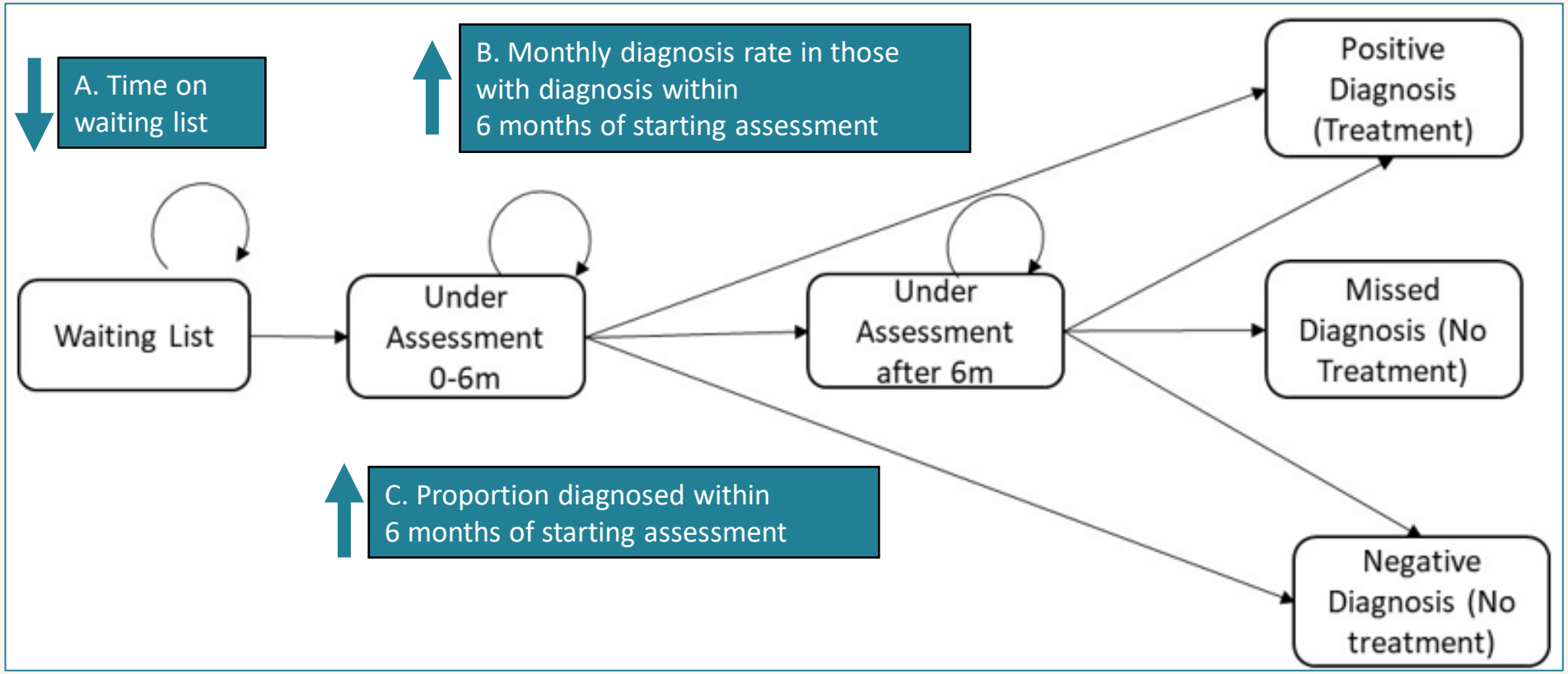
For further details see section 5.2 of the EAR

EAG's model structure

Diagnosis

Model parameters that differ when QbTest use is modelled (compared to standard assessment alone)

Arrow indicates direction of impact of adding QbTest compared to standard assessment alone



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m: months

For further details see section 5.2 of the EAR

Key model inputs and assumption

Input	Standard Ass	Source	QbTestAll	Source
A. Mean time on waiting list*	11.06 months	FOCUS + AQUA + assumption	9.36 months	FOCUS + AQUA + assumption
B. Monthly diagnosis rate in those with diagnosis within 6 months of starting assessment*	0.76	FOCUS	1.44 HR applied	AQUA
C. Proportion diagnosed (with ADHD or not) within 6 months of starting assessment*	59%	AQUA	76%	AQUA
D. Prevalence of ADHD for those diagnosed within 6 months of starting assessment	86%	AQUA	73%	AQUA

- In the base-case it was assumed that there was no impact of the QbTest on diagnostic accuracy (this was varied in scenario analyses).
- The total cost of QbTest administration was £50.86, which included the unit costs per test, as well as 30 minutes of Band 4 nurse time. This was varied for other technologies in scenario analysis.

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* Explored in scenario analysis. HR: Hazard Ratio

For further details see section 5.3 of the EAR

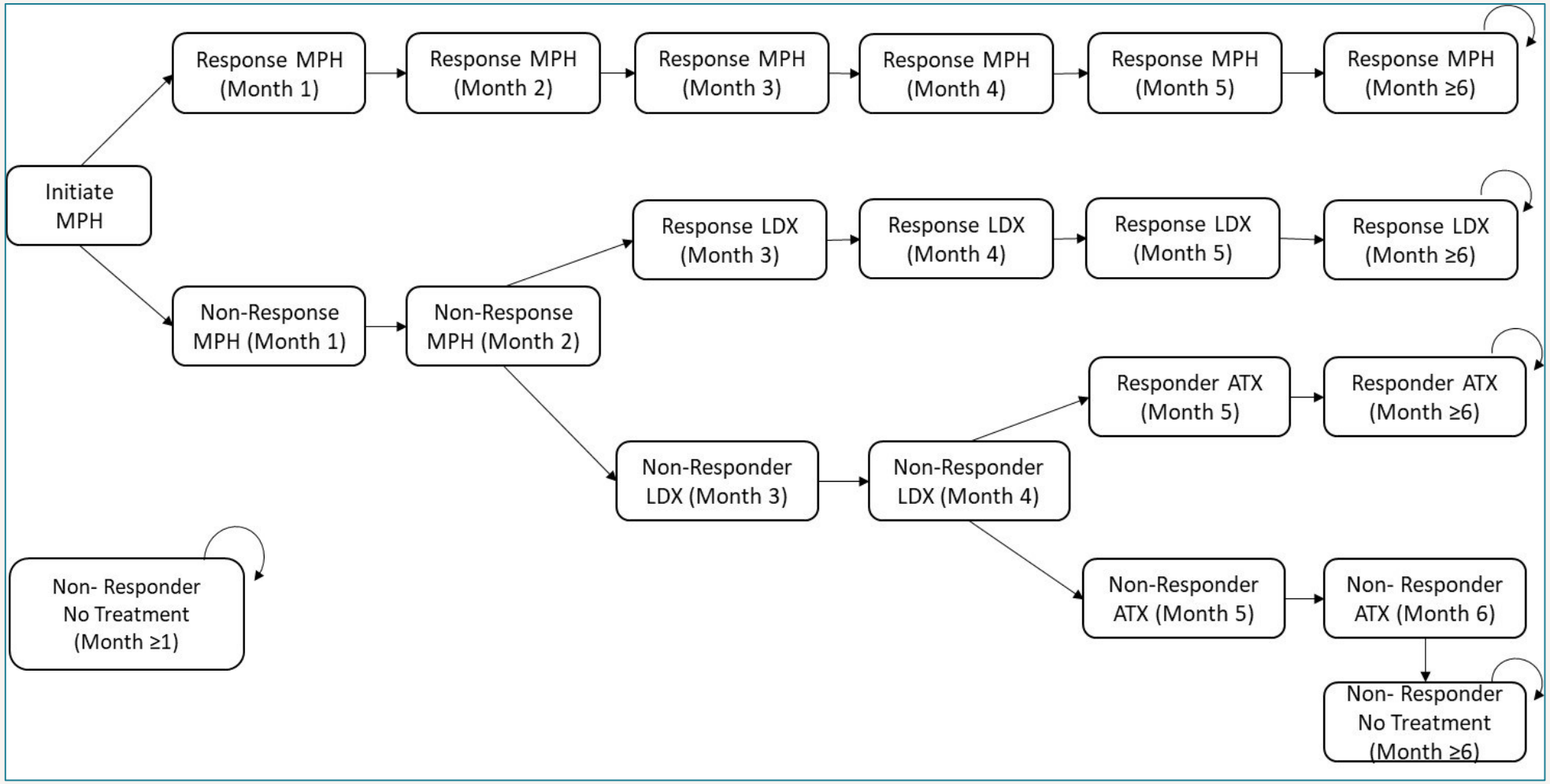
EAG's model structure

Following diagnosis for people with ADHD

Model assumes patients with an ADHD diagnosis initiate pharmacological treatment following NICE guidance.

Diagnosed ADHD (True positives)

Diagnosed No ADHD (False negatives and missed diagnosis)



NICE

MPH: Methylphenidate hydrochloride, LDX: Lisdexamfetamine mesylate, ATX: Atomoxetine

EAG's model structure

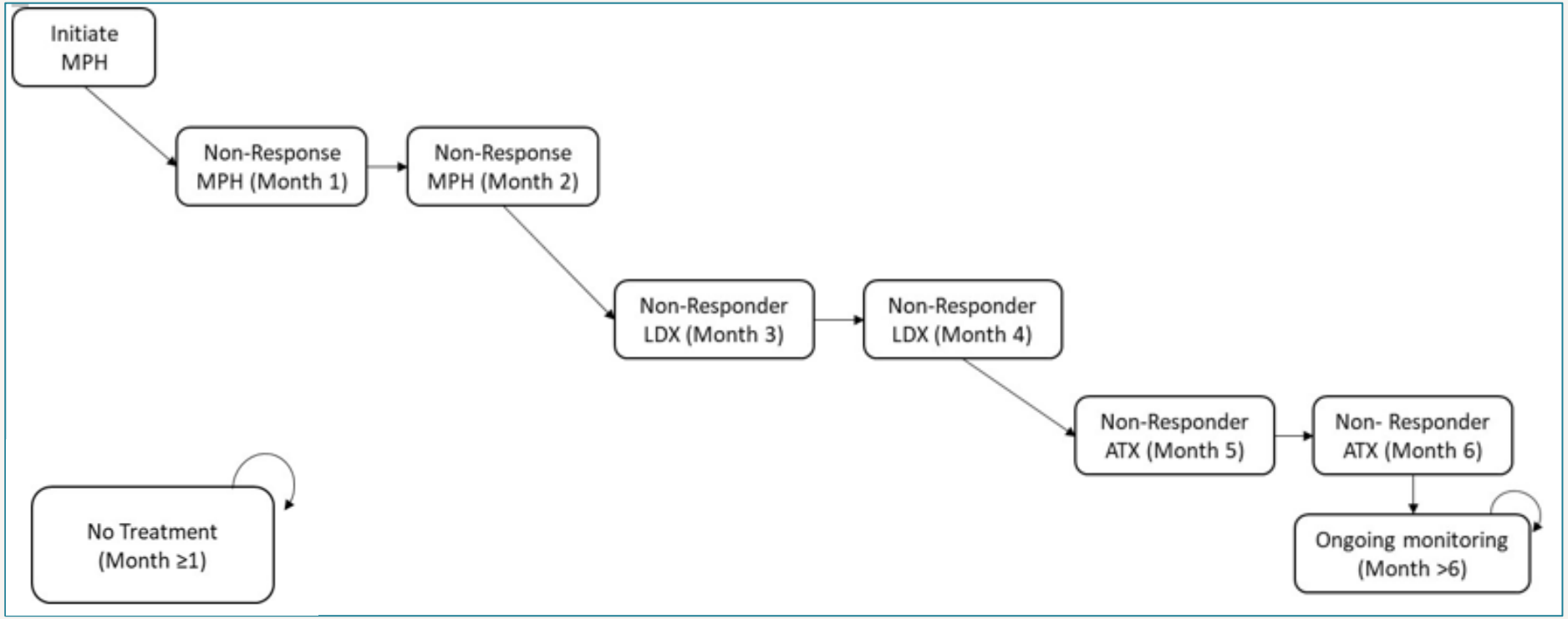
Following diagnosis for people without ADHD

Model assumes patients with an ADHD diagnosis initiate pharmacological treatment following NICE guidance.

Diagnosed ADHD (False positives)

None in base case

Diagnosed No ADHD (True negatives)



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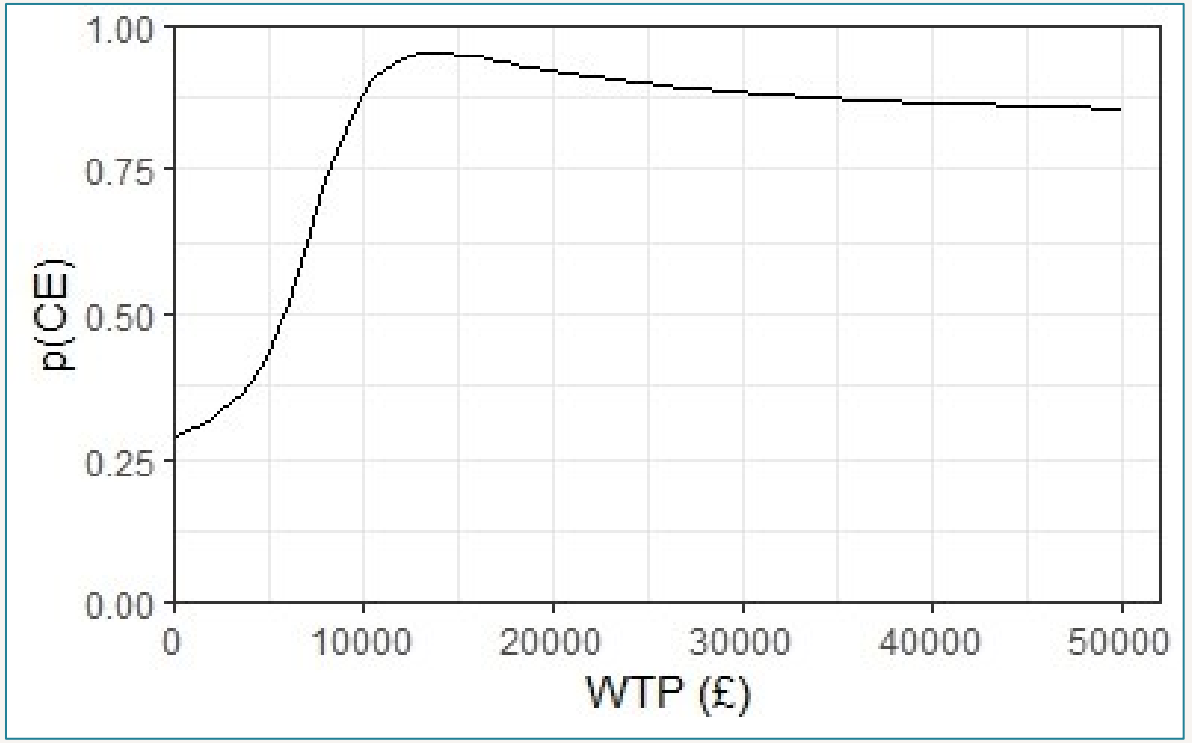
MPH: Methylphenidate hydrochloride, LDX: Lisdexamfetamine mesylate, ATX: Atomoxetine

Base case results

	Total Costs (discounted)	Total QALYs (discounted)	Incremental Costs	Incremental QALYs	ICER	Mean INB £20K WTP	Prob (CE)	Mean INB £30K WTP	Prob (CE)
Standard	£6,005	6.9083	-	-	-	-	-	-	-
QbTestAll	£6,243	6.9469	£238	0.0385	£6,184	£533	92%	£918	88%

Cost-effectiveness acceptability curve

Probability QbTestAll is cost-effective compared to Standard assessment



ICER: Incremental Cost Effectiveness Ratio; INB: Incremental Net Benefit; WTP: Willingness-to-pay; Prob(CE): Probability of being cost-effective

For further details see section 5.5.1 of the EAR

QbTestUnclear test strategy

Objective 2: diagnosis in people referred with suspected ADHD for whom current assessment cannot reach a diagnosis (QbTestUnclear)

- Due to limited data the EAG were only able to explore cost-effectiveness of QbTest used for complex cases by making a strong assumption that this would only be used for those where a diagnosis was not made in 2 appointments (including the initial appointment).
    - All patients receive standard assessment, and those patients who do not receive a diagnosis after 2 appointments are offered QbTest, the results of which are available at the 3rd appointment.

EAG: This scenario assumes no impact on diagnosis rates or other parameters than test cost, and so should be interpreted accordingly.

Proportion with unclear diagnosis	Incremental Costs	Incremental QALYs	ICER	Mean INB £20K WTP	Prob CE	Mean INB £30K WTP	Prob CE
Base case 0.0	£238	0.0385	£6,184	£533	0.922	£918	0.884
0.5	£213	0.0385	£5,531	£556	0.933	£941	0.895
0.9	£237	0.0387	£6,115	£538	0.926	£925	0.890

NICE

ICER: Incremental Cost Effectiveness Ratio; INB: Incremental Net Benefit; WTP: Willingness-to-pay; Prob(CE): Probability of being most cost-effective

For further details see section 5.5.2 of the EAR

Scenario analyses

- The EAG ran 40 scenario analyses, varying parameters relating to:
  - time waiting for an assessment
  - time from assessment to diagnosis
  - diagnostic test accuracy
  - costs
  - utilities
- Most scenarios did not have a large impact on the cost effectiveness result. In most scenarios the QbTestAll strategy remained cost effective.
- Scenarios that had a larger impact on overall results are described in the following slides.

NICE

For further details see section 5.5.2 of the EAR

Scenario analysis

Higher costs for treatment response and non-response

- In scenario analysis 5, healthcare resource use costs related to staff time for responders and non-responders to ADHD treatment were varied to higher costs per month from other studies identified: Zimovetz (2016) and King (2006).

Scenario	Responder	Non-responder
Base case (NG87)	£38.06	£76.11
5a (Zimovetz 2016)	£170.52	£325.90
5b (King 2006)*	£191.45	£285.71

NICE NG87 Guideline highlights concerns about potential bias in Zimovetz (2016) due to industry funding, and that King (2006) was based on limited clinical data.

- A higher proportion of patients initiate treatment and start treatment more quickly under QbTestAll strategy and incur these costs.

Alternative response costs	Incremental Costs	Incremental QALYs	ICER	Mean INB £20K WTP	Prob CE	Mean INB £30K WTP	Prob CE
Base case NG87	£238	0.0385	£6,184	£533	92%	£918	88%
Zimovetz 2016	£845	0.0382	£22,109	-£81	48%	£302	85%
King 2006*	£960	0.0392	£24,472	-£175.33	37%	-£216.76	80%

NICE

ICER: Incremental Cost Effectiveness Ratio; INB: Incremental Net Benefit; WTP: Willingness-to-pay; Prob(CE): Probability of being most cost-effective

*Updated to correct error in original EAR

For further details see section 5.5.2 of the EAR

Scenario analysis

Proportion who received a diagnosis within 6 months

- Scenario 15 varied the proportion of people receiving a diagnostic decision within 6 months of starting assessment when using QbTest.
  - Scenario 15a uses the lower confidence interval from AQUA. Scenario 15b uses the same proportion as standard assessment (that is, no benefit from using QbTest).

Proportion with diagnosis within 6m	Incremental Costs	Incremental QALYs	ICER	Mean INB £20K WTP	Prob CE	Mean INB £30K WTP	Prob CE
Base case (0.76)	£238	0.0385	£6,184	£533	92%	£918	88%
15a (0.689)	-£87	0.0035	**Dominates**	£157	71%	£192	62%
15b (0.598)	-£497	-0.0408	£12,198 (**SW Quadrant**)	-£318	20%	-£726	14%

NICE

ICER: Incremental Cost Effectiveness Ratio; INB: Incremental Net Benefit; WTP: Willingness-to-pay; Prob(CE): Probability of being most cost-effective

For further details see section 5.5.2 of the EAR

Scenario analysis

Diagnosis rate

The EAG modelled a scenario (2) which used different Hazard Ratios (HRs) for the rate of diagnosis for QbTestAll versus standard assessment from AQUA subgroup analysis by age.

- A lower HR (0.82) for adolescents (12 to 17 years), leads to higher costs and lower QALYs compared to the base case.

Scenario	HR
Base case (6 to 17 yrs)	1.44
2a (Children 6 to 12 yrs)	1.84
2b (Adolescents 12 to 17 yrs)	0.82

EAG: This scenario relies on all other model inputs being unchanged for adolescents, in particular the proportion who receive a diagnosis within 6 months, which is a big driver of the cost-effectiveness results (see previous slide). There were no data on proportion with a diagnosis at 6 months for the 2 age subgroups.

Alternative rate of diagnosis HR	Incremental Costs	Incremental QALYs	ICER	Mean INB £20K WTP	Prob CE	Mean INB £30K WTP	Prob CE
Base case (HR 1.44)	£238	0.0385	£6,184	£533	92%	£918	88%
2a (Children 1.84)	£242	0.0432	£5,593	£623	95%	£1,055	92%
2b (Adolescents 0.82)	£312	0.0248	£12,604	£183	65%	£431	69%

NICE

ICER: Incremental Cost Effectiveness Ratio; INB: Incremental Net Benefit; WTP: Willingness-to-pay; Prob(CE): Probability of being cost-effective

For further details see section 5.5.2 of the EAR

Scenario analysis

Proportion with no further assessment after no diagnosis within 6 months (Missed diagnosis)

Scenario 6 investigated reducing the proportion of people who do not go on to receive further assessment, if they have not received a diagnosis within 6 months.

- All 3 values in scenarios 6a to 6c make the QbTest cost-saving

Scenario	Proportion
Base case	0.82
6a	0.00
6b	0.25
6c	0.50

EAG: We have no evidence to inform the proportion without a diagnosis within 6 months who go on for further assessment.

Proportion with missed diagnosis	Incremental Costs	Incremental QALYs	ICER	Mean INB £20K WTP	Prob CE	Mean INB £30K WTP	Prob CE
Base case (0.82)	£238	0.0385	£6,184	£533	92%	£918	88%
6a (0.00)	-£676	0.0132	**Dominates**	£941	100%	£1,073	100%
6b (0.25)	-£402	0.0209	**Dominates**	£821	100%	£1,030	98%
6c (0.50)	-£121	0.0289	**Dominates**	£699	98%	£988	95%

NICE

ICER: Incremental Cost Effectiveness Ratio; INB: Incremental Net Benefit; WTP: Willingness-to-pay; Prob CE: Probability of being most cost-effective

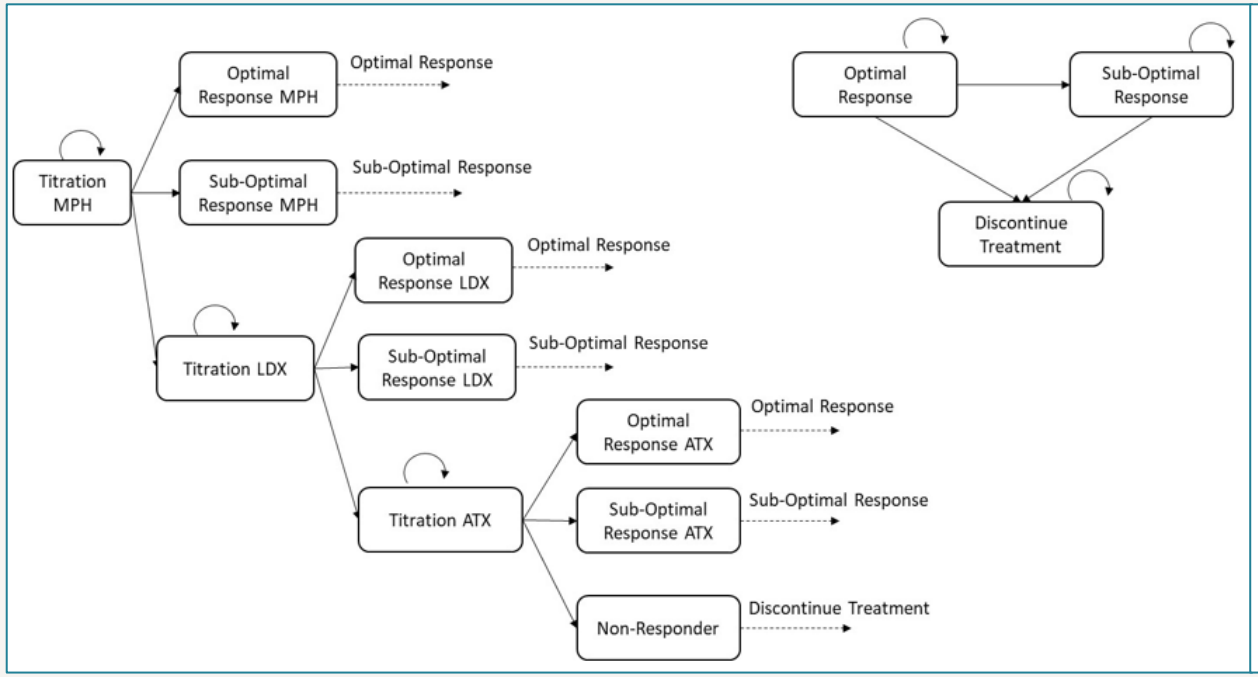
For further details see section 5.5.2 of the EAR

EAG model structure – Medication monitoring

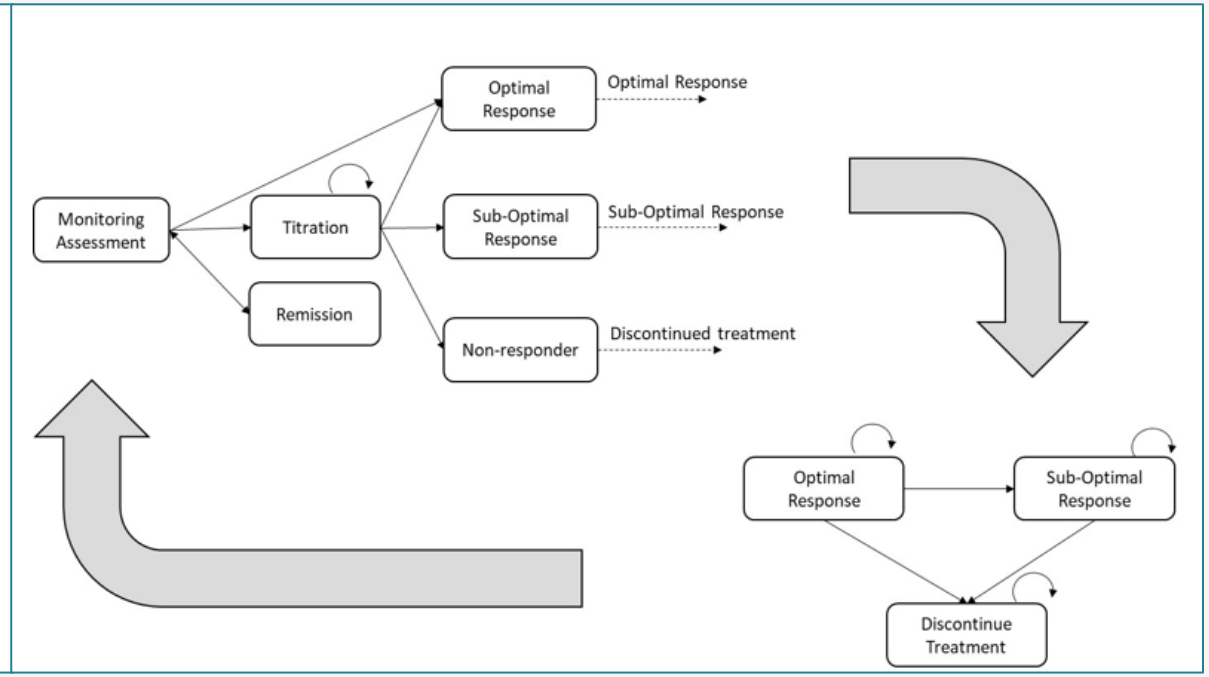
The EAG did not identify sufficient evidence to assess the populations from objectives 3 or 4

3. evaluating medication effectiveness during initial dose titration and treatment decisions for people with a diagnosis of ADHD
4. during long-term treatment monitoring for people with a diagnosis of ADHD

Proposed model structure: dose titration (objective 3)



Proposed model structure: long-term monitoring (objective 4)



Issues for consideration (1)

A. AQUA Trial

- The EAG's model largely relies on data from a single study: the AQUA trial (Hollis [2018])
  - Study assessed QbTest used for diagnosis in children and adolescents
  - No data to run model for subgroups (including people with mental health, behavioural or neurodevelopmental conditions)
  - Cost-effectiveness of other technologies was only available using the same data as QbTest, just varying technology costs.

EAG: Main analyses are only directly applicable for children and adolescents. Whether the tests perform differently in subgroups remains a key uncertainty.

B. Children and adolescents

- Limited data from AQUA were available split for younger children (6 to 12 years) and adolescents (12 to 17)
  - Rate of diagnosis for those with a diagnosis within 6 months was the only parameter varied.
  - QbTest use in adolescents appeared less cost-effective

EAG: Limited data from the AQUA trial suggested that effects on time to diagnosis may be greatest in younger children (age 6 to 12) than in adolescents

Issues for consideration (2)

C. Key parameter uncertainties

- QbTest was cost effective in most scenario analyses, except when:
  - higher costs for responders / non-responders on treatment used,
  - no increase in QbTest impact on proportion who receive a diagnosis within 6 months

D. Testing for people for whom standard assessment cannot reach a diagnostic decision (objective 2)

- Scenario analyses, using strong assumptions, had slightly higher net benefit than the base case.

E. Uncertainty of the cost-effectiveness of technologies in the evaluation of treatment effectiveness

- Due to a lack of data, no cost effectiveness estimates were produced.

F. Potential impacts of technologies that are not captured in the model

- Impact on the number of diagnostic decision appeals and repeat assessments.
- Impact on the availability of ADHD medications.
- Any benefits on educational attainment, forming and maintaining relationships, self-esteem, and wide-ranging long-term outcomes including social function, education, criminality, alcohol use, substance use, and occupational outcomes.

NICE National Institute for Health and Care Excellence

Thank you

Patient Group Submission Template for Diagnostic Technologies

NICE
Health Technology Assessment (HTA) on

Qb test for the assessment of attention deficit hyperactivity disorder (ADHD)

Please read the accompanying guide fully before completing this submission template.

Information about your organisation	
Organisation name	The National Network of Parent Carer Forums CIC
Contact person's name	Jo Harrison
Role or job title	Director and East of England Representative
Email	eastofengland@nnpcf.org.uk
Telephone	XXXXXXXXXX
Postal address	124-128 City Road, London, EC1V 2NX
Organisation type	Patient/carer organisation (e.g. a registered charity) x Informal self-help group Unincorporated organisation Other, please state:
Organisation purpose (tick all that apply)	Advocacy x Education x Campaigning Service provider Research Other, please specify:
What is the membership of your organisation (number and type of members, region that your group represents, demographics, etc)? 130,000 members covering the whole of England, we work with DfE, DHSC, NHSE and other organisations. We are a pan disability organisation that represents parent carers. We are a community interest company and as such we cannot campaign.	

Patient Group Submission Template for Diagnostic Technologies

Please look at our website www.nnpcf.org.uk

Declarations	
Do you have any conflicts of interest? No	
Did anyone outside your organisation help you prepare this submission?	No
If yes – who helped you and in what way? Please tell us if the people helping you were paid and if they have any conflicts of interest. **NA**	
Are you willing for this submission to be shared on our website?	Yes (but please omit telephone number)
We may invite you to a scoping meeting where this technology is to be discussed. Would a member of your group be willing to join such a meeting (this may be in person or virtually)?	Yes - already listed as a stakeholder and attended workshop 30/10/23

Patient Group Submission Template for Diagnostic Technologies

Impact of the symptoms, condition or disease on patients

1. How do symptoms and/or the condition or disease affect patients' lives or experiences?

ADHD impact on children and young people is vast.

Inattention, can mean that detail-oriented tasks, can be difficult, which can lead to mistakes, or admission of information in tasks, which can impact on a child and young person's ability to engage and at times succeed in education, without the right support and this will also follow through to adulthood and employment,

Hyperactivity and impulsivity can impact on a child being able to engage in learning through typical classroom environments and will often need support to remain "on task", will need to be supported with movement breaks, due to inability to sit still for period of time/duration of a typical lesson. Movement may often appear inappropriate and not age related, with the need to run or climb. Language and communication skills may be impacted, with talking to much, overtaking, blurting out responses, unable to take age related turn-taking roles conversations.

Difficulties with task focus, organisation skills, time keeping can not only impact not on education and employment but with simple day to day tasks such as engaging in play, sports and social activities, household tasks such as tidying a bedroom, helping with chores, hygiene and self-management, learning to manage finances.

Sleep can also be impacted, as can a person's mental wellbeing.

All the above can impact a child and young person, and if they are not provided with the right support at the right time, can impact on their ability to achieve their full potential within education, increase the risk of school exclusions, make them more vulnerable to crimes and gangs of which will impact on a young person's transition into adulthood to reaching their full potential.

Impact of the symptoms, condition or disease on family and carers

2. How do symptoms and/or the condition or disease affect carers/unpaid care-givers and family?

Families are impacted on a day-to-day basis. Families are not always able to timely access the right information and support to enable them to better understand and support their child and young person.

Many Parent/Carers will face having to work reduces hours, or give up work to manage their child's needs, especially where the right support in education is not provided and a lack of social care and mental wellbeing care is provided. When in employment parents and carers will often need to prioritise their caring responsibilities over work, and this can often be a short notice, which can be problematic for employers.

This increased the number of families who become reliant on benefits, live in poverty and struggle with debt. This can also impact on housing.

The impact on siblings of a child with ASHD, can be far reaching, as rhey to will have to learn to manage the behaviours and needs of their siblings, may finer it more difficult to engage in play, turn taking and communication with their sibling., The increase needs of their sibling, may also mean parent and carers time can often be prioritised with the needs of sibling. This can all impact on the siblings own wellbeing,

Experiences and availability of current diagnostic technologies

3. What role do currently available diagnostic technologies play in helping patients manage their symptoms and/or the condition or disease?

The QB test, for some allows a quicker more efficient diagnostic process.

The QB test is not routinely used by all ICBs and commissioned providers for the assessment and diagnostic process.

Whilst some child and young people, find the assessment process manageable, it has been reported than some children find the process overwhelming which can impact on the efficiency of the test.

A diagnosis or a greater understanding of need, where a diagnosis it not provided, allows, the professionals, families and importantly the child or young person to better understand their strengths and needs and aid them in accessing the right support. If technology can support this to be done quicker then a manual

assessment, where deems appropriate, it improves more timely access to support for children and young people.

4. What unmet information needs do people currently have due to the lack of an available diagnostic technology for their symptom or condition?

A lack of diagnosis can be a barrier for support. A digital offer than allows for more efficient identification of need.

Currently long waiting lists are a barrier to access early intervention. Child and young person misses school/college/work and this has other implications and includes mental health and self-esteem. If a Child or young person in not able to engage in a meaningful way in their community, this will also impact on the family's overall wellbeing and ability to work as mentioned in Q2.

Patient Group Submission Template for Diagnostic Technologies

About the diagnostic technology being assessed

5. What are the most important things people would like to gain from the information provided by, and/or the use of, the diagnostic technology being assessed?

Children and young people, families, and professionals to have a better understanding of need.

The ability for the child and young person to be able to identify, understand, manage their needs and to be able to develop and celebrate their strengths, leading to independence and a successful transition to adulthood and being able to reach their full potential.

6. For those people with experience of this diagnostic technology, what difference did the information provided by, and/or the use of, the technology make in their lives or the lives of family and carers?

Increased understanding of need, ability to empower families to have a better understanding of their child and young person and who to support them.

Improved wellbeing of families, when the technology leads to the child and young person to be able to access the right support.

That said, some families reported higher anxieties in the child and your person in the lead up to and directly after the use of the assessment technology. Good Quality information to empower children and young people and their families is needed in order to reduce these anxieties.

7. For those without experience of this diagnostic technology, but who are aware of studies or other sources of evidence of value, what are the expectations/limitations of having the information provided by the diagnostic technology and/or using the diagnostic technology?

As previously referenced the QB Test is not currently routinely accessible by all families, due to commissioning arrangements at "place".

Some families will prefer historical assessment processes as they have more confidence in the process.

For some children and young people, the digital assessment process is efficient and well met, for others it can be overwhelming.

Families may feel frustrated if they cannot access.

Confidence in the process, needs to be managed, especially where assessments are borderline, and a re-assessment is provided.

Some families, feel concerned that the assessment will not allow for a complete understanding if their child and could lead to a diagnosis not being provided.

It is important that the children, young people and their families are given sufficient information in a clear and accessible manager to ensure they understand the digital assessment and enable them to have confidence in the process.

Additional information

8. Please include any additional information you believe would be helpful in assessing the value of the diagnostic technology (e.g. equality issues, ethical or social issues and/or socio-economic considerations).

We need to ensure that those who accessing the QB Test are able to engage in the process effectively and the any co-morbidities such as a learning disability does create an inequality which would impact unfairly on the outcome of the assessment.

We also need to be mindful of digital poverty and any basic digital understanding that would be required to access a digital assessment, that again should the child or young person not have create an unfair disadvantage.

Patient Group Submission Template for Diagnostic Technologies

Key messages

9. In up to five statements please list the most important points of your submission.

The digital assessment should not unfairly disadvantage any person and Alternative methods of assessment should still be considered where appropriate.

It is important that the technology will enable quicker and more efficient diagnosis to enable access to support.

Clear and accessible information must be provided to children young people and their families regarding the digital assessment process and the outcome of the assessment clearly explained.

Following assessment children young people and their families, must be provided access to the right support that meets their needs.

Clinical and cost effectiveness of technologies for the assessment of attention deficit hyperactivity disorder: a systematic review and economic model

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Declared competing interests of the authors

None of the authors have any competing interests.

Rider on responsibility for report

The views expressed in this report are those of the authors and not necessarily those of the NIHR Evidence Synthesis Programme. Any errors are the responsibility of the authors.

Keywords

Systematic Review
Economic Model

Summary of changes made to the report following the consultation process prior to the 1st diagnostic assessment committee meeting

Section/Location	Change made
Scientific summary, Results section, Objective 1 sub-section, last para	Added "at £20,000/QALY" for clarification.
Section 5.3.8, sub-section "Costs relating to use of the technologies", end of sub-section	We have added more detail on the costs of Nesplora AULA and EFSim, and described 2 additional scenario analyses. We also added text to highlight that the scenarios using the costs for Nesplora AULA and EFSim should not be interpreted as cost-effectiveness analyses of those technologies.
Table 19, columns 5 and 6	Costs have been corrected
Section 5.3.10, subsection "Utilities for ADHD patients who do and do not respond to treatment", end of sub-section	Added sentence to explain an additional scenario analysis on utilities for responders and non-responders
Table 27, Scenario 4	Added scenarios 4(e) and 4(f) using costs for Nesplora AULA and EFSim provided by the companies.
Table 27, Scenario 5	Corrected costs for responders and non-responders
Table 27, Scenario 17	New scenario added to explore assumptions on utilities, as requested by consultation comments
Section 5.5.2, subsection "Results Scenarios relating to diagnostic test accuracy", 2nd para	Added text to give more explanation of the results from Scenario 6, as requested by the NICE technical team
Section 5.5.2, subsection "Scenarios relating to costs", 2nd para	Corrected text describing results for scenario 5b with corrected costs for responders and non-responders
Section 5.5.2, subsection "Scenarios relating to utilities", 1st para	Added a paragraph describing the results from the new scenario 17 exploring different assumptions on the utilities for responders and non-responders (or not on treatment)
Table 31, Scenarios 4(e) and 4(f)	Added rows with results for additional scenarios 4(e) and 4(f)
Table 31, Scenario 5(b)	Corrected results for scenario 5(b) with corrected costs for responders and non-responders
Table 31, Scenarios 17(a), 17(b), and 17(c)	Added rows with results for additional scenarios 17(a), 17(b) and 17(c)

Table 35, entry for "Fernandez-Martin PR-H, Rocio Canovas, Rosa Diaz-Orueta, Unai Martinez de Salazar, Alma Flores, Pilar. Data-driven profiles of attention-deficit/hyperactivity disorder using objective and ecological measures of attention, distractibility, and hyperactivity. European child & adolescent psychiatry 2023[Epub ahead of print]"	Reason for exclusion has been corrected to "Does not report on one of the outcomes of interest"

Abstract

Background

Attention Deficit Hyperactivity Disorder (ADHD), is characterized by inattention, impulsivity, and hyperactivity. Diagnosis is complex and time consuming. Medication requires careful selection and dose titration. Technologies for objective measures of ADHD that use motion sensors to measure hyperactivity (“sensor CPT”) may help improve the diagnostic process and medication management, when used in addition to clinical assessment.

Objective

To determine whether sensor CPT are clinically and cost-effective to the NHS. Specific objectives were to determine the effectiveness of sensor CPT for:

1. Diagnosis of ADHD in people referred with suspected ADHD

2. Diagnosis of ADHD in people referred with suspected ADHD for whom current assessment cannot reach a diagnosis

3. During initial dose titration and treatment decisions for people with ADHD

4. Evaluating treatment effectiveness during long-term treatment monitoring for people with ADHD

Design

Systematic review and economic model.

Results

Objective 1 (29 studies – 25 QbTest, 2 EF Sim, 2 Nesplora Kids): Most evidence was in children. The AQUA trial was the only study to evaluate the QbTest in combination with clinical assessment and included a comparison with clinical assessment alone. Accuracy was similar (p=0.14), but the study was at high risk of bias. The AQUA trial reported that adding QbTest to the diagnostic process resulted in fewer appointments to reach a diagnosis, reduced consultation time, greater clinician confidence, and exclusion of the diagnosis in a more children. Findings were supported by limited data from uncontrolled before-after studies. Qualitative and survey data reported increased clinician confidence in clinical decision making, reduced time to diagnostic decision and improved communication. Barriers to implementation included staffing, training, technology requirements, and length and repetitive content of the test. We found QbTest in addition to clinical assessment was likely cost-effective due to reduced time waiting for assessment, reduced appointments until diagnosis, and a higher proportion receiving treatment benefits.

Objective 3 (6 studies): All evaluated QbTest and most had quality concerns. Qualitative and survey data suggested that healthcare staff and families valued the QbTest for dose titration, checking medication utility, and improving medication adherence. Some data suggested that results may not increase patient understanding and some clinicians highlighted logistical challenges.

No studies were identified for objectives 2 and 4.

Conclusions

Our results suggest that QbTesting as part of the diagnostic work-up for ADHD in children (age <18 years), when used in combination with clinical assessment, is cost-effective. This finding was robust to assumptions made in the model. There are insufficient data on other sensor CPT, in adults or on medication management.

Future work

- Diagnostic accuracy study evaluating comparing each of the sensor CPT plus clinical assessment. This should consider accuracy across different patient subgroups.
- Trial comparing patient outcomes and process measures in adults and children tested with and without sensor CPT with separate analyses for difficult to diagnose patients
- Trial evaluating the role of sensor CPT in medication management, including long-term follow-up

Limitations

Lack of good quality data on all tests, both for diagnosis and medication management, particularly when evaluated in combination with clinical information

Study registration

The protocol was registered on the PROSPERO database (CRD42023482963).

Funding details

This report was commissioned by the NIHR Evidence Synthesis Programme as project number NIHR136009.

Word count: 500 words

Scientific Summary

Background

Attention Deficit Hyperactivity Disorder (ADHD), is a neurodevelopmental disorder characterized by persistent patterns of inattention, impulsivity, and hyperactivity that can significantly impact daily functioning.

Diagnosis of ADHD is complex and relies on a clinician's judgment combined with information such as questionnaires, third-party reports, patient history, and behavioural observations. ADHD is frequently associated with other neurodevelopmental and psychiatric conditions, which can complicate the diagnosis and management of ADHD. It usually takes an average of 2 to 3 appointments and around 2.5 hours of clinic time to reach a diagnosis of ADHD. NHS waiting times for ADHD assessment are long, with patients often waiting more than 2 years. One treatment option for ADHD is medication. Identifying the most suitable medication and dose for a particular patient can be challenging.

A number of rating scales and tests are available to help diagnose ADHD, but none have sufficient accuracy to be used as a stand-alone diagnostic tool. There are a number of technologies for objective measures of ADHD that use motion sensors to measure hyperactivity (referred to as "sensor CPT"). These may help to improve the diagnostic process for people with ADHD and to improve medication management, when used in addition to standard clinical assessment.

Objectives

The overall aim of this project was to determine whether sensor CPT are clinically and cost-effective to the NHS.

Objective 1: What is the diagnostic accuracy and clinical- and cost-effectiveness of sensor CPT for the diagnosis of ADHD in people referred with suspected ADHD?

Objective 2: What is the diagnostic accuracy and clinical- and cost-effectiveness of sensor CPT for the diagnosis of ADHD in people referred with suspected ADHD for whom current assessment cannot reach a diagnosis?

Objective 3: What is the clinical- and cost-effectiveness of sensor CPT in evaluating medication effectiveness during initial dose titration and treatment decisions for people with a diagnosis of ADHD?

Objective 4: What is the clinical and cost-effectiveness of sensor-based CPT for evaluating treatment effectiveness during long-term treatment monitoring for people with a diagnosis of ADHD?

Methods

Clinical effectiveness review

A systematic review was conducted. Studies that evaluated the QbMini, QbTest (6-12 and 12-60), QbCheck, EF Sim, EF Sim Web Version, Nesplora Kids and Nesplora adults, alone or in combination with clinical assessment for ADHD, were eligible for inclusion. We included

randomised controlled trials (RCTs), non-randomised studies of interventions including before-after studies (NRSI), diagnostic test accuracy (DTA) studies, surveys and qualitative evaluations that reported on eligible outcomes.

Four databases and two trial registries were searched. We screened trial registries, reference lists of reviews and study reports, relevant websites and information submitted by test manufacturers.

Title and abstract screening were conducted by two reviewers independently. Inclusion assessment, data extraction, and risk of bias assessment were performed by one reviewer and checked by a second. Risk of bias was assessed with the following tools: RoB 2 (RCTs), ROBINS-I (NRSI), QUADAS-2 (DTA studies), CASP checklist (qualitative studies), Q-SSP (survey studies).

For each objective, we provided a narrative summary of study details, risk of bias, and results. Random and fixed effects meta-analysis was performed to generate summary effect estimates. Forest plots were produced to show individual and summary effect estimates with 95% confidence intervals (CIs). Fisher's exact test was used to compare estimates of accuracy where studies evaluated multiple index tests. Qualitative evidence was synthesised based on guidance from Joanna Briggs Institute.

Cost effectiveness model

We developed a *de novo* model for sensor CPTs for the diagnosis of ADHD in people referred with suspected ADHD. We only evaluated the QbTest in addition to clinical assessment vs clinical assessment alone for children and adolescents, due to lack of evidence on the inputs needed for our model for other sensor CPTs and populations. A Markov model structure was used to capture the process of waiting for assessment, assessment, diagnosis and treatment. We populated the model using evidence identified in the clinical effectiveness review, a review of cost-effectiveness studies of diagnostic tests and models of treatment for ADHD, and further targeted searches as required.

Results

Objective 1

We included 29 studies (38 reports) for objective 1: two RCTs (one of these also provided data on accuracy; both included a survey and qualitative sub-study), 20 DTA studies (two included a survey of patient views), five uncontrolled before-after implementation studies (2 also provided information on patient/clinician views – 1 survey and qualitative evaluation, 1 survey) and two studies that only reported on patient and clinicians acceptability of sensor CPTs. Most studies evaluated the QbTest, two evaluated EF Sim and two evaluated Nesplora Kids; there were no studies of EF Sim web or of Nesplora Adults. The majority of the evidence was in children.

Five studies evaluated the accuracy of the QbTest in combination with clinical information, only one of these (the AQUA trial) evaluated the accuracy in combination with clinical judgement, as would be used in practice. However, data from the AQUA trial were limited due to inclusion of only those who had a diagnostic decision at 6 months and limitations

with the reference standard. There is therefore no reliable data on the accuracy of any of the sensor CPTs when used in combination with clinical judgement.

Estimates of the accuracy of the sensor CPTs alone were heterogeneous, and so results should be interpreted with caution. Summary estimates of the accuracy of the QbTest suggested that sensitivity was highest when the sub-components were combined into an overall measure (summary sensitivity 79%, 95% CI 69, 86%) but specificity was lower (summary specificity 59%, 95% CI 42, 74%) than when sub-categories were assessed individually. There was little evidence of a difference between the accuracy of the three sub-categories of activity, impulsivity and inattention. One study of Nesplora Kids and two studies of EF Sim reported similar estimates of accuracy to studies of the QbTest, but this was based on very limited information from studies at high risk of bias.

Three studies provided a direct comparison between sensor CPT and non-sensor CPT, one study (the AQUA trial) provided a direct comparison between clinical diagnosis combined with QbTest with the accuracy of clinical diagnosis alone, and one compared the accuracy of the QbTest alone to the accuracy of QbTest plus clinical information. One study reported that an overall measure from EF-Sim was more sensitive than the non-sensor CPT omission errors measure (p=0.03), but was less specific (p=0.07). There was no difference between the overall EF Sim measure and the other two CPT measures. Two studies provided a direct comparison between the Conners' CPT II and the QbTest (12-60). One reported that Qb measures were more sensitive ($p \leqslant 0.01$) but less specific than the two Conners' CPT measures, whilst the other reported that the QbTest was less sensitive (p<0.01) with no difference in specificity. The AQUA trial compared QbTest plus clinical judgement to a control group using the standard diagnostic process. The two groups had very similar specificity but sensitivity was slightly higher in the clinical diagnosis alone group (96%, 95% CI 87 to 100) compared to the group where diagnosis incorporated the QbTest (86%, 95% CI 72 to 95), but there was no statistical evidence of a difference between groups (p = 0.14). One study in older adults presented a comparison between models based on the QbTest alone and a model that incorporated a clinical measure of ADHD symptoms. The model that incorporated the clinical information was much more sensitive (91%, 95% CI 83, 96) than the QbTest alone (56%, 95% CI 45, 66; p<0.01)). There was no evidence for a difference in specificity (p=0.11).

Five studies evaluated the impact of the QbTest on process measures. All were conducted in the UK and were restricted to children and adolescents. The AQUA trial randomised children to be assessed for ADHD with or without the QbTest as part of the diagnostic process. This study was judged at high risk of bias for time-to-event outcomes as a large proportion of participants (80/250) were uninformatively censored from the analysis as they dropped out or were discharged from the clinic and so did not have a diagnosis at 6 months. It was at low risk of bias for other outcomes, except cost of clinic appointments which was judged at unclear risk. The other four studies were retrospective record reviews, where data for those evaluated for ADHD prior to implementation of the QbTest were compared to data for those evaluated after the implementation of the QbTest. The largest of these studies, Focus ADHD, was affected by the Covid-19 pandemic as the QbTest was implemented over the same period as the pandemic. All four studies were judged at serious risk of bias; none adjusted for potential confounding factors. The AQUA trial reported a number of benefits

associated with adding QbTest to the diagnostic process including fewer appointments to reach a diagnosis, reduced consultation time, increased proportion of patients with a diagnosis, greater clinician confidence in the diagnostic decision, and exclusion of the diagnosis in a greater proportion of children. They also reported that cost of clinic appointments were less in the QbTest arm compared to the control arm. Limited data from the before-after studies found that following implementation of the QbTest fewer consultations were required to reach a diagnosis. These studies also reported other benefits included reduced time to reach a diagnosis (two studies), and reduced costs of testing.

Eight studies provided data on clinician and/or patient and carer views of sensor CPTs for the diagnosis of ADHD. Most of the studies were judged to have some methodological concerns due to a lack of detail reported on the methodology used. Five evaluated the QbTest through interviews, surveys or focus groups. These reported that clinicians felt the test increased confidence in clinical decision making, and both clinicians and families felt it may reduce the time to diagnostic decision. Clinicians and families also felt that the test helped to improve communication. Although, some families felt that the test results were not properly explained to them and did not help them to understand symptoms or how diagnoses were made. Barriers to implementation included staffing, training, and technology requirements. Patients and caregivers highlighted concerns with the length and repetitive content of the test, and staff in one study reported that patients struggled with sensory discomfort and stress during the test. One study of QbCheck reported that participants found it easy to use, however this was from a brief 3-question survey conducted as part of a DTA study. Two survey studies evaluated EF Sim. One of these, funded by the test manufacturer, reported positive findings concerning acceptability for teachers and psychologists who had implemented the test. The other study also reported positive acceptability from a short survey to children who had used the test in a DTA study.

We found that QbTest in addition to clinical assessment is likely to be cost-effective, with incremental costs of £238.35 and incremental QALYs of 0.0385 per person evaluated for ADHD. The resulting incremental cost-effectiveness ratio (ICER) is £6183 per QALY gained, which is cost-effective at a willingness to pay (WTP) threshold of £20,000 per QALY. The mean incremental net benefit (probability of being cost-effective) is £532.55 (92%) and £918 (84%) at WTP of £20,000 and £30,000 per QALY, respectively. These findings were driven by reduced time waiting for assessment, reduced appointments until diagnosis, and a higher proportion receiving a diagnosis so that more patients with ADHD receive treatment benefits.

We found that our overall conclusions were robust to most of our modelling assumptions. However, if the state costs for responders / non-responders on treatment were assumed to be higher, then QbTest in addition to clinical assessment would not be cost-effective at £20,000/QALY, due to the higher proportion who initiate treatment and incur the higher costs. Also, if the proportion of patients with a diagnosis within 6 months for QbTest in addition to clinical assessment is lower (closer to that for clinical assessment alone), then QbTest in addition to clinical assessment becomes cost-saving but also incurs lower or even

less QALYs than clinical assessment alone. In this scenario, the cost savings do not justify the quality of life reductions.

Objective 2

We did not identify studies that met inclusion for objective 2. We ran some exploratory analyses which demonstrated that if there are no consequences in terms of diagnostic accuracy then using sensor CPTs on the subset of those where a diagnosis is not reached after 1 or 2 appointments would be more cost-effective than using sensor CPTs on all patients, because the test cost is incurred for only some patients.

Objective 3

Six studies were included for objective 3; all evaluated the QbTest. One DTA study evaluated the accuracy of QbTest as part of dose titration against the reference standard of "good outcome" at 1-year follow-up. However, the QbTest formed part of the reference standard which is likely to overestimate the accuracy of the test and so it is not possible to draw strong conclusions from this study.

One study (the QUOTA trial) provided data on process measures, however it was a small feasibility trial that was not designed and powered to formally evaluate the impact on outcomes. Three RCTs (the AQUA trial and two feasibility RCTs: FACT and QUOTA) and two implementation studies provided interview or survey data on patient and clinician views of the QbTest for medication management and dose titration. Most of the studies had concerns regarding quality due to lack of information on study design. Findings suggested that healthcare staff and families mostly valued the role of the test for dose titration, checking medication utility, and improving medication adherence. However, two surveys of patients suggested that the results of the QbTest may not have helped them to understand medication decisions, and some clinicians highlighted that using the QbTest for medication management can present logistical challenges due to having to schedule more appointments.

Objective 4

We did not identify any studies that met inclusion for objective 4.

There was insufficient evidence on model inputs to be able to evaluate cost-effectiveness for objectives 3 or 4.

Conclusions

There was a lack of good quality data on all tests, both for diagnosis and medication management, particularly when evaluated in combination with clinical information. Our results suggest that QbTesting as part of the diagnostic work-up for ADHD in children (age <18 years), when used in combination with clinical assessment, is cost-effective. We found this finding was robust to nearly all assumptions made in the model. There are insufficient data on other sensor CPT, in adults or on medication management.

There are a number of areas where further work is required:

- Diagnostic accuracy study evaluating comparing each of the sensor CPT plus clinical assessment. This should consider accuracy across different patient subgroups.
- Trial comparing patient outcomes and process measures in adults and children tested with and without sensor CPT with separate analyses for difficult to diagnose patients
- Trial evaluating the role of sensor CPT in medication management, including long-term follow-up

Study registration

The review was registered at PROSPERO (CRD42023482963).

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Plain English Summary

What is the problem?

Attention deficit hyperactivity disorder (ADHD) is a common condition that affects behaviour in both children and adults. People with ADHD may find it hard to concentrate, act without thinking and be unable to sit still. This can get in the way of daily life.

ADHD is usually diagnosed by a specialist (an expert in ADHD) based on the person's history, behaviour and symptoms. The expert will typically observe the person and interview the person and others in their life (e.g. partners, parents or teachers).

It can take a long time to be diagnosed with ADHD and the person may have to go to lots of appointments. ADHD is also sometimes confused with mental health conditions that have similar symptoms, making it harder to diagnose.

Tests have been developed that may improve how ADHD is diagnosed and followed up. These tests involve the person doing a computer-based task which measures behaviours associated with ADHD (e.g. ability to concentrate and to control movement) and include the use of sensors to track movement. These tests may reduce the number of appointments needed and could increase the likelihood of diagnosing ADHD correctly. They might also be able to help work out if treatments are working properly.

What did we do?

We wanted to know whether using these new tests to help diagnose ADHD will mean that more people are correctly told whether or not they have ADHD, whether these tests help diagnose ADHD faster, and whether the tests can be used to correctly tell us how well ADHD treatments work. We also wanted to know whether these tests are a good use of NHS money. We looked at existing research and developed cost models to answer these questions.

What did we find?

We found very limited good quality data. Our findings suggest that using QbTest is likely to help diagnose ADHD more quickly, using fewer appointments, and may allow a diagnosis to be made in more people. It is likely to represent a good use of NHS money.

Word count: 342words

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Definition of Terms and List of Abbreviations

Term	Definition
AE	Adverse Event
AHSN	Academic Health Science Network
AQ-10	Autism Spectrum Quotient-10
ASD	Autism spectrum disorders
ASRS	ADHD symptom rating scale (Swedish version)
ASEBA	Achenbach System of Empirically Based Assessment
ATX	Atomoxetine
AUC ROC	Area Under the Receiver Operating Characteristics Curve
BNF	British National Formulary
CAARS-E	Conners Adult ADHD Rating Scale
CAARS-S:L	Conners' Adult ADHD Rating Scale (German version)
CAMHS	Children and Adolescent Mental Health Services
CAP	Child and Adolescent Psychiatry
CASP	Critical Appraisal Skills Programme
CEA	Cost-Effectiveness Analysis
CGAS	Children's Global Assessment Scale
CGI-S	Clinical Global Impression Severity Scale
CI	Confidence interval
CINAHL	Cumulative Index Nursing and Allied Health Literature
CPI	Consumer Price Inflation
CPT	Continuous Performance Tests
CRD	Centre for Reviews and Dissemination
DAC	Diagnostics Advisory Committee
DAR	Diagnostics Assessment Report
DCD	Developmental coordination disorder
DEX	Dexamfetaminesulphate
DIVA	Diagnostic Interview for ADHD in Adults
DSM-4	Diagnostic and statistical manual of mental disorders, fourth edition
DSM-4-TR	Diagnostic and statistical manual of mental disorders, fourth edition, text revision
DSM-5	Diagnostic and statistical manual of mental disorders, fifth edition
DTA	Diagnostic test accuracy
EAG	Evidence Assessment Group
EMA	European Medicines Agency
EPR	Electronic patient records
EQ-5D	EuroQol 5 dimensions
EQA	External Quality Assessment
FBB-ADHS-V	Fremdbeurteilungsbogen für Vorschüler mit Aufmerksamkeits- und Hyperaktivitätsstörungen
FN	False Negative
FP	False Positive
FU	Follow-up
GBP	Great Britain Pound
GDS	Gordon's diagnostic system

Term	Definition
GP	General Practitioner
GXR	Guanfacine Extended-Release
HCP	Healthcare Professional
HR	Hazard Ratio
HRQoL	Health Related Quality of Life
HTA	Health Technology Assessment
ICD	International Classification of Diseases
ICER	Incremental Cost-Effectiveness Rario
ICTRP	International Clinical Trials Registry Platform
INB	Incremental net benefit
IQ	Intelligence quotient
IQR	Interquartile range
IR	Immediate release
IRR	Incidence Rate Ratio
IT	Information technology
ITT	Intention to treat
JBI	Joanna Briggs Institute
K-SADS-PL	Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime Version
KiTAP	Test of Attentional Performance for Children (child version)
LCI	Lower Confidence Interval
LDX	Lisdexamfetamine
MPH	Methylphenidate
NA	Not Applicable
NASS	Non-adoption, abandonment, scale-up, spread, sustainability
NHS	National Health Service
NHS EED	NHS Economic Evaluations Database
NI	No information
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health and Care Research
NPV	Negative predictive value
NR	Not reported
NRSI	Non-randomised study of interventions
OCD	Obsessive compulsive disorder
ONS	Office for National Statistics
OR	Odds Ratio
OROS	Osmotic release oral system
PADHD	Prediction of ADHD
p(CE)	Probability cost-effective
PHE	Public Health England
PN	Probably no
PPV	Positive predictive value
PRESS	Peer Review of Electronic Search Strategies
PSA	Probabilistic Sensitivity Analysis

Term	Definition
PSS	Personal Social Services
PSSRU	Personal Social Services Research Unit
PTSD	Post Traumatic Stress Disorder
PY	Probably Yes
QALY	Quality Adjusted Life Year
Q-SSP	Quality Assessment Checklist for Survey Studies in Psychology
RCT	Randomized Controlled Trial
RD	Risk Difference
REML	Restricted Maximum Likelihood
RR	Relative Risk
RRR	Relative Risk Reduction
SCID-I	Structured Clinical Interview for DSM-4 v1
SCID-II	Structured Clinical Interview for DSM-4 v2
SD	Standard deviation
SDQ	Strengths and Difficulties Questionnaires
SE	Standard error
SLI	Specific language impairment
SN	Strong No
SNAP-IV	Swanson Nolan and Pelham Questionnaire
SROC	Summary receiver operating characteristics
SY	Strong Yes
TAG	Technology Appraisal Group
TAP	Test of Attentional Performance for Children
TN	True Negative
TOVA	Test of variables of attention
TP	True Positive
TR	Time Ratio
UCI	Upper confidence interval
UK	United Kingdom
UKAS	United Kingdom Accreditation Service
US	United States
USA	United States of America
VR	Virtual reality
VR-CPT	Virtual reality continuous performance test
WHO	World Health Organisation
WN	Weak no
WTP	Willingness to pay
WY	Weak Yes
YOI	Young Offenders Institution

1 Background and Definition of Decision problem

Sections of this Chapter have been reproduced from the review protocol, available at the NICE website.[1]

1.1 Epidemiology and burden of ADHD

Attention Deficit Hyperactivity Disorder (ADHD), is a neurodevelopmental disorder characterized by persistent patterns of inattention, impulsivity, and hyperactivity that can significantly impact daily functioning.[2] Different subtypes can be defined based on these key features:

- Inattentive subtype
- Hyperactive-impulsive subtype
- Combined subtype (both inattentive and hyperactive-impulsive)

The exact cause of ADHD is unknown but is generally considered to involve multiple genetic and environmental factors that lead to altered brain neurochemistry and structure. ADHD is estimated to affect around 2 to 7% of school-aged children and young people, with an average estimate of around 5%.[3] There has been a substantial increase in the proportion of children diagnosed with ADHD over the past 30 years, with rates doubling between 2003 and 2018.[4] Increasing awareness of ADHD among healthcare professionals, educators, and the general public has contributed to higher rates of diagnosis.[3] ADHD often persists into adulthood - studies suggest that around 15% of adults will continue to meet full diagnostic criteria for ADHD, 65% will continue to show symptoms which impact on their life, whereas around 20% will have no symptoms or impairment in adulthood.[5] Certain population may be more likely to have ADHD – a 2018 meta-analysis estimated that up to 1 in 4 prisoners had a diagnosis of ADHD,[6] although a more recent re-analysis of this data reported that, after accounting for an outlier and restricting to studies that used random sampling of adults in prison, prevalence was much lower at around 4.5% in men.[7]

ADHD can have a significant impact on individuals' academic, social, and occupational functioning. Children with ADHD may struggle in school, have difficulty forming and maintaining relationships, and experience low self-esteem.[8, 9] In adulthood, untreated ADHD can lead to challenges in employment, relationships, and mental health.[10] ADHD is often accompanied by substantial comorbidity including substance use, depression, anxiety and accidents.[11] Symptoms of inattention can make even basic tasks such as reading, watching television and multi-tasking challenging.[12] Among adults, there is an expectation of being able to function independently but difficulty maintaining attention can make this very challenging.[12] However, there are also positive effects of ADHD, with a recent qualitative study highlighting that sometimes acting on impulse can have positive effects leading perhaps to a fulfilled and exciting life.[12] The burden of ADHD extends beyond the affected individuals to their families, schools, and the healthcare system – a UK based study highlighted the impact of ADHD on the quality of life of children with ADHD and of their siblings.[8] The economic burden includes healthcare costs, educational support services, and lost productivity for individuals and caregivers.

ADHD is usually diagnosed in childhood, with symptoms often becoming noticeable when a child starts school.[13] Boys are more commonly diagnosed with ADHD than girls, with a male-to-female ratio estimated at around 3:1.[3, 14] People with ADHD may seem restless, have trouble concentrating and may act on impulse.[13] Boys present differently from girls – they often display disruptive behaviour prompting referral, whereas girls are more likely to have the inattentive subtype, making it less likely for girls to be referred for evaluation of ADHD. Symptoms of ADHD may change with age, with symptoms relating to hyperactivity becoming harder to detect with age, whilst those relating to inattentiveness persist.[5, 15]

1.2 Current diagnostic and care pathway

1.2.1 Referral

The NICE guideline on ADHD diagnosis and management (NG87) provides guidance on the diagnostic pathway for ADHD.[16] However, this can be seen as best practice and is not always reflected in reality in the NHS. The guidance suggests that children and young people with suspected ADHD should be referred from community settings to secondary care for further investigation – this is often to a paediatrician with those with significant mental health comorbidities and adolescents often referred to child and adolescent mental health services (CAHMS). Community referral is usually made by a health, education, or social care professional, for example the GP, educational psychologist, or school special educational needs coordinator. Exact referral and care pathways vary locally.[16]

NICE guidelines recommend that adults presenting with symptoms suggestive of ADHD who do not have a childhood diagnosis of ADHD should be referred to secondary care for further assessment by a mental health specialist with training in the diagnosis and treatment of ADHD. Referral is usually made from primary care or general adult psychiatric services. Adults who were diagnosed and treated for ADHD as children, or people who present with symptoms suggestive of continuing ADHD, should be referred for further assessment.[16]

The NICE guidelines highlight that the following groups have a higher likelihood of having ADHD than the general population, and so a lower threshold for referral may be appropriate in these groups:[16]

- people born preterm
- looked-after children and young people
- children and young people diagnosed with oppositional defiant disorder or conduct disorder
- children and young people with mood disorders
- people with a close family member diagnosed with ADHD
- people with epilepsy
- people with other neurodevelopmental disorders (e.g. autism spectrum disorder, tic disorders, and learning difficulties)
- adults with a mental health condition

- people with a history of substance misuse
- people known to the Youth Justice System or Adult Criminal Justice System
- people with acquired brain injury.

The guidelines also highlight that ADHD is likely to be under-recognised in girls and women who may be less likely to be referred for ADHD assessment, may be less likely to be diagnosed with ADHD and may be more likely to receive an incorrect diagnosis of another mental health or neurodevelopmental condition.[16]

1.2.2 Diagnosis

Assessment and diagnosis of ADHD is a complex process that typically relies on a clinician's judgment and involves gathering information from multiple sources, such as assessment questionnaires, third-party reports, patient history, and behavioural observations. This approach is largely subjective and can lead to concerns regarding the reliability and consistency of the diagnosis.[17] It is also resource intensive – it usually takes an average of 2 to 3 appointments and around 2.5 hours of clinic time to reach a diagnosis of ADHD.[18] Guidelines from The Royal College of Psychiatrists in Scotland suggest that in most cases the assessment and diagnosis of ADHD in adults will require 2 to 3 one hour sessions.[19] Whilst children are usually assessed face-to-face in clinic, assessment for adults is often done remotely. This avoids the need to travel long distances to centralised assessment centres and also means that family members can join the consultation from different locations. Waiting times for a diagnosis through the NHS can also be lengthy – a recent survey based on people who had signed a petition to ask for improved ADHD assessment, suggested that 10% of respondents had been waiting between 2 and 3 years for an ADHD assessment and 24% had waited between 1 and 2 years.[20] Proportions were slightly higher for children, with 14% waiting between 2 and 3 years for an ADHD assessment, and 30% waiting between 1 and 2 years. A recent paper suggests that a realistic estimate for time to diagnosis for adults newly referred for assessment is likely to be 5-10 years.[21] The average time to diagnosis in children is reported to be 18 months.[22]

The NICE guideline on ADHD diagnosis and management (NG87) recommends diagnosis based on a combination of psychosocial assessment, patient history, symptoms and behaviour.[16] To make a diagnosis of ADHD, symptoms of hyperactivity/impulsivity and/or inattention should meet the diagnostic criteria of DSM-5 or ICD-11[23, 24] and should cause at least moderate psychological, social and/or educational impairment. This should be based on interview and/or direct observation in multiple settings. Impairment should be pervasive occurring in at least 2 important settings including social, familial, educational and/or occupational settings.[16] The guidance highlights that the diagnosis should only be made by a specialist psychiatrist, paediatrician or other appropriately qualified healthcare professional with training and expertise in the diagnosis of ADHD.[16]

ADHD is frequently associated with other neurodevelopmental and psychiatric conditions. Common co-occurring conditions include autism spectrum disorders (ASD), personality

disorders, learning disabilities, anxiety disorders, mood disorders, conduct disorders and developmental trauma.[2] The presence of these comorbidities can complicate the diagnosis and management of ADHD.[5] Diagnosis can also be more challenging amongst those in the criminal justice system.

A number of rating scales are available to help diagnose ADHD. The most commonly evaluated rating scales include Achenbach System of Empirically Based Assessment (ASEBA), Conners Scales, DSM-4 based ratings scales (e.g., the ADHD Rating Scale IV), and the Strengths and Difficulties Questionnaire (SDQ). A recent systematic review of these tools concluded that although most tools have excellent overall diagnostic accuracy (area under the curve, AUC, ranged from 0.76 to 1.00), a single measure completed by a single reporter is unlikely to have sufficient accuracy for clinical use.[25] This finding is reflected in the NICE guidelines, which state that a diagnosis should not be made solely on the basis of such scales.[16]

Other tests that can help with the diagnosis include Continuous Performance Tests (CPT). These are computer-based tests that assess an individual's sustained attention and impulse control. Examples of these tests include: Test of variables of attention (TOVA), Gordon's diagnostic system (GDS) and Conners' CPT. These tests are designed to be used alongside clinical assessment as part of the diagnostic pathway for ADHD. A systematic review found mixed evidence on the clinical utility of CPT as an assessment tool. They highlighted that such tests should not be used as a stand-alone diagnostic tool and suggested that combining CPTs and an objective measure of activity may be particularly useful as a clinical tool and worthy of further pursuit.[26] These tests are not explicitly mentioned in the NICE guidelines.

1.2.3 Management and treatment of ADHD

Managing ADHD requires a multidisciplinary approach, with NICE guidance recommending that individuals with ADHD should have a comprehensive, holistic shared treatment plan that addresses psychological, behavioural and occupational or educational needs.[16] The treatment plan should be developed through discussion with those affected by ADHD and their families – this should be an ongoing process and should undergo regular review. Recommendations on treating ADHD vary according to age, with slightly different recommendations for those under 5 years, children and young people aged over 5 years and adults. Treatment plans will be tailored to the individual but are likely to encompass some or all of the following:[27]

Behavioural Interventions: Behavioural therapies are used to improve organizational skills, impulse control, and self-regulation. Parent training and classroom management strategies are often included.

Educational Support: For children and young people, schools are encouraged to provide support, such as Individual Education Plans (IEPs) and accommodations to address academic challenges.

Psychosocial Support: Individual or family counselling may be recommended to address emotional and psychological issues.

Lifestyle and Self-Care: Encouraging a healthy lifestyle with regular exercise, a balanced diet, and adequate sleep is important. Developing structured routines and organization skills can also be beneficial.

Awareness and Education: Parents, caregivers, and individuals with ADHD are provided with education and support to help them understand the condition and learn strategies for managing symptoms.

Medication: Medications, such as stimulants (e.g., methylphenidate or amphetamine-based drugs) or non-stimulants (e.g., atomoxetine, guanfacine, clonidine), may be prescribed based on the severity of symptoms and individual response.[28]

Medication should only be given to those with ADHD if their symptoms are *"still causing a significant impairment in at least one domain after environmental modifications have been implemented and reviewed."*[16] However, due to the length of time that it currently takes to receive a diagnosis, by which time most people will have pursued a range of techniques and strategies to manage their difficulties, medication is often started soon after diagnosis. Medication is not recommended in those under 5 without a second specialist opinion, ideally from a tertiary centre.[16] Before starting medication a detailed baseline assessment is required. Medication is usually started at a low dose that is gradually increased as needed.[27] The optimal dose will balance treatment effectiveness against severity of any adverse effects. Potential adverse effects vary according to which medication is prescribed but include: small increases in blood pressure, decreased appetite, trouble sleeping, headaches, stomach aches, drowsiness, dizziness, diarrhoea, nausea and vomiting and mood changes including feeling aggressive, irritable, depressed, anxious or tense.[27] Treatment is considered optimal when patients demonstrate reduced symptoms, positive behaviour change, improvement in education, employment, and relationships, with tolerable adverse effects. Achieving optimal treatment requires regular review, assessment, and adjustment of medication.

Once a patient has started treatment, NICE guidelines recommend regular monitoring to assess effectiveness and adverse effects. They recommend that those taking medication should record adverse events, ideally using an adverse effect checklist. Treatment effectiveness should be monitored using standard symptom and adverse effect rating scales.[16] There are two stages to monitoring treatment effectiveness. The initial stages is during the dose titration phase, when patients are reviewed frequently, until they are on a stable dose of medication. After this they are monitored at least annually, mainly to assess whether the treatment remains effective and to assess side effects.

1.3 Technologies of interest

Technologies of interest for this appraisal include technologies that combine a continuous performance test (CPT) with an objective and standardised measure of motor activity for the assessment of ADHD. We use the term **"sensor CPT"** to refer to these tests. CPTs that do not incorporate the objective and standardised measures of motor activity are referred to as **"non-sensor CPT".**

1.3.1 QbTest (QbTech Ltd.)

The QbTest is a CE-marked, class I medical device designed for use to aid in the assessment of ADHD and in the evaluation of treatment interventions in those with ADHD aged 6 to 60 years. It combines computerised assessments with a high-resolution motion tracking system to evaluate three core symptoms of ADHD: attention, impulsivity, and hyperactivity.

The QbTest involves a computer-based task that typically takes 15 to 20 minutes to complete. There are three versions of the test for different age groups to control for developmental differences in cognitive abilities: QbMini for those aged 4-5 years, QbTest (6-12 years) for children aged 6 to 12 years and QbTest (12-60) for those aged 12 to 60 years. This version is also referred to as the QbTest Plus. During the test, the individual is required to respond to specific stimuli by pressing a button – they are required to distinguish between "targets" and "non-targets". To monitor motor activity during the test, the individual wears a headband. This motion tracking system records and measures hyperactivity and other motor-related behaviours.

Table 1 Overview of differences between different versions of the QbTest

Feature	QbMini[29, 30]	QbTest(6-12)	QbTest(12-60)
Age group	4-5 years	6 to 12 years	12 to 60 years
Stimulus	Yellow smiley face and yellow circle without smiley face	Grey circle and grey circle with a cross	Red circle, blue circle, red square and blue square
Target	Yellow smiley face	Grey circle	Matching pair - identical in shape and colour to the stimulus immediately preceding it
Stimulus rate	One stimulus every two seconds	One stimulus every two seconds (0.5 Hz).	one stimulus every two seconds (0.5 Hz).
Time stimulus is visible	2 seconds	100 milliseconds	200 milliseconds
Total number of stimulus presented	300	450	600
Target to non-target ratio	50:50	50:50	25:75

To administer the QbTest, a private and quiet room with a computer, desk and chair is needed. Trained healthcare assistants or nurses can oversee the test, and a trained clinician interprets the results. Test results are compared to a normative group of individuals of the same sex and age who do not have ADHD. Outputs of the test are visually reported, detailing the performance in each of the three symptom domains of ADHD (activity, attention, and impulsivity) and the level of deviation from non-ADHD score and are sent directly to the clinician. Results are expressed as the Q-Score for sub-categories of activity, impulsivity and inattention. Q-scores reflect the deviation of the participant's performance (in standardised units) from the mean score of the normative group. There is no standard threshold for defining a positive Q-score as the scores are only meant to inform the diagnosis – the clinician combines the QbTest data with questionnaire responses and observational information for a comprehensive assessment.

The QbTest was implemented across 69 NHS trusts between 2020 and 2023 as part of an Academic Health Science Network (AHSN) initiative known as "Focus ADHD" which aimed to improve the diagnosis of ADHD in children and young people.[22, 31] A recent NICE Medical Innovation Briefing highlighted that the QbTest should be used as an addition to routine clinical assessment, not as a standalone test. It also highlighted uncertainties in that the evidence reviewed included potentially inappropriate populations and did not use a parallel clinical assessment.[32]

1.3.2 QbCheck (QbTech Ltd.)

QbCheck is the same as the QbTest, but is designed for remote testing and can be used without a healthcare professional present. Like the QbTest, it is a CE-marked class I medical device, indicated for use as an online tool to aid in the clinical assessment of ADHD and in the evaluation of treatment interventions in those with ADHD aged 6 to 60 years. It combines an online computerised continuous performance task (CPT) with a webcam motion tracking system and, like the QbTest, results are compared to a normative group without ADHD, with results reported in the same way as for the QbTest. In addition to the QbTest, the test-taker performs an ability test that gives important information of the test-takers ability to manage the test situation.

The QbCheck requires a laptop or computer with a stable internet connection in an appropriate location. The test uses the built-in web camera rather than the advanced motion tracking system used for the QbTest. As with the QbTest, there are two different versions targeted at the different age groups – the test stimulus are the same for the QbCheck as for the QbTest. The test can be administered remotely and observed by trained healthcare assistants or nurses and interpreted by a trained clinician alongside questionnaire responses and observational data.

1.3.3 EFSim Test (previously known as ARVO and EPELI) (Peili Vision Company)

The EFSim is a virtual reality (VR) game designed for children and young people aged 8 to 13 years. It is CE marked as a class I medical device. It involves completing everyday tasks

within a simulated home environment and is intended to be used alongside existing clinical assessments for ADHD.

The game consists of a 25-minute in-game session played on an Oculus Go head-mounted display and its hand controller. During gameplay, motion tracking sensors in the goggles and controller capture the participant's movements. An updated version of the EFSim Test that includes eye movement (saccades) tracking is due to be available in early 2024.The test assesses various performance indicators related to ADHD, including attention, hyperactivity, impulsivity, memory, time management, planning, behaviour regulation, task efficiency, and efficiency of information processing.

A web-based, remote version of the EFSim Test is also in development. This is due to be available in early 2024.

1.3.4 Nesplora Attention Adults Aquarium (Giunti psychometrics)

The Nesplora Attention Adults Aquarium is a Class I CE-marked, virtual reality continuous performance test (VR-CPT) suitable for people aged 16 to 90 years. It measures symptoms of ADHD including auditory and visual attention, impulsivity, motor activity and reaction time. It is intended to be used alongside current ADHD clinical assessment.

The test involves an 18 to 22 minute computerised task that is conducted whilst wearing a VR headset and headphones. It requires a virtual reality device, computer, stable internet connection, and headband headphones. The person undertaking the test uses a handheld button to respond to both visual and auditory stimuli. Results are available immediately, and are visually reported, detailing a score for the following categories: attention, inhibitory control (impulsivity), motor activity, processing speed, distractibility, and vigilance. This score is calculated by comparing to a normative data set of people without ADHD of the same sex and age. All measures for sustained attention and inhibition are obtained separately for auditory and visual modalities and for the two modalities combined.

1.3.5 Nesplora Attention Kids Aula (Giunti psychometrics)

The Nesplora Attention Kids Aula is a Class I CE-marked VR-CPT. It is very similar to Nesplora Attention Adults Aquarium but is aimed at young people aged 6 to 16 years – the test also involves a computerised task, measures the same ADHD symptoms as the adult version and is performed and interpreted in the same way as the adult version.

1.4 Place of the technology in the diagnostic and treatment pathway

There are four potential roles for the new technologies in the diagnostic and treatment pathway. In all cases, the tests should be used alongside healthcare professional assessment:

1. As part of the initial diagnostic assessment for all people referred with suspected ADHD

2. As part of the initial diagnostic assessment for people where a diagnostic decision cannot be reached using current assessment methods.
3. To assess medication effectiveness during initial dose titration and treatment decisions in people with a diagnosis of ADHD
4. To assess treatment (pharmacological or non-pharmacological) effectiveness for long-term treatment monitoring for people with a diagnosis of ADHD

2 Objectives

Sections of this Chapter have been reproduced from the review protocol, available at the NICE website.[1]

The overall aim of this project was to determine whether technologies for objective measures of ADHD that use motion sensors to measure hyperactivity are clinically and cost-effective to the NHS. We defined the following objectives to address this aim:

1. What is the diagnostic accuracy and clinical- and cost-effectiveness of technologies that combine measures of cognition and motor activity for the diagnosis of ADHD in people referred with suspected ADHD?
2. What is the diagnostic accuracy and clinical- and cost-effectiveness of technologies that combine measures of cognition and motor activity for the diagnosis of ADHD in people referred with suspected ADHD for whom current assessment cannot reach a diagnosis?
3. What is the clinical- and cost-effectiveness of technologies that combine measures of cognition and motor activity in evaluating medication effectiveness during initial dose titration and treatment decisions for people with a diagnosis of ADHD?
4. What is the clinical and cost-effectiveness of technologies that combine measures of cognition and motor activity for evaluating treatment effectiveness during long-term treatment monitoring for people with a diagnosis of ADHD?

3 Assessment of clinical effectiveness

Sections of this Chapter have been reproduced from the review protocol, available at the NICE website.[1]

We conducted a systematic review to summarise the evidence on the clinical effectiveness and diagnostic accuracy of technologies that combine measures of cognition and motor activity for diagnosis and management of ADHD. The systematic review followed the principles outlined in the Centre for Reviews and Dissemination (CRD) guidance for undertaking reviews in health care, the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy and the NICE Health Technology Evaluations Manual.[33-35] The review is reported according to PRISMA-2020, PRISMA-DTA and PRISMA-E guidelines.[36-38] The review was registered on the PROSPERO database (CRD42023482963).

3.1 Inclusion and exclusion criteria

Studies that fulfilled the following criteria were eligible for inclusion:

3.1.1 Technology (intervention/index test)

Technologies that combine a continuous performance test (CPT) with an objective and standardised measure motor activity for the assessment of ADHD. We use the term **"sensor CPT"** to refer to these tests. Eligible tests are: QbMini, QbTest (6-12 and 12-60), QbCheck, EF Sim, EF Sim Web Version, Nesplora Kids and Nesplora adults alone or in combination with clinical assessment for ADHD by a healthcare professional.

3.1.2 Population

Objective 1: Adults and children referred for evaluation of suspected ADHD
Objective 2: Adults and children referred for evaluation of suspected ADHD in whom a diagnosis had not been made through standard assessment processes
Objective 3: Adults and children with a diagnosis of ADHD undergoing initial dose titration and treatment decisions
Objective 4: Adults and children with a diagnosis of ADHD being monitored for treatment effectiveness

3.1.3 Setting

Secondary care or remote assessment settings. Studies in which some participants (e.g. control groups) were enrolled in other settings were also eligible.

3.1.4 Comparator

Any diagnostic assessment for ADHD that did not include the technology of interest. Studies that compared two or more technologies of interest were also eligible for inclusion. For evaluation of diagnostic test accuracy, studies that reported a direct comparison of the accuracy of one of the technologies of interest and another CPT (e.g. Connor's CPT) were also included. These are referred to as "**non-sensor CPT**".

3.1.5 Reference standard (diagnostic accuracy studies only)

Any reported diagnostic assessment for ADHD.

3.1.6 Study designs

For assessment of *clinical effectiveness* we included randomised controlled trials (RCT) or non-randomised study of interventions (NRSI). For evaluation of *diagnostic test accuracy*, we included diagnostic test accuracy (DTA) studies of any design including one gate (also known as diagnostic cohort or cross-sectional studies) and multi-gate (also known as diagnostic case-control studies) designs. Qualitative studies were eligible if they provided data on any of the specified outcomes. Where data were not available on any of the specified outcomes from the designs listed, we also considered UK based observational studies that included a control group (e.g. before-after study).

3.1.7 Outcomes

Studies were required to report at least one of the following outcomes of interest for this appraisal:

- Test performance (diagnostic accuracy) e.g. sensitivity, specificity, area under the ROC curve (AUC)
- Test failure
- Time to assessment or to reach a diagnostic decision
- Use of NHS and PSS services (such as the number and length of clinical appointments prior to diagnosis)
- Impact on clinical decision-making
- Confidence of healthcare professionals in assessment
- Ease of use/acceptability for clinicians
- Use of interventions (such as ADHD medication)
- Morbidity
- Mortality
- Health related quality of life
- Ease of use/acceptability for patients or carers
- Patient and carer experience
- Costs related to using the technologies
- Cost of training staff to operate technology and interpret results
- Costs of resources associated with diagnosing and reviewing ADHD
- Cost of interventions to help manage ADHD Heath-related quality of life

Existing systematic reviews were included if they fulfilled inclusion criteria, were judged as low risk of bias based on the ROBIS tool,[39] had searches conducted within the past year, and stratified the synthesis as described in our synthesis section (section 3.5), otherwise they were used a source of potentially relevant studies.

3.2 Study identification

Studies were identified using bibliographic and non-bibliographic search methods following guidance in the NICE Health Technology manual.[34]

3.2.1 Bibliographic searching

The following databases were searched:

- MEDLINE (Ovid)
- EMBASE (Ovid)
- PsycINFO (Ovid)
- CINAHL (Cumulative Index to Nursing and Allied Health Literature) (EBSCOhost)

We used sensitive search strategy based on terms for each of the technologies eligible for inclusion and for the manufacturers of these technologies. Full search strategies are reported in Appendix 1.

3.2.2 Non-bibliographic search methods

Completed and ongoing trials were identified through searches of the following trial registries:

- ClinicalTrials.gov via www.clinicaltrials.gov
- WHO International Clinical Trials Registry Platform (ICTRP) via www.who.int/clinical-trials-registry-platform

Additional relevant studies were identified by:

- Screening reference lists of any reviews (systematic or non-systematic) identified by our searches
- Reviewing the reference lists of any primary study report included at full-text
- Hand searching the websites of the manufacturer/or licence holders for each test
- Information submitted by test manufacturers

3.2.3 Managing the searches

Search results were exported to EndNote 20 for deduplication using the default deduplication settings and manual review of records. Search results were then exported from EndNote to Microsoft Access for screening.

3.3 Review strategy

Two reviewers independently screened titles and abstracts identified by the searches. Full copies of all reports considered potentially relevant were obtained and two reviewers independently assessed these for inclusion. Disagreements were resolved through discussion.

The three test manufacturers (Peili Vision, Nesplora and QbTech) submitted reports containing information about the tests and citations to potentially relevant reports. One

reviewer extracted all relevant information and citations from the test manufacturer submissions into a separate document for each manufacturer in Microsoft Word. One reviewer screened each citation as follows: 1) checked our review searches to see if it had been identified already 2) if it had not been identified by our searches, or identified by our searches but only screened at title and abstract stage, we located the full text report, saved it and assessed it for inclusion. Any queries were discussed with a second reviewer.

Data were extracted using standardised data extraction forms developed in Microsoft Access or Microsoft Word depending on the quantity of data available. Data extraction forms were piloted on a small sample of papers and adapted as necessary. Data were extracted by one reviewer and checked in detail by a second reviewer. Any disagreements were resolved through discussion.

Data were extracted on the following: study design (RCTs, DTA studies, before-after implementation study, qualitative, survey), objective that study addresses, funding sources (public, industry, mixed), country, setting, inclusion criteria, ADHD sub-type, test details (test, threshold), comparator or reference standard test(s), sample size and outcomes specified in inclusion criteria (section 3.1).

We considered the PROGRESS-Plus population factors, where reported. [40] PROGRESS-Plus is an acronym that describes characteristics that contribute to health inequity. PROGRESS stands for: place of residence, race/ethnicity/culture/language, occupation, gender/sex, religion, education, socioeconomic status, and social capital. “Plus” stands for any additional factors considered important for the specific topic under review. We extracted the following “Plus” factors:

- personal characteristics associated with discrimination: characteristics of relevance to the current review include age, sex, ethnicity, learning disability, neurodevelopmental disorders (including autism spectrum disorders and personality disorders), developmental trauma
- looked after children
- features of relationships e.g. exclusion from school
- time-dependent relationships e.g. instances where a person may be temporarily at disadvantage
- people in the Youth Justice System or Adult Criminal Justice System

We extracted whether each PROGRESS-Plus factor was reported at baseline (y/n), the baseline data concerning the factor as reported by the authors, and whether the study reports results data stratified by the factor. Where stratified data were reported, these were extracted.

Dichotomous clinical effectiveness data were extracted as number of patients with events and/or number of events and total number of patients in each treatment arm. For categorical data, we extracted details on the categories assessed, the total number of

patients in each treatment arm and the number of patients in each outcome category. For continuous clinical effectiveness data we extracted means/medians together with ranges, standard deviations (SD), standard errors (SE), and/or confidence intervals (CIs) for the outcome at baseline, follow-up and for change from baseline in each treatment group. For all types of clinical effectiveness data, summary effect estimates together with 95% CIs and p-values for comparisons between groups together with details on the methods of analysis, any variables controlled for in the analysis and the test statistic were extracted.

Accuracy data were extracted as 2x2 tables comparing the ADHD test against the reference standard, where available. The area under the Receiver Operating Characteristic (ROC) curve (AUC) was also extracted, with 95% confidence interval or standard error. Where 2x2 tables were not reported in the paper, these were calculated from estimates of sensitivity and specificity together with the total number of patients with and without ADHD. For one study,[41] 2x2 tables were approximated from reported point estimates for sensitivity, specificity, PPV and NPV, the total sample size, and an assumption that the proportion of individuals excluded from the test accuracy evaluation was the same in both the QbTest (6-12) and the QbTest (12-60) groups. Where standard errors or confidence intervals were not reported for an AUC estimate, these were estimated from the AUC and number of patients with and without ADHD, using the R package auctestr.[42 43] If a measure of accuracy (e.g. sensitivity, specificity, AUC) was reported without providing the information needed to calculate 2x2 tables, then these data were extracted.

Where multiple sets of 2x2 data were reported in a single study, for example for different tests, test components, target conditions, ADHD subtypes, thresholds, or subgroups of interest, all data were extracted. For studies comparing two or more index tests (at least one of which was a sensor CPT) and a reference standard, if full cross-classifications of test results (2x2x2 data) were reported, these were also extracted.

For studies that reported data on qualitative interviews or survey data, data were extracted on the following: author (year), study name, country, language, setting, study design, funding, and sensor CPT. For each relevant study component (e.g. interview with young people; survey with healthcare professionals), we extracted information about participants, sampling strategy, data collection and analysis.

Where studies were only available as abstracts, or where insufficient data were reported in a study to extract the required information, study authors were contacted for additional information.

3.4 Quality assessment strategy

The methodological quality of included RCTs was assessed using the updated Cochrane Risk of Bias Tool (RoB 2).[44] DTA studies were assessed for methodological quality using QUADAS-2.[45] Before-and-after implementation studies were assessed using the ROBINS-I tool.[46] Studies that contributed qualitative data were assessed with an amended version of the

CASP checklist for qualitative studies (we excluded question 10 “how valuable is the research?”).[47] Studies that contributed survey data were assessed with the Quality Assessment Checklist for Survey Studies in Psychology (Q-SSP).[48] One reviewer assessed the quality of included studies and this was checked by a second reviewer. Any disagreements were resolved by consensus or discussion with a third reviewer.

3.5 Synthesis methods

For each of the four objectives, a narrative summary of included studies is presented. This includes a summary of study characteristics (e.g. study designs, sample size, geographical location, year, age group, test evaluated), outcomes reported and study quality. We also narratively summarised whether studies reported baseline data for PROGRESS-Plus characteristics, and whether the studies report results data stratified by these characteristics.

We stratified the synthesis on whether the tests were evaluated in isolation or in combination with clinical assessments, and on specific sensor CPT tests evaluated. For each test, the analysis was further stratified on the test subcategory evaluated. We had intended to conduct subgroup analyses based on the following subgroups, however there were only sufficient data available to stratify on age:

- Age (children, young people, and adults)
- Sex
- Ethnicity
- People with mental health, behavioural and neurodevelopmental conditions
- People with developmental trauma
- People in the Youth Justice System or Adult Criminal Justice System
- Looked-after children

Where sufficient data were available, meta-analysis was carried out to generate summary effect estimates. We only had sufficient data on test accuracy outcomes (sensitivity, specificity and AUC) to perform meta-analysis. If a single study reported multiple estimates of 2x2 data that could have been included in a single meta-analysis, we selected one set of data for each analysis based on the following hierarchy:

- If multiple control groups were available, we selected the control group most similar to the group in which the test will be used in practice:
    - Control group of participants who had been evaluated for suspected ADHD and in whom the condition was ruled out selected in preference to other groups
    - Diseased controls selected in preference to healthy controls
- Where results were reported for multiple thresholds we selected the threshold most similar to that evaluated in other studies
- If data were reported for the whole population and separately for specific population subgroups we selected data for the full population

Where at least two sets of 2x2 data were available, meta-analysis of sensitivity and specificity was performed using the metadta command[49] in the Stata statistical software package.[50] For analyses based on at least three sets of 2x2 data, bivariate random effects meta-analyses of sensitivity and specificity was performed, with binomial likelihoods.[51, 52] Where only two sets of 2x2 data contributed to a meta-analysis, we used univariate fixed effects meta-analysis. Study-level and pooled results were plotted as coupled forest plots and in ROC space. In ROC space, uncertainty around summary results from bivariate and univariate analyses are represented with 95% confidence ellipses or 95% confidence intervals (CIs) respectively. Subgroup analysis was performed by QbTest (6-12) and QbTest (12-60). We did not have sufficient studies for formal investigation of other sources of heterogeneity. We also produced summary estimates of the AUC using inverse-variance random effects models. These were fitted using the metagen command[53] within the 'meta' package of the R statistical software package.[54]

Where studies compared the accuracy of two index tests, we produced plots showing estimates and 95% CI for the two tests in the same population. We tested for differences between estimates of sensitivity or specificity using Fisher's exact test.[55]

If two or more qualitative studies were identified that reported data on the same outcomes, we used the meta-aggregative approach to qualitative synthesis based on guidance from the Joanna Briggs Institute (JBI).[56] One reviewer (ET) extracted themes from the included studies and then organised them into conceptual categories. This was checked by a second reviewer (AOS). We extracted direct quotes to evidence what the synthesised themes presented. Where conflicted information, or negative cases, were identified, these were pursued further to enhance methodological rigour. Where available, data from survey studies were also used to evidence the themes presented, clearly marked in the full synthesis in Appendix 3 as additional "findings from quantitative data".

3.6 Protocol changes

The following changes were made to the methods specified in the review protocol[1]:

- We clarified the eligibility criteria for study setting to make it clear that studies with control groups recruited in other settings were eligible: "Studies in which some participants (e.g. control groups) were enrolled in other settings (e.g. community setting) were also eligible."
- We broadened our inclusion criteria for comparative studies to also include data from studies that compared the accuracy of sensor CPTs (alone or in combination with clinical diagnosis) with the accuracy of clinical diagnosis alone.
- We identified one study of the QbMini. Although the original protocol did not specify that this test would be eligible, as it very similar to the QbTest, just aimed at younger children, this was also included.

4 Results of clinical effectiveness review

4.1 Results of the searches

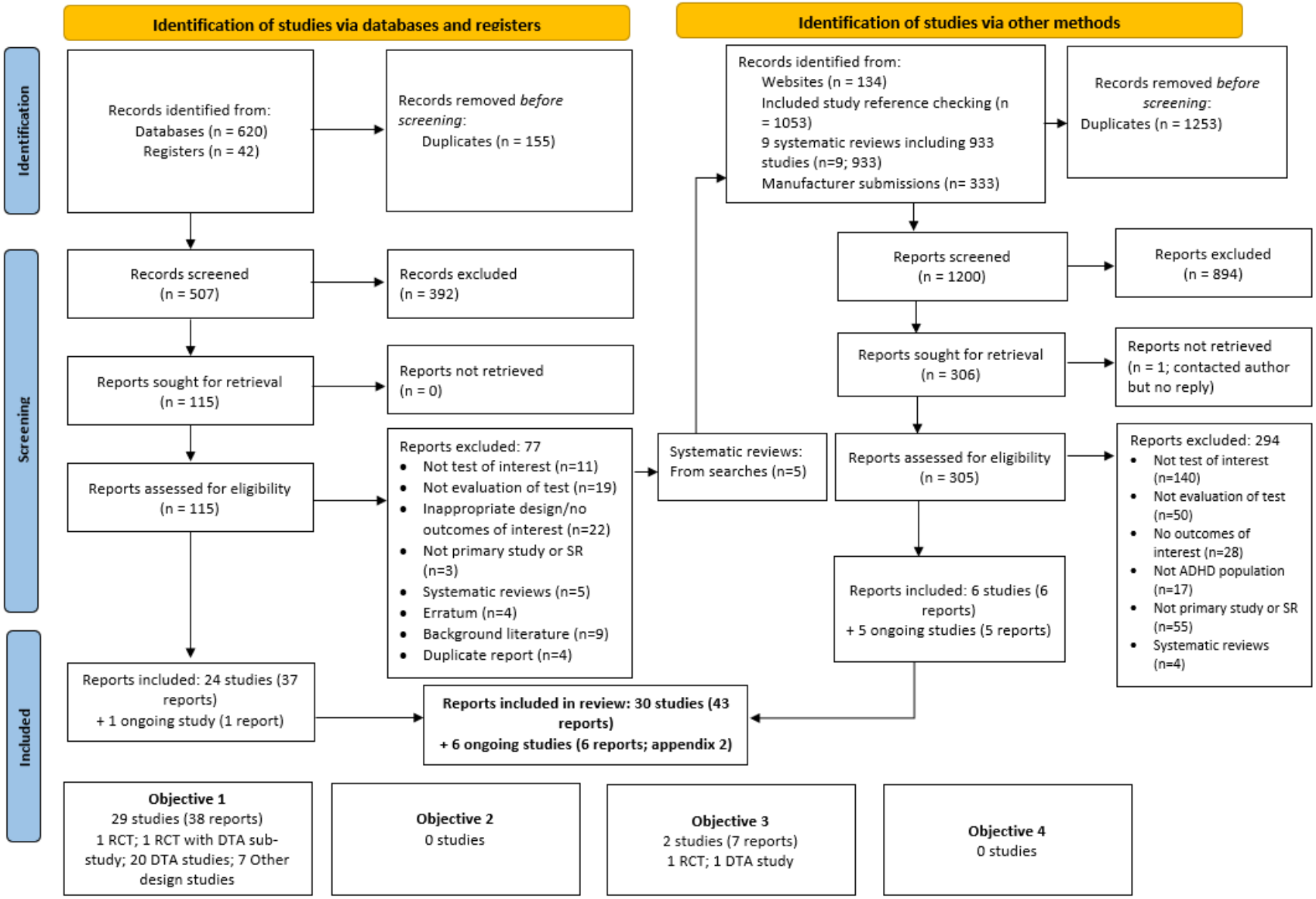
The searches of bibliographic databases and trials registries identified 507 unique reports. Additional methods of study identification (website checking, reference checking of included studies, checking studies included in systematic reviews and checking manufacturer submissions) identified 1200 unique reports. In total, 30 studies in 43 reports were included in the review (see Figure 1). We identified 9 systematic reviews.[26, 30, 57-63] None of these fulfilled the criteria specified for inclusion of systematic reviews and so they were screened to identify potentially relevant studies.

Most studies evaluated the QbTest, there was one study of the QbCheck, one of QbMini, two of Nesplora Aula and two of the EF Sim test. Three studies were only reported as conference abstracts – two DTA studies,[64, 65] and one implementation study.[66] The authors of these studies did not respond to our request for a full publication. All included studies were reported in English, except for one conference abstract of a DTA study, which was reported in Spanish and we translated it using Google Translate.[65] The translation was checked by a native Spanish speaker to ensure it was an accurate summary of the abstract. We could not locate the full text for one unpublished potentially relevant study for the QbTest that we identified by checking references of the included studies.[67]

We contacted the authors of nine studies to request additional data or to clarify information presented in the study reports. Five responded to our requests, including the authors of four DTA studies,[18, 68-70] and one implementation study.[71] Four did not respond to our requests, including three DTA studies[41, 64, 72] and one implementation study.[66]

We identified six ongoing studies. One ongoing study was identified by our searches.[73] This study is evaluating the EFSim test in children aged 8 to 13 years and includes a group with diagnosed ADHD and a normally developing control group. Five ongoing studies were highlighted in the submissions from the manufacturers, with limited detail (no NCT number or reference to study provided). Peili Vision reported that several pilots using the EFSim test are being set up in spring 2024 in the UK to implement it as part of an early triage tool (no further information provided). [redacted] Appendix 2 provides an overview of included and ongoing studies.

Figure 1 Prisma flow chart



4.2 Objective 1: Diagnostic accuracy and clinical-effectiveness of sensor CPTs for the diagnosis of ADHD in people referred with suspected ADHD

We included 29 studies (38 reports) for objective 1: two RCTs (one of these also provided data on accuracy,[18] both also included a survey and qualitative sub-study),[18, 74] 20 DTA studies[29, 41, 64, 65, 68-70, 72, 75-86] (two included a survey of patient views on the acceptability of the test),[77, 79] five uncontrolled before-after implementation studies[31, 66, 71, 87, 88] (2 also provided information on patient/clinician views – 1 survey and qualitative evaluation),[31] 1 survey[71] and two studies that only reported on patient and clinicians acceptability of sensor CPTs.[89, 90]

4.2.1 Impact of sensor CPTs for diagnosis of ADHD on patient outcomes

Only one study, the FACT UK based feasibility RCT, considered the impact of sensor CPTs on patient outcomes.[74] As this study was a feasibility trial, the primary objective was to determine the feasibility of conducting a full trial, rather than to compare outcomes between intervention groups. This study was conducted in the very specific population of boys with symptoms of possible ADHD aged 15 to 18 years in young offenders institutions in England. It compared usual care combined with the QbTest(12-60) to usual care alone in 60 boys (30 in each treatment group). Follow-up was poor, with only 32% of participants followed up at 6 months, although the authors report that this was affected by COVID-19 restrictions. As shown in Appendix 3, this study reported baseline data on four Progress-Plus characteristics (sex, ethnicity, education, and time-dependent relationships). Due to the feasibility design, small sample size, and low follow-up rates it was not possible to draw conclusions regarding clinical effectiveness from this study.

4.2.2 Diagnostic accuracy of sensor CPTs for diagnosis of ADHD

Twenty-one studies (28 reports) evaluated the accuracy of sensor CPTs for the diagnosis of ADHD (Table 3 and Table 4). One of these studies was an RCT (AQUA trial) included in section 4.2.3, which also reported a DTA substudy;[18] all others were DTA studies. Table 3 provides a summary of study characteristics for these studies.

The majority of studies evaluated the QbTest (6-12 or 12-60 depending on age), with single studies evaluating the QbMini and QbCheck (online) versions of this test. There was only one study of EF sim (reported as Epeli test) and two of Nesplora Kids; there were no studies of EF-sim web or of Nesplora Adults. Most studies evaluated the accuracy of the tests in isolation, three evaluated the accuracy of the QbTest in combination with some form of clinical assessment,[18, 82, 85] and one evaluated the test both in isolation and combined with clinical assessment.[80] Three studies provided a direct comparison of the accuracy of the sensor CPT with that of a non-sensor CPT,[68, 77, 84] and one compared the accuracy of QbTest combined with clinical information with QbTest alone.[18] Fifteen studies used the DSM-4 or 5 criteria for the diagnosis of ADHD as the reference standard, with single studies using ICD-10,[77] K-SADS-PL interview,[85], independent consensus diagnosis using DAWBA.[18, 91] One reported that the diagnostic process was according to the clinic's standard diagnostic

procedure without providing any further details,[41] one used an assessment of disruptive behaviour pathway used locally as the standard.[64], and one did not report any details about a reference standard (conference abstract). [65] Table 2 provide an overview of the reference standards used in the included studies.

Table 2 Overview of the reference standards used in the studies that contribute accuracy data to objective 1

Reference standards	Details
DSM-4 diagnostic criteria[92]	Fourth edition of the Diagnostic and Statistical Manual of Mental Disorders. The DSM contains standardised diagnostic criteria for mental disorders, used by healthcare professionals to guide diagnosis. For ADHD, it includes 18 symptoms divided into two domains: inattention and hyperactivity/ impulsivity. At least six symptoms in one domain are required for diagnosis.[93]
DSM-5 diagnostic criteria[94]	Fifth and most recent version of the Diagnostic and Statistical Manual of Mental Disorders. The same 18 symptoms and domains are included as in DSM-4, but there were also several changes to the handbook including (but not limited to): only five symptoms are required in one domain for adult diagnosis (still six for younger persons); examples have been added to facilitate application across the lifespan; co-morbid diagnosis with autism spectrum disorder is now allowed; ADHD moved to "neurodevelopmental disorders" chapter.[93]
DSM (version not specified)	The Diagnostic and Statistical Manual of Mental Disorders (as above).
ICD-10[95]	The International Classification of Diseases 10 (ICD-10) is the tenth revision of the classification system (the current version is ICD-11) created by the World Health Organisation to provide a standardised way to report and code mortality and morbidity data. The classification contains codes for diseases, signs and symptoms, abnormal findings, complaints, social circumstances, external causes of injury or diseases. The ICD-10 calls ADHD "hyperkinetic disorder" and requires hyperactivity, inattention and impulsivity to be present. The ICD-10 diagnostic criteria for ADHD are more restrictive than DSM criteria.[96]
Independent consensus diagnosis using the DAWBA.[91]	The Development and Wellbeing Assessment (DAWBA) consists of interviews and rating scales to generate an ICD-10 or DSM-5 psychiatric diagnoses in 5-16 year olds. It involves a parent interview, an interview for young people aged 11+, a teacher questionnaire and a computer-assisted clinical diagnostic rating based on the information. Clinical raters use the computer-generated rating to decide whether to accept or overturn the computer diagnosis (or lack of diagnosis) after reviewing all the information.
K-SADS-PL[97]	The Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version interview (K-SADS-PL) is a semi-structured diagnostic interview to assess mental disorders including but not limited to ADHD, Schizophrenia, and Major Depressive Disorder. The schedule has six components (developmental history, diagnostic screening

Reference standards	Details
	interview, completion checklist supplement to screen for additional disorders, appropriate diagnostic supplements (review presence/ absence of symptoms for other disorders), supplementary lifetime diagnosis checklist (summarises which disorders have been present from first episode to now), children's global assessment scale (level of functioning). It generates DSM-3-R and DSM-4 diagnoses.[97]
Diagnostic process according to clinic's standard diagnostic procedure - no further information.	NA
Assessment of disruptive behaviour pathway used locally as the standard	NA
Not reported	NA

Ten studies used the more reliable one-gate design (also known as diagnostic cohort or cross-sectional study) where a single group of participants was enrolled and all then received both the index test and reference standard. Five of these single-gate studies enrolled adults with suspected ADHD referred for ADHD assessment in secondary care.[70, 76, 83, 84, 86] Two studies enrolled children only – of these, one recruited children with suspected ADHD, autism, or another neurodevelopmental disorder,[69] and one recruited children who had screened positive for ADHD and were referred for further ADHD assessment.[68] One study enrolled adolescents with a high occurrence of neurodevelopmental disorders, including ADHD.[72] The remaining two single-gate studies included mixed populations: one enrolled children and adolescents who had been referred for their first ADHD assessment (and enrolled in the AQUA trial QbOpen arm),[18] and one enrolled children and adults referred for evaluation of suspected neurodevelopmental or psychiatric disorder.[41] Ten studies used a multi-gate design (also known as diagnostic case-control study) where two or more separate groups of participants were enrolled – one with known ADHD and one or more without ADHD, participants then received the sensor CPT. Eight studies had a two-gate design, in which they enrolled an ADHD group (cases) and one control group. Seven of these studies enrolled healthy controls[65, 75, 77, 79-81, 85] and one enrolled controls with Autism.[82] One study enrolled four groups: an ADHD group (cases) and three different control groups (a group who had been assessed for ADHD and in whom this had been ruled out, a group with bipolar disease, and healthy controls)[78] and another enrolled three groups (an ADHD group, a group with specific language impairment, and healthy controls).[29] For the four-gate study we selected the group that had been assessed for ADHD as the control group to use for the analysis; for the three gate study we used the group with specific language impairment. One study had an unclear study design, with limited study details reported in a conference abstract.[64]

Studies were conducted almost exclusively in Europe with eight studies conducted in Sweden; one study was a multi-national study that included sites in the USA in addition to Germany and Sweden. One study was conducted in a population-based setting recruiting participants from a twins registry, one study (reported in a conference abstract only) did not

report setting,[65] and all other studies were conducted in secondary care (e.g. recruiting participants from specialized ADHD outpatient clinics, neuropsychiatric centers, University ADHD outpatient clinics, or child and adolescent mental health services), although some included controls recruited from community settings (e.g. university, waiting areas, schools, workplaces). Five studies were at least partly funded by industry, and in a further two studies the authors either worked for the test manufacturer or developed the test.

Eight studies were conducted in adults, five in children (aged 6 to 12 years), two in children and adolescents (12-18 years) with single studies in children aged 5 years, children aged 5-15 years, children (age not specified), adolescents, adolescents and adults and older adults. The majority of studies included more male participants than female participants, particularly in the ADHD groups, although five studies included slightly higher proportions of female participants.

Twenty out of 21 DTA studies reported baseline data on at least one PROGRESS-Plus characteristic. The one study that did not report on PROGRESS-Plus was a conference abstract with limited detail on the population.[65] Data on place of residence were reported by two studies (10%);[78, 85] ethnicity by one study (5%);[18] occupation by four studies (19%).[78, 81, 84, 86]; sex by 18 studies (86%); religion by 0 studies (0%); education by 8 studies (38%)[72, 77, 78, 80, 81, 84-86]; socioeconomic status by 3 studies (14%)[77, 81, 82]; social capital by 0 studies (0%). Baseline data on neurodevelopmental/ learning disorders were reported by 13 studies (62%), and data on mental health disorders were reported by 11 studies (52%). Features of relationships (e.g. marital status, household set-up, major school problems) were reported by three studies (14%).[72, 78, 81] None of the studies reported data stratified by PROGRESS-Plus characteristics. Appendix 3 presents the PROGRESS-Plus data extracted from each study.

Table 3 Overview of studies that provide information on the diagnostic accuracy of sensor CPTs for the diagnosis of ADHD

Feature	Category	Number of studies
Design	One-gate (diagnostic cohort/cross-sectional)	10
	Multi-gate (diagnostic case-control)	10
	Unclear	1
Test evaluated	QbTestPlus	10
	QbTest or QbTestPlus	4
	QbTest	2
	QbMini	1
	QbCheck	1
	EPELI (EFSim)	1
	Nesplora AULA	2
Combination with clinical information	Test evaluated alone	17
	Test evaluated in combination with clinical information	3
	Both	1
Comparison with other tests	Accuracy of other CPT compared with accuracy of sensor CPT	3

Feature	Category	Number of studies
	Comparison with clinical diagnosis alone	1
	No comparison	19
Reference standard	DSM-4 diagnostic criteria	9
	DSM-5 diagnostic criteria	5
	DSM (version not specified)	1
	Independent consensus diagnosis using DAWBA (based on DSM-5 and ICD-10)	1
	K-SADS-PL interview	1
	ICD-10	1
	Diagnostic process according to clinic's standard diagnostic procedure - no further information.	1
	Assessment of disruptive behaviour pathway used locally as the standard	1
	Not reported	1
Country	Sweden	8
	Germany	3
	UK	3
	The Netherlands, Germany and Sweden	1
	Sweden and Germany	1
	Finland	1
	Germany, Sweden and the USA	1
	Spain	1
	Not reported	2
Setting	Secondary Care	19
	Population based	1
	Not reported	1
Funding	Non-industry	6
	Non-industry (but the authors developed the test)	1
	Mixed (non-industry & industry)	4
	Industry (authors employed by QbTech)	1
	Not reported but one author employed by QbTech	1
	Unfunded	3
	Not reported	4
	“Not applicable” (no further information)	1
Sample size (number analysed)	<50	1
	50-100	4
	100-200	7
	200-500	6
	>500	1
Age group	Children aged 5 years	1
	Children (6-12 years)	5
	Children (5-15 years)	1
	Children (6-12 years) & adolescents (12-18 years)	2
	Children (age not reported)	1
	Adolescents (12-18 years)	1
	Adolescents (12-18 years) & adults	1
	Adults	8
	Older adults	1
% male	<25%	0

Feature	Category	Number of studies
	25-50%	5
	50-75%	11
	>75%	2
	Unclear	3

Table 4 Details of studies that provided information on the diagnostic accuracy of sensor CPTs for the diagnosis of ADHD

Author, Design & Location	Test	Population and reference standard
QbTest combined with clinical assessment		
Bijlenga (2019)[80] Netherlands, Germany & Sweden; two-gate design (healthy controls)	QbTest (12-60); QbTest (12-60) + Clinical judgment (Symptom severity self-report scale)	ADHD group: **Adults** (age 55+); DSM-4-TR ADHD diagnosis (n=97) Healthy controls: Adults (age 55+) with score below cutoff on symptom severity measures (n=112) matched on age and gender
Emser (2018)[85] Germany; two-gate design (healthy controls)	QbTest (6-12) or QbTest (12-60) + objective clinical assessment (KiTap and TAP)	**Children and Adults** ADHD: DSM-4-oriented clinical interview by experienced clinician including KSADS and rating scales (n=68). Controls: No established or suspected ADHD diagnosis or family history of ADHD, unclear how assessed. Age/gender matched at group level (n=68)
Groom (2016)[82] UK; Two-gate design (ADHD controls)	QbTest (12-60) + Clinical judgment (Conners Adult Rating Scale and Autism Quotient-10)	**Adults (age 18-60 years)** ADHD group (n=32): DSM-5 diagnosis of ADHD. Autism (ASD) group (n=25): ICD10 diagnosis of Asperger's syndrome
Hollis (2018)[18] UK; one-gate design	QbTest (6-12 or 12-60) + clinical judgement Clinical judgement alone	**Children & Adolescents** (age 6-17 years) enrolled in AQUA trial Consensus diagnosis using DAWBA[91]. QbTest group: ADHD confirmed (n=43); no-ADHD (n=43) Control group: ADHD confirmed (n=51); no-ADHD (n=25)
QbTest alone		
Adamou (2022)[83] UK; one-gate design	QbTest (12-60)	**Adults** referred to Specialist Adult ADHD and Autism service DSM-5 - ADHD confirmed (n=38) vs no ADHD (n=31)
Bijlenga (2019)[80] Netherlands, Germany & Sweden; two-gate design (healthy controls)	QbTest (12-60); QbTest (12-60) + Clinical judgment (Symptom severity self-report scale)	ADHD group: **Adults** (age 55+); DSM-4-TR ADHD diagnosis (n=97) Healthy controls: Adults (age 55+) with score below cutoff on symptom severity measures (n=112) matched on age and gender
Brunkhorst-Kanaan (2020)[70] Germany; one-gate	QbTest (12-60)	**Adults** referred to specialist outpatient clinic for suspected ADHD diagnosis **DSM-5**: Diagnostic Interview for ADHD in Adults (DIVA) interview. ADHD confirmed (n=94); no ADHD (n=20)

Author, Design & Location	Test	Population and reference standard
Edebol (2013)[81] Sweden & Germany; Two-gate design (healthy controls)	QbTest (12-60)	ADHD group: **Adults** diagnosed with ADHD following clinical assessment adhering to DSM-4. Non-ADHD control group: Healthy **adults** with no known psychiatric diagnoses.
Edebol (2012)[78] Sweden; four-gate design (diseased and healthy controls)	QbTest (12-60)	ADHD group: DSM diagnosis (version not specified) (n=53) B/B group: diagnosed with borderline / bipolar (n=45) Disconfirmed ADHD (n=29)[retained for analysis] Healthy controls (n=179)
Edebol (2011)[86] Sweden; one-gate design	QbTest (12-60)	**Adults** awaiting clinical assessment of ADHD. DSM-4 - clinical assessments. ADHD confirmed (n=12) and no ADHD group (n=7)
Hult (2018)[69] Sweden; one-gate	QbTest (6-12)	**Children** (age 6-12 years) with suspected ADHD, autism, or another neurodevelopmental disorder. Diagnosis based on DSM-4; assessed by multi-professional team. ADHD confirmed (n=124); no-ADHD (n=58)
Johansson (2018)[72] Sweden; one-gate	QbTest (12-60)	**Adolescent** (age 15) population with high occurrence of neurodevelopmental disorders, including ADHD **K-SADS-PL** interview confirmed ADHD (n=89) and no ADHD (n=248)
Pettersson (2018)[84] Sweden; one-gate design	QbTest (12-60)	**Adults** referred for ADHD assessment; ADHD diagnosed based on expert clinical assessment (DSM-4), SCID-I, SCID-II. ADHD confirmed (n=60) and no ADHD group (n=48)
Sharma (2009)[64] UK; unclear design	QbTest (6-12) or QbTest (12-60)	**Children & Adolescents** (aged 5-15 years, n=50) selected from QbTest database, which were evaluated for ADHD as per local protocol or as diagnosed by child/ family guidance Assessment of disruptive behaviour pathway used locally as standard; no. with/ without ADHD not reported.
Soderstrom (2014)[76] Sweden; one-gate	QbTest (12-60)	**Adults** referred to neuropsychological clinic for ADHD assessment **DSM-4**: Clinical assessment confirmed ADHD (n=41) and no ADHD (n=20)
Stevanovic (2023)[41] Sweden; one-gate	QbTest (6-12) & QbTest (12-60)	**Children** and **adults** referred for evaluation of suspected neurodevelopmental/ psychiatric disorder. Diagnosis based on clinic's standard diagnostic procedure (no further information). ADHD confirmed (n=708); no-ADHD (n=220)
Tallberg (2019)[68] Sweden; one-gate	QbTest (6-12)	**Children** who screened positive for ADHD and were referred for further assessments in Child and Adolescent Psychiatry (CAP) clinic. Diagnosis based on DSM-4. ADHD confirmed (n=80); no-ADHD (n=38)
QbMini		
Hamadache (2021)[29] Germany; three-gate design (healthy and diseased controls)	QbMini	**Children** (age 5): ADHD based DSM-4 (n=37) Specific language impairment (n=27)

Author, Design & Location	Test	Population and reference standard
		Healthy controls: tested at pre-schools and found to be normally developing (n=55)
QbCheck		
Ulberstadt (2020)[79] Germany, Sweden, USA Two-gate (healthy controls)	QbCheck	**Adolescents and adults** (12-59 years) Cases: DSM-5 diagnostic criteria (n=69). Controls: Healthy controls; those with high levels of inattention/hyperactivity/ impulsivity according to DSM-5 excluded (n=73).
Nesplora Kids (AULA)		
Rufo-Campos(2012)[65] Not reported; two-gate	Nesplora Kids (AULA)	**Children** (age not reported) ADHD group: children diagnosed with ADHD – no further information reported (n=62) Non-ADHD group: children without ADHD diagnosis - no further information reported (n=62)
Zulueta (2019)[75] Spain; two-gate (healthy controls)	Nesplora Kids (AULA)	**Children** (age 6-16 years) ADHD group: fulfilled DSM-5 criteria; recruited from outpatient department (n=213) Healthy control group: from schools and neurology clinics minimal ADHD symptoms and no other behavioural disorder (n=194 included)
EPELI		
Seesjarvi (2022)[77] Finland; two-gate (healthy controls)	EPELI	**Children** (age 9-12 years) ADHD group (n=38): ADHD diagnosis by licensed physician using ICD-10 Non-ADHD group (n=38): No mental or behavioural disorder; matched to cases.

Risk of bias

Only three of the 21 studies were judged at low risk of bias across all QUADAS-2 domains, three were judged at unclear risk of bias and fifteen were judged at high risk of bias (Table 5 and Table 44 in Appendix 2).

Eleven studies were judged at high risk of bias for the **patient spectrum** domain. Ten studies were judged high risk because they used a two-gate design where studies recruited a group of patients with known ADHD and a group without ADHD, either a healthy control group or a group of patients with an alternative diagnosis. One other study (the AQUA trial) was judged as high risk for this domain because participants were only eligible for the DTA sub-study if they had a diagnostic decision at 6 months (94/123 participants in QbTest group and 76/127 in the control group).

None of the studies were judged at high risk of bias for the **index test** domain although nine were judged at unclear risk of bias as they did not provide sufficient information on how the sensor CPT was evaluated or on the threshold to determine a "positive" test result. Whilst the QbTest does not specify a threshold for positivity so there is no standard threshold that

can be applied, it is important that study authors pre-specify any threshold that is used to dichotomise results.

Four studies were judged at high risk of bias for the **reference standard** domain –one study used the K-SADS-PL criteria (Table 2) which is not specific for ADHD and so may not be as accurate as DSM or ICD criteria, and in two studies information on the sensor CPT was available to the person interpreting the reference standard results, in one of these the ADHD diagnosis was made based on criteria used within the clinic rather than on accepted criteria such as the DSM-5 criteria. The AQUA trial used independent consensus diagnosis by two independent child psychiatrists based on the DAWBA criteria, which is considered an accepted reference standard. However, it was judged at high risk of bias for the reference standard domain as in 123/241 participants, DAWBAs were missing from one informant (i.e. either parent or teacher) meaning the independent assessors did not have access to this information when making a diagnosis. A further seven studies were judged at unclear risk of bias – five did not provide sufficient information to judge whether the reference standard was interpreted blind to the index test results and in three studies it was unclear whether the reference standard was likely to correctly classify participants as having ADHD.

Eight studies were judged at high risk of bias for the **flow and timing** domain due to a large number of enrolled participants not being included in the analysis.

Table 5 Results of the QUADAS-2 assessment of risk of bias in DTA studies included for objective 1

	Patient selection	Index test	Ref stand	Patient flow	Overall bias	Rationale
Adamou (2022)[83]	☺	☺	?	☺	?	Unclear whether ref standard interpreted blind to QbTest results.
Bijlenga (2019)[80] *Qb test alone*	☹	?	☺	☹	☹	Two-gate design. No information on threshold. High proportion of drop-outs (25/234).
Brunkhorst-Kanaan (2020)[70]	☺	☺	☺	☺	☺	No concerns
Edebol (2013)[81]	☹	☺	☺	☹	☹	Two-gate design. 4/55 ADHD group excluded from analysis.
Edebol (2011)[86]	☺	☺	☺	☺	☺	No concerns
Edebol (2012)[78]	☹	☺	?	☺	☹	Four-gate design. Limited details on reference standard.
Emser (2018)[85]	☹	?	☺	☺	☹	Two-gate design. No information on threshold for Qb-Test + clinical assessment or on blinding of ref standard.
Groom (2016)[82]	☹	?	☺	☹	☹	Two-gate design. No information on blinding of QbTest to case/control status. No detail on threshold. High proportion of drop-outs (5/37 in ADHD group).
Hamadache (2021)[29]	☹	?	☺	☺	☹	Mutli-gate design. Limited details on QbMini.

	Patient selection	Index test	Ref stand	Patient flow	Overall bias	Rationale
Hollis (2018)[18]	☹	☺	☹	☺	☹	Participants eligible for DTA sub-study if diagnostic decision had been made at 6months (QbOpen eligible sample n=94/123; QbBlind n=76/127) Ref standard diagnosis made using limited data for around 50% participants as either parent or teacher assessment missing.
Hult (2015)[69]	☺	☺	☺	☺	☺	No concerns
Johansson (2018)[72]	☺	?	☹	☹	☹	Reference standard K-SADS-PL – not ADHD specific and so may not correctly diagnose ADHD. High proportion of participants excluded from 2x2 table.
Pettersson (2018)[84]	☺	☺	?	☺	?	Unclear if reference standard blind to QbTest result.
Rufo-Campos(2012)[65]	☹	?	?	?	☹	Two-gate design; no details about conduct/ interpretation of index test, reference standard, or flow and timing
Seesjarvi (2022)[77]	☹	?	☺	☹	☹	Two-gate design; patients with other listed comorbidities excluded from cases and controls. No information on whether Epeli test interpreters were blinded to diagnosis; high proportion excluded from 2x2 table.
Sharma (2009)[64]	?	?	?	?	?	Very limited information available from conference abstract
Soderstrom (2014)[76]	☺	☺	☹	☺	☹	Clinicians aware of QbTest results when interpreting reference standard.
Stevanovic (2023)[41]	☺	☺	☹	☹	☹	Unlikely that ref standard interpreted blind to index test; insufficient details on reference standard but was based on clinic records not DSM criteria. High proportion of drop-outs.
Tallberg (2019)[68] - accuracy	☺	?	?	☹	☹	High proportion of missing data. Unclear if ref standard was blinded to QbTest; was not blinded to other tests evaluated.
Ulberstadt (2020)[79]	☹	?	☺	☹	☹	Two-gate design. Unclear who interpreted the test and if blinded to ADHD status. 7/149 patients were not included in 2x2 table.
Zulueta (2019)[75]	☹	?	☺	☺	☹	Two-gate design. No information on test interpretation or threshold.

Concerns regarding applicability

Six studies were judged at low concerns regarding applicability, three at unclear concerns and 12 at high concerns (Table 5 and Table 44 in Appendix 2). All ten studies that used a two-gate design were considered to have concerns regarding applicability as they did not enrol a group of participants with suspected ADHD. Two of the one-gate studies were also considered to have concerns regarding applicability as they enrolled a selected subgroup to assess for ADHD – both enrolled participants with a high level of neurodevelopmental/ neuropsychological disorders. Concerns regarding applicability were high for the index test for one study – in this study the conduct of the QbTest did not follow the manufacturers instructions. In a further 11 studies the applicability was judged as unclear for the index test

as there were insufficient details on how the sensor CPT was performed. Five studies were judged at unclear concerns regarding applicability for the reference standard domain as there were insufficient details on the reference standard to determine how this was classifying ADHD.

Table 6 Results of the QUADAS-2 assessment of concerns regarding applicability of DTA studies included for objective 1

	Patients	Index test	Ref stand	Overall	Rationale
Adamou (2022)[83]	☺	☺	☺	☺	No concerns
Bijlenga (2019)[80]	☹	☺	☺	☹	Two-gate design
Brunkhorst-Kanaan (2020)[70]	☺	?	☺	?	Limited details on test conduct
Edebol (2013)[81]	☹	☺	☺	☹	Two-gate design
Edebol (2011)[86]	☺	☺	☺	☺	No concerns
Edebol (2012)[78]	☹	☺	?	☹	Four-gate design; Limited details on reference standard
Emser (2018)[85]	☹	?	☺	☹	Two-gate design; Limited details on test conduct
Groom (2016)[82]	☹	?	☺	☹	Two-gate design; Limited details on test conduct
Hamadache (2021)[29]	☹	?	☺	☹	Three-gate design. Limited details on test conduct
Hollis (2018)[18]	☺	☺	☺	☺	No concerns
Hult (2015)[69]	☺	☺	☺	☺	No concerns
Johansson (2018)[72]	☹	?	?	☹	High proportion of neuro-developmental disorders - unlikely to be reflective of population with symptoms of ADHD.
Pettersson (2015)[84]	☺	☺	☺	☺	No concerns
Rufo-Campos(2012)[65]	☹	?	?	☹	Two-gate design. Limited details on index test conduct & interpretation; no details about reference standard
Seesjarvi (2022)[77]	☹	?	☺	☹	Two-gate deign; Limited details on test conduct
Sharma (2009)[64]	?	?	?	?	Very limited information available from conference abstract
Soderstrom (2014)[76]	☺	☺	☺	☺	No concerns
Stevanovic (2023)[41]	☹	☹	?	☹	Children referred for evaluation of various neuropsychological conditions (not just ADHD). Test conduct did not follow manufacturers instructions.
Tallberg (2019)[68] - accuracy	?	?	☺	?	Children had screened positive for ADHD and so were referred for further evaluation – unclear if representative of review population.
Ulberstadt (2020)[79]	☹	?	☺	☹	Two-gate design. Limited details on test conduct.
Zulueta (2019)[75]	☹	?	☺	☹	Two-gate design. Limited details on test conduct.

Accuracy of QbTest plus clinical information

Four studies[18, 80, 82, 85] provided information on the accuracy of QbTest in combination with clinical information; one of these studies reported results separately for QbTest (12-60) and for QbTest (6-12) (Figure 2). We did not identify any studies of any of the other sensor CPTs in combination with clinical information.

The Hollis (2019) AQUA trial was the only study to combine the QbTest information with clinical assessment in the same way that it would be used in practice. Other studies constructed prediction models that combined information from specific clinical scales with results from the QbTest. The Hollis (2019) and Groom (2016) studies used an overall combined output from the QbTest. Bijlenga (2019) used information from the hyperactivity and inattention domains and Emser used individual QbTest outputs. Table 7 provides a summary of the clinical information used and how studies combined this with QbTest results. As the type of clinical information and QbTest data used varied across studies, it was not considered appropriate to pool data.

The AQUA trial used the more reliable one-gate design, all others used a two-gate design. Risk of bias was high for all studies that used a two-gate design. The AQUA trial was also judged at high risk of bias due to limitations with the reference standard and restriction to those with a diagnosis at 6 months.

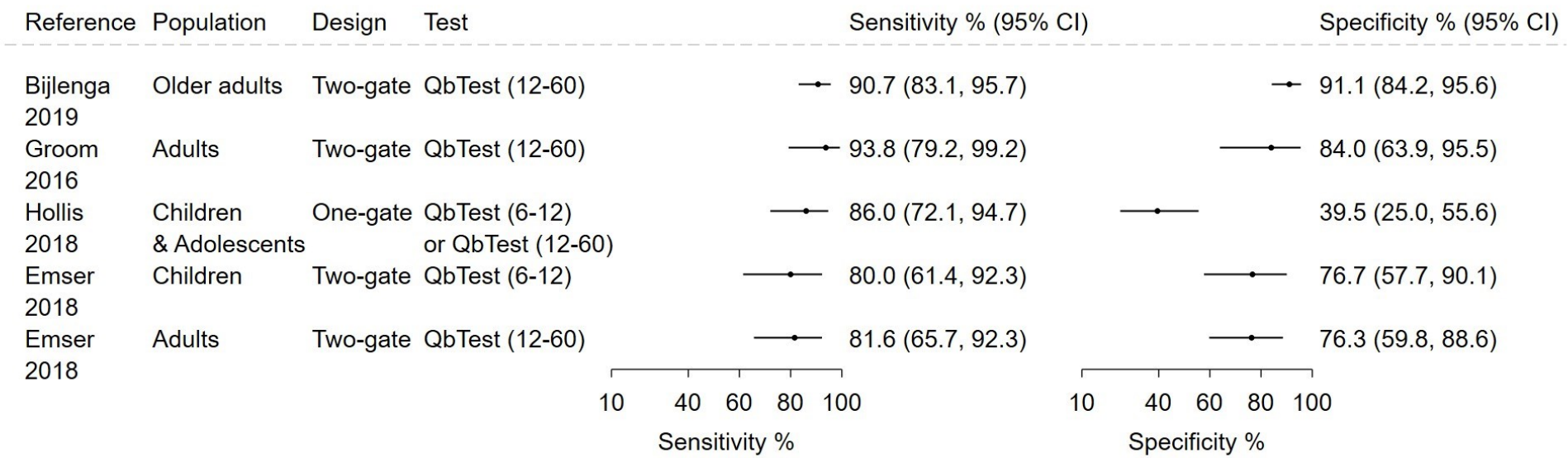
Estimates of sensitivity ranged from 80% (95% CI 61, 92%) to 94% (95% CI 79, 99%). Estimates of specificity ranged from 40% (95% CI 25% to 56%) to 91% (95% CI 84, 96%), but were above 76% for all but the AQUA trial. It is likely that the limited information available to those making the reference standard diagnosis may have resulted in the diagnosis being too stringent - this would have resulted in more false-positive results leading to an underestimate of specificity. Restriction to those with a diagnosis at 6 months is likely to have overestimated the accuracy of the test, as those without a diagnosis are more likely to be a difficult to diagnose group.

Table 7 Overview of how studies combined clinical information with QbTest results

Study author (date)	Details of "QbTest + clinical information"
Bijlenga (2019)[80]	QbTest + self-reported ADHD symptom severity: Several self-report questionnaires were used to assess symptom severity, ADHD-RS was used in the Netherlands, which assesses the DSM-4-TR ADHD symptoms.[98] In Sweden, the Swedish version of the ADHD Symptom Rating Scale (ASRS v1.1) was used which also assesses DSM-4-TR ADHD criteria.[99] In Germany, the German version of the Conners' Adult ADHD Rating Scale (self-report long version) (CAARS-S:L) was used, which assesses DSM-4 ADHD criteria.[100] In order to establish a unified symptom severity outcome, the total scores per patient were transformed into a 0% to 100% score, taking into account the score range of each measure. This unified outcome was called the "ADHD symptom severity score". The authors conducted two binary logistic regressions- the first model included only QbTest factors (QbHyperactivity and QbInattention) and the second model included

Study author (date)	Details of "QbTest + clinical information"
	both QbTest factor scores and self-reported ADHD symptom severity. Estimates of sensitivity and specificity were derived from the models; details on how this was done were not reported.
Emser (2018)[85]	QbTest + objective clinical assessment (KiTap and TAP): Three subtests from the TAP (test battery of attention)[101] and KiTAP (child version of the test battery of attention)[102] were used: Go/NoGo task, divided attention and sustained attention. The authors provided accuracy of ADHD diagnosis using the output from the QbTest and TAP tasks. The authors developed prediction models that combined the QbTest components and TAP assessment variables. Estimates of sensitivity and specificity were derived from the models; details on how this was done were not reported.
Groom (2016)[82]	QbTest + Conners Adult Rating Scale and Autism Quotient-10: Self- and observer-reported symptom ratings were collected from all participants using the E-ADHD Subscale of the Conners Adult ADHD Rating Scale (CAARS-E),[103] which measures ADHD symptoms, and the Autism Quotient-10 (AQ-10), which screens for autism spectrum disorders.[104] The authors conducted binary logistic regression to combine data from the QbTest composite score with data from the CAARS-E and AQ-10. Sensitivity and specificity were calculated based on the % of participants correctly assigned to the ADHD and ASD control groups.
Hollis (2018)[18]	Usual diagnostic workup (typically this included an interview with the child and their family, and the completion of at least one standardised informant-based behavioural assessment measure) with QbTest results available to clinician

Figure 2 Forest plot showing estimates of sensitivity and specificity with 95% confidence intervals for studies that evaluated sensor CPTs in combination with clinical assessment



Accuracy of QbTest

Thirteen studies evaluated the accuracy of the QbTest alone (Figure 3, Figure 4Figure 5 and Figure 5). Three studies evaluated the version for children aged 6-12,[41, 68, 69] 10 studies evaluated the version for older children and adults aged 12-60,[41, 70, 72, 76, 78, 80, 81, 83, 84, 86] one evaluated both versions,[64] and one evaluated both versions, reporting data separately for the different age-groups.[41] Where reported, thresholds ranged from 1.25 to 1.5, with most studies using a threshold of 1.5. Estimates of the accuracy of QbTest evaluated in isolation were generally lower than when evaluated in combination with clinical judgement

QbTest – Overall

Six studies reported an overall measure of QbTest based on the three subcategories – all evaluated the version in adolescents or adults. Three studies, all by Edebol,[78, 81, 86] evaluated a measure that they called "prediction of ADHD (PADHD)". This was based on qualitative analyses of raw scores from the different QbTest subcategories. The studies by Johansson and Adamou based the total score on the mean of the three subcategory scores.[72, 83] Two studies were judged at high risk of bias as they used a two-gate design[83, 86] the others were judged at low risk of bias.

Estimates of sensitivity ranged from 67% (95% CI 57, 77%) to 87% (95% CI 75, 95%) with a summary estimate of 79% (95% CI 69, 86%). Estimates of specificity were slightly lower and ranged from 41% (95% CI 24, 61%) to 83% (95% CI 77, 88%) with a summary estimate of 60% (41, 76%). There was some suggestion that sensitivity was higher in two gate studies, the highest estimate of specificity was from a two-gate study that enrolled a healthy control group. None of the studies reported AUC data for the overall combined measure, although one provided AUC data for the QbTest subcategories.[72] None reported data on sensitivity and specificity for the QbTest subcategories.

One study (not shown on the plots) conducted in older adults and judged at low risk of bias, only provided data for a combination of scores across the QbActivity and QbInattention subcategories.[80] Estimated sensitivity was 56% (95% CI 45, 66%) and specificity was 83% (75%, 0.89%). Another study (not shown on plots), available only as an abstract, did not provide any information on what QbTest output were used for the analysis.[64] This study reported a sensitivity of 96% (95% CI 82, 100%) and specificity of 81% (95% CI, 58 95%).

QbTest – sub-categories

Six studies evaluated the accuracy of subcategories of the Qbtest – QbActivity, QbImpulsivity or QbInattention. One of the studies provided data separately for the QbTest (6-12) and QbTest (12-60) versions of the test. Two studies were judged at high risk of bias as they used a two-gate design, the others were at low risk of bias. All studies provided data on the AUC – all provided data on the QbActivity and QbInattention scores and five provided data on the QbImpulsivity scores (Figure 5). Summary estimates of AUC were similar across the three domains ranging from 0.58 (95% CI 0.55, 0.61) to 0.63 (95% CI 0.58, 0.68). The summary estimate of sensitivity was lowest for QbImpulsivity (42%, 95% CI 32, 52%), followed by QbInattention (46%, 95% CI 38, 54%) and was highest for QbActivity (60%, 95%

CI 47, 7s%), although confidence intervals overlapped for all estimates. Summary estimates of specificity were similar for QbImpulsivity (78%, 95% CI 67, 86%) and QbInattention (77%, 95% CI 63, 87%) and was lower QbActivity (64%, 95% CI 78, 77%), although confidence intervals also overlapped for these estimates. There was little evidence of a difference in accuracy of the tests between adults and children for all accuracy measures across all domains. Note that summary estimates that combined data from the different age groups are more different than summary estimates stratified based on age. This is because the combined data are summarised using random effects models whereas stratified data are summarised using fixed effects models due to the small number of studies.

QbCheck

One study, Uberstadt (2020)[79] evaluated the accuracy of the QbCheck test – the remote version of the QbTest. This study used a two-gate design with healthy controls and so was considered at high risk of bias. Estimated sensitivity for the overall results (unclear how this was calculated) was 83% (95% CI 72, 91%) and specificity was 79% (95% CI, 68, 88%) (Figure 6). Estimates of sensitivity and specificity were not reported for the individual components of the QbCheck test, but AUC data were reported (Figure 5). Estimates ranged from 0.73 (95% CI 0.65, 0.81) to 0.81 (95% CI 0.74, 0.88) with confidence intervals overlapping for all estimates.

QBMini

One study, Hamadache (2021)[29] evaluated the QbMini test – the version of the QbTest designed for children aged 4-5 years. This study was judged at high risk of bias as it used a two gate design with two control groups – healthy controls and those with specific language impairment. We selected the group with language impairment for analysis, as healthy controls are more likely to overestimate specificity. The study only reported AUC data for the three subcategories of the test – QbActivity, QbInattention and QbImpulsivity. The AUC were close to 0.5 suggesting no discriminative ability of the test (
Figure 7).

Accuracy of EFSim Test (previously known as ARVO and EPELI)

Only one study provided data on the accuracy of the EFSim test – referred to in the paper as the EPELI test. This study was judged at high risk of bias as it used a two-gate design with healthy controls in which controls were matched to cases – this is not appropriate for evaluation of test accuracy. There was also a high proportion of missing data from the 2x2 table. It reported estimates of sensitivity, specificity and AUC for various subcategories of the tests as well as for a single overall measure. AUC estimates ranged from 0.70 (95% CI 0.58 to 0.82) for the overall measure to 0.83 (95% CI 0.74, 0.92) for the Task Efficacy measure (Figure 5). Estimates of sensitivity ranged from 61% (95% CI 43, 76%) for the Actions measure to 76% (60, 89%) for the Navigation Efficacy and Overall measures. Estimates of specificity ranged from 55% (95% CI 38, 71%) for the overall measure to 89% (95% CI 75, 97%) for the Task Efficacy and Actions measures.

Accuracy of Nesplora Attention Kids Aula

Two studies evaluated the accuracy of the Nesplora Attention Kids AULA test; there were no studies of the adult version of this test. Both studies were judged at high risk of bias as they used a two-gate design with healthy controls.[75] One study reported an overall estimate of sensitivity of 68% (95% CI 61, 74%) and specificity of 75% (95% CI 68, 81%). The other study available only as an abstract, reported that the test had an overall accuracy of 93.5% but did not provide any further information or report data separately for sensitivity and specificity.

Figure 3 Forest plot showing individual study and summary estimates of sensitivity and specificity with 95% confidence intervals for studies that evaluated the QbTest stratified according to QbTest domain

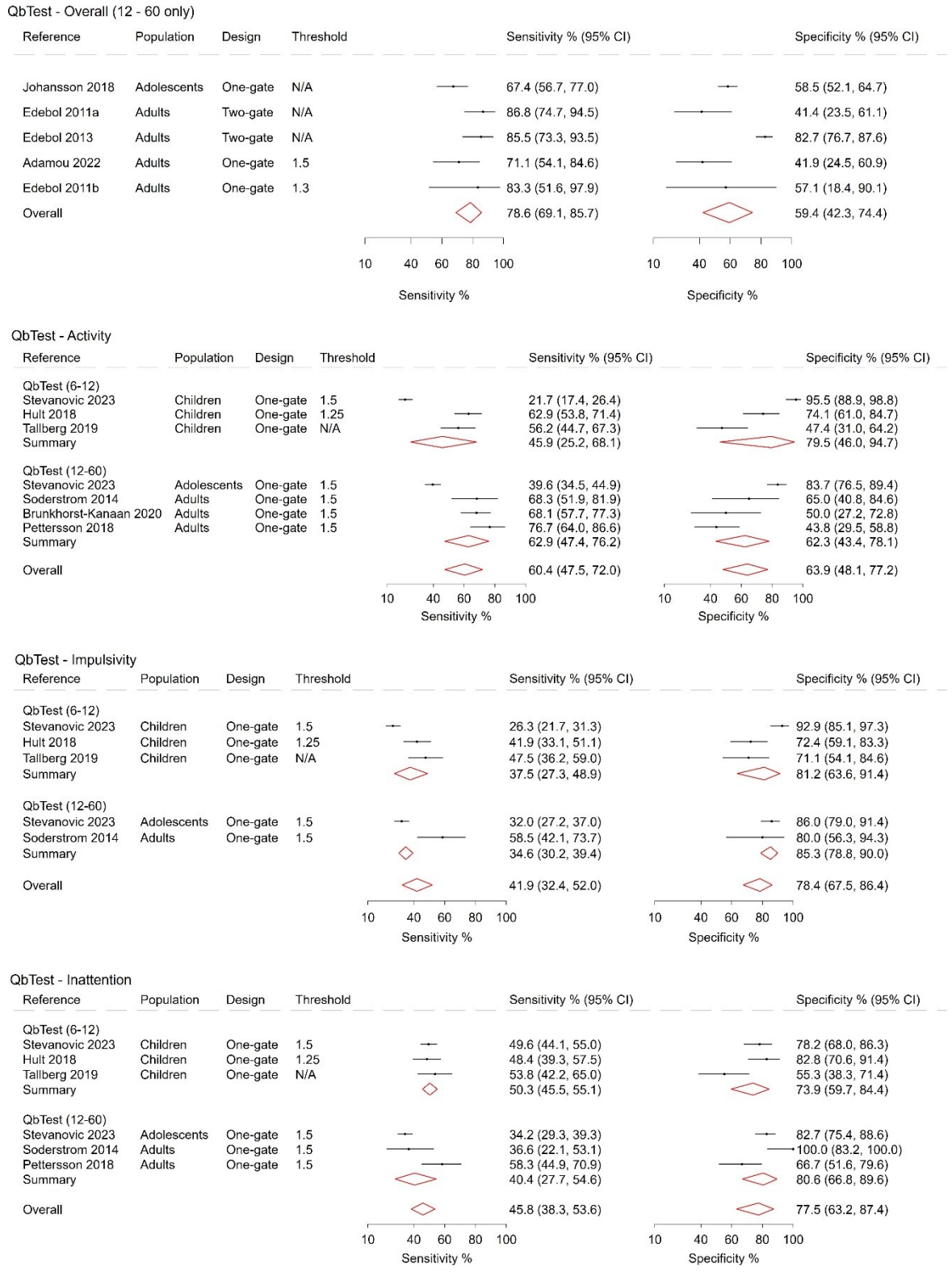


Figure 4 Individual study and summary estimates of sensitivity and specificity with 95% confidence intervals plotted in SROC space for studies that evaluated the QbTest, stratified according to QbTest domain

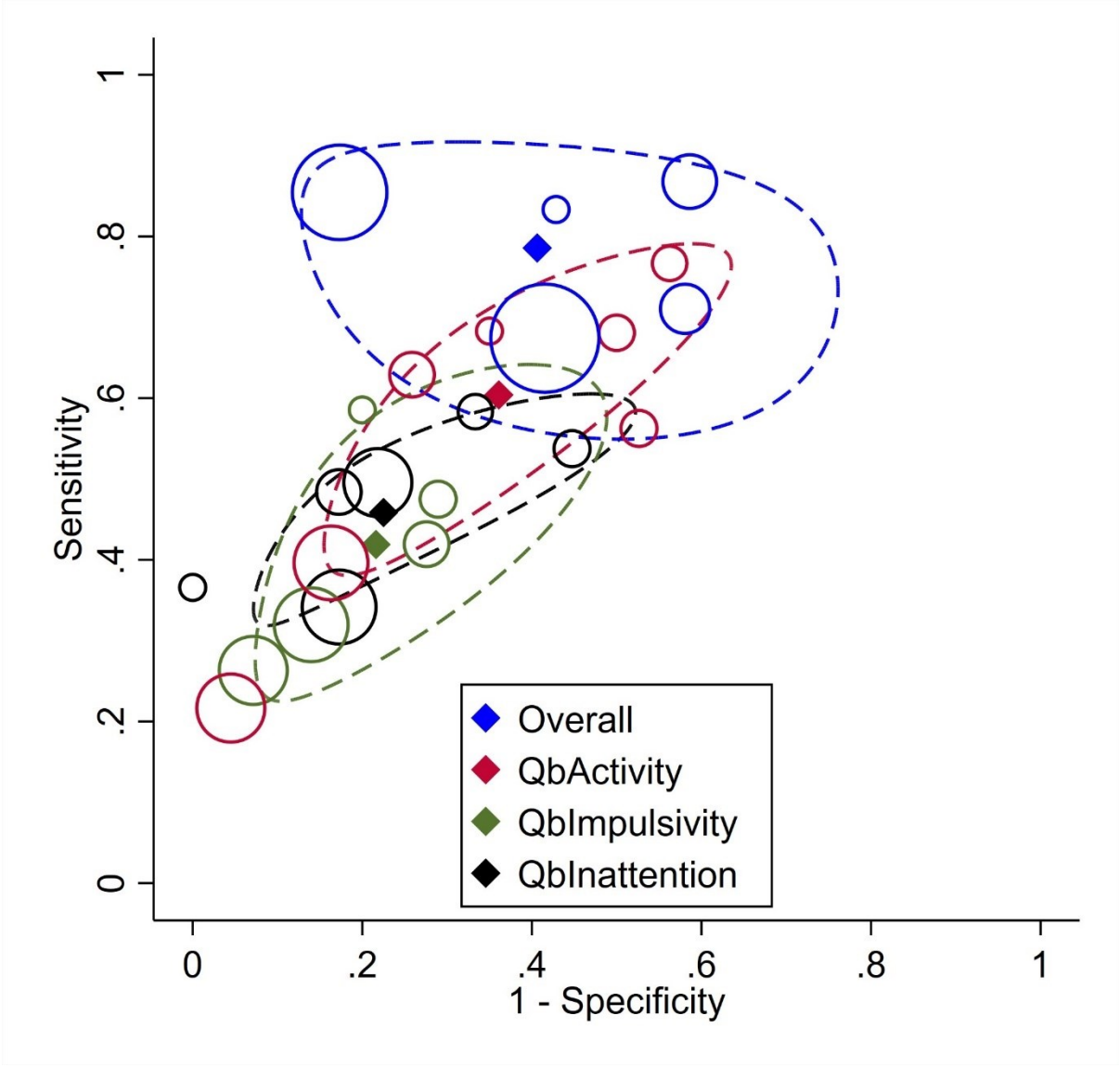


Figure 5 Forest plot showing estimates of area under the receive operator characteristic curve (AUC) with 95% confidence intervals for studies that evaluated the QbTest stratified according to QbTest domain

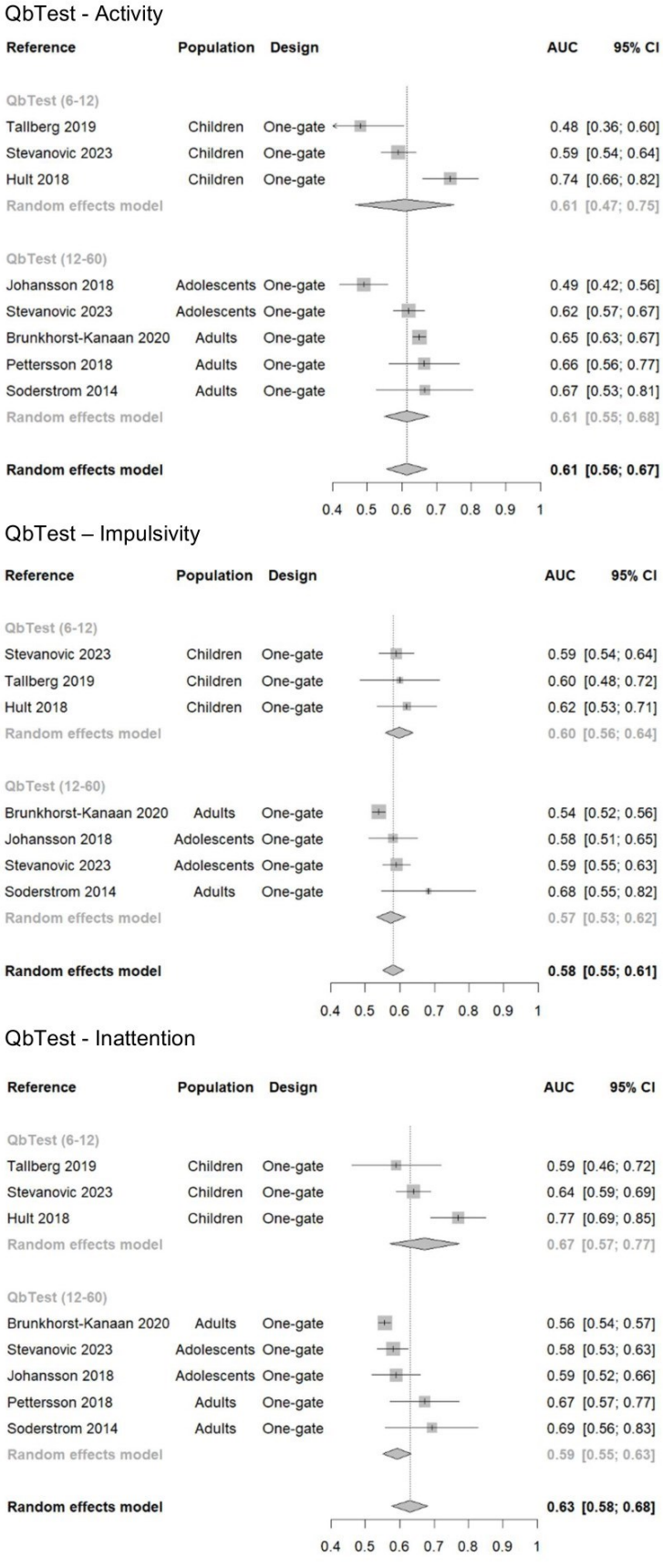


Figure 6 Forest plot showing estimates of sensitivity and specificity with 95% confidence intervals for sensor CPTs that were evaluated in single studies

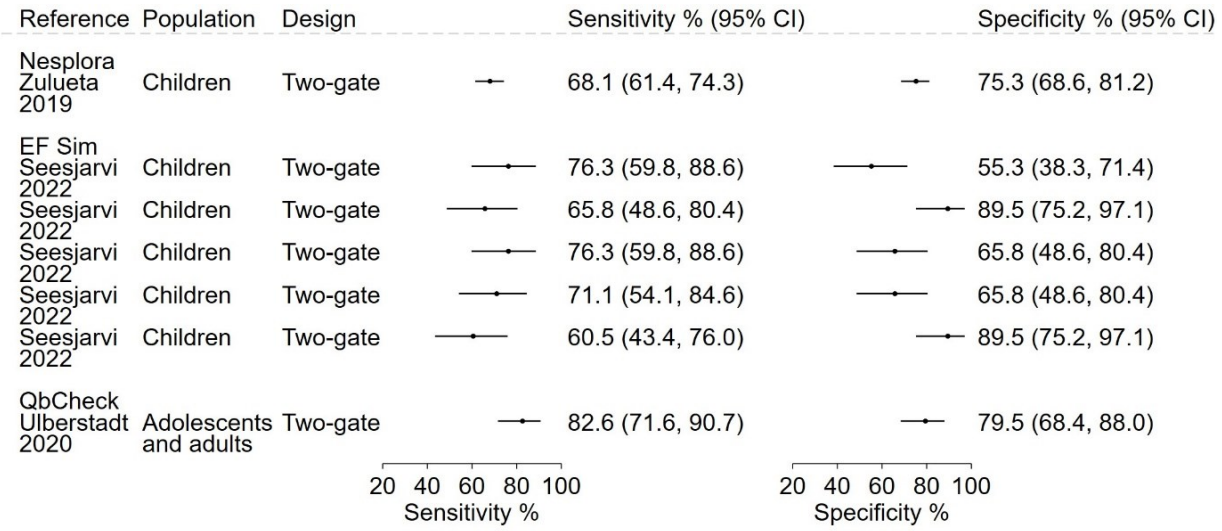
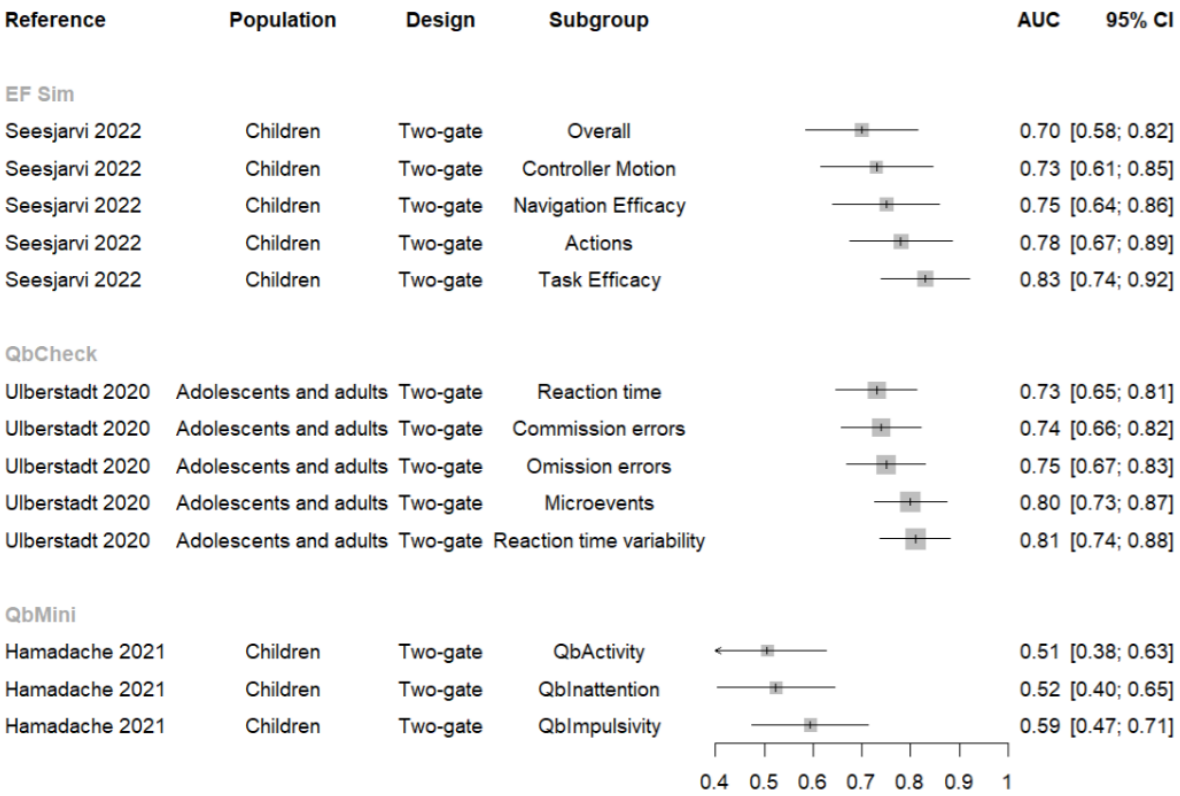


Figure 7 Forest plot showing estimates of area under the receive operator characteristic curve (AUC) with 95% confidence intervals for sensor CPTs that were evaluated in single studies



Comparison of sensor CPTs with non-sensor CPTs or clinical diagnosis alone

Three studies provided a direct comparison between non-sensor CPT and sensor CPTs,[68, 77, 84] one study compared QbTest alone to QbTest combined with clinical symptoms,[80] and the AQUA trial compared QbTest combined with clinical diagnosis to clinical diagnosis alone. [18] Results are summarised in Figure 8 and Figure 9. There were insufficient data to allow full cross-classification of results. Formal comparisons between estimated sensitivity and specificity was performed for each measure reported in each study (Table 8).

Four studies provided a paired comparison of tests i.e. all participants received both tests; the AQUA trial randomised participants to diagnosis incorporating the QbTest or to clinical diagnosis alone. Both designs are considered appropriate to compare the accuracy of multiple index tests. Four studies were judged at high risk of bias and one at unclear risk of bias. The only limitations in the studies identified by the QUADAS-C assessments in addition to those identified by the standard QUADAS-2 assessment, were that the only study in which information was provided on whether each tests was interpreted blind to the other was the AQUA trial, as participants were randomised to testing groups.

Seesjarvi (2022)[77] compared three measures from a non-sensor CPT[105] with the EF Sim test. The overall EF Sim measure was more sensitive than the non-sensor CPT omission errors measure (p=0.03), but was less specific (p=0.07). There was no difference between the overall EF Sim measure and the other two CPT measures.

Petterson (2018)[84] and Tallberg (2019)[68] provided a direct comparison between the Connors' CPT II[106] and the QbTest (12-60). The Petterson study reported that all three of the Qb measures (QbActivity, QbInattion and QbOmmision errors) were more sensitive (p≤0.01) but less specific than CPT II commission errors and CPT II reaction time variability. There was no difference for QbTest reaction time variance. In contrast, Tallberg reported that the QbTest was less sensitive (p<0.01) than the CPT II with no difference in specificity.

The AQUA trial[18] compared QbTest (6-12) or QbTest (12-60) plus clinical judgement ("QbOpen"), to a control group using the standard diagnostic process ("QbBlind"; in this group the QbTest was also conducted, but the results were not shared with the clinician or used to guide diagnosis). Both groups were evaluated against independent consensus diagnosis using DAWBA, the limitations with this reference standard are highlighted above. The two groups had very similar specificity: 40% (95% CI 25 to 56) for QbOpen and 36% (95% CI 1 to 58) for QbBlind (OR 1.16 (95% CI 0.38, 3.71), p-value = 0.80). Sensitivity was slightly higher in the QbBlind group (96%, 95% CI 87 to 100) compared to the QbOpen group (86%, 95% CI 72 to 95), but there was no statistical evidence of a difference between groups (OR 0.26 (95% CI 0.02, 1.53), p-value = 0.14).

The study by Bijlenga (2019)[80] in older adults presented a comparison between models based on the QbTest alone and a model that incorporated a clinical measure of ADHD symptoms (Table 7). The model that incorporated the clinical information was much more

sensitive (91%, 95% CI 83, 96) than the QbTest alone (56%, 95% CI 45, 66; p<0.01)). There was no evidence for a difference in specificity (p=0.11).

Figure 8 Forest plot showing estimates of sensitivity and specificity with 95% confidence intervals for studies that compared multiple index tests

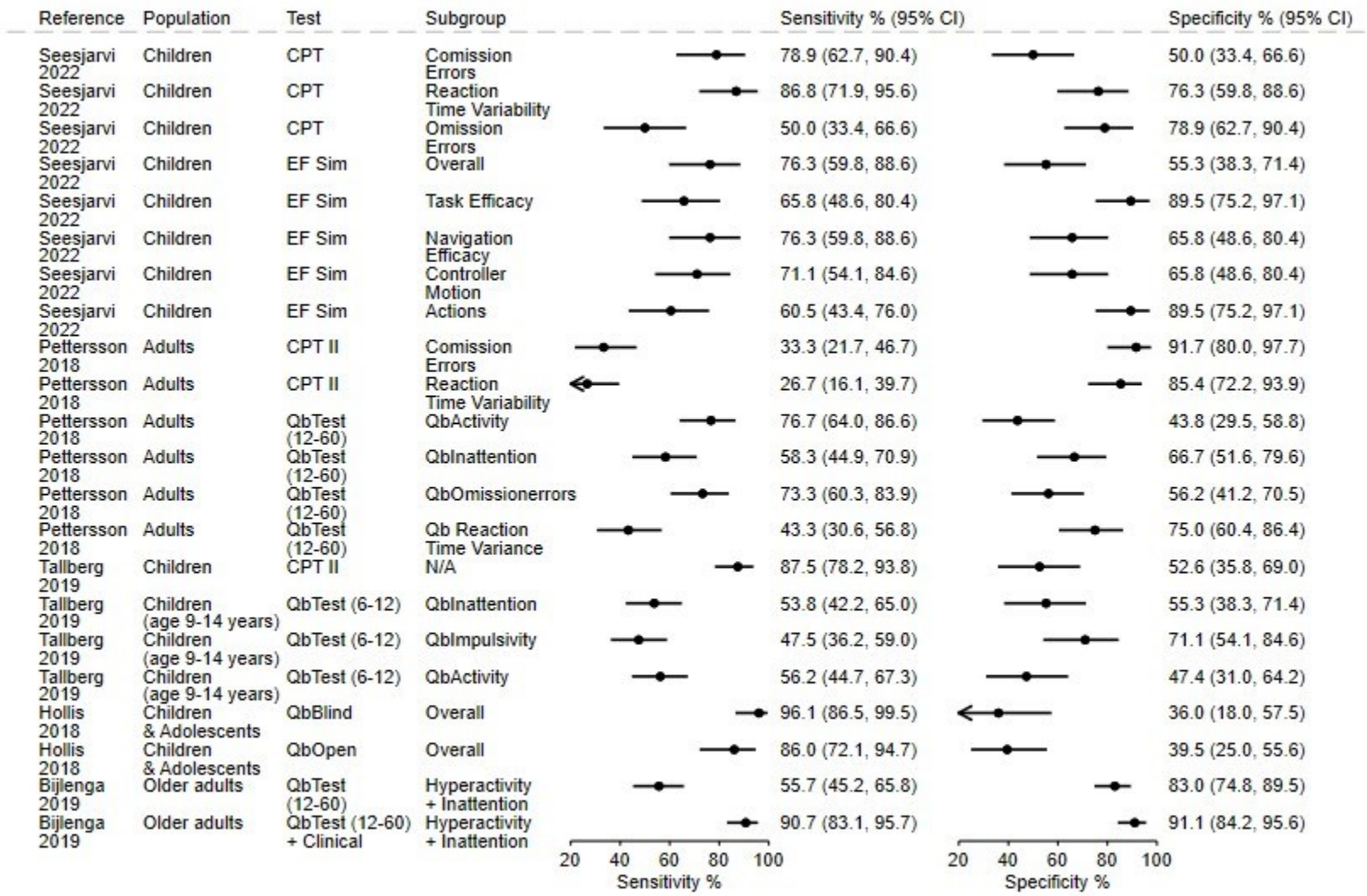


Figure 9 Forest plot showing estimates of area under the receive operator characteristic curve (AUC) with 95% confidence intervals studies that estimated the accuracy of a non-sensor CPT and sensor CPT on the same participants

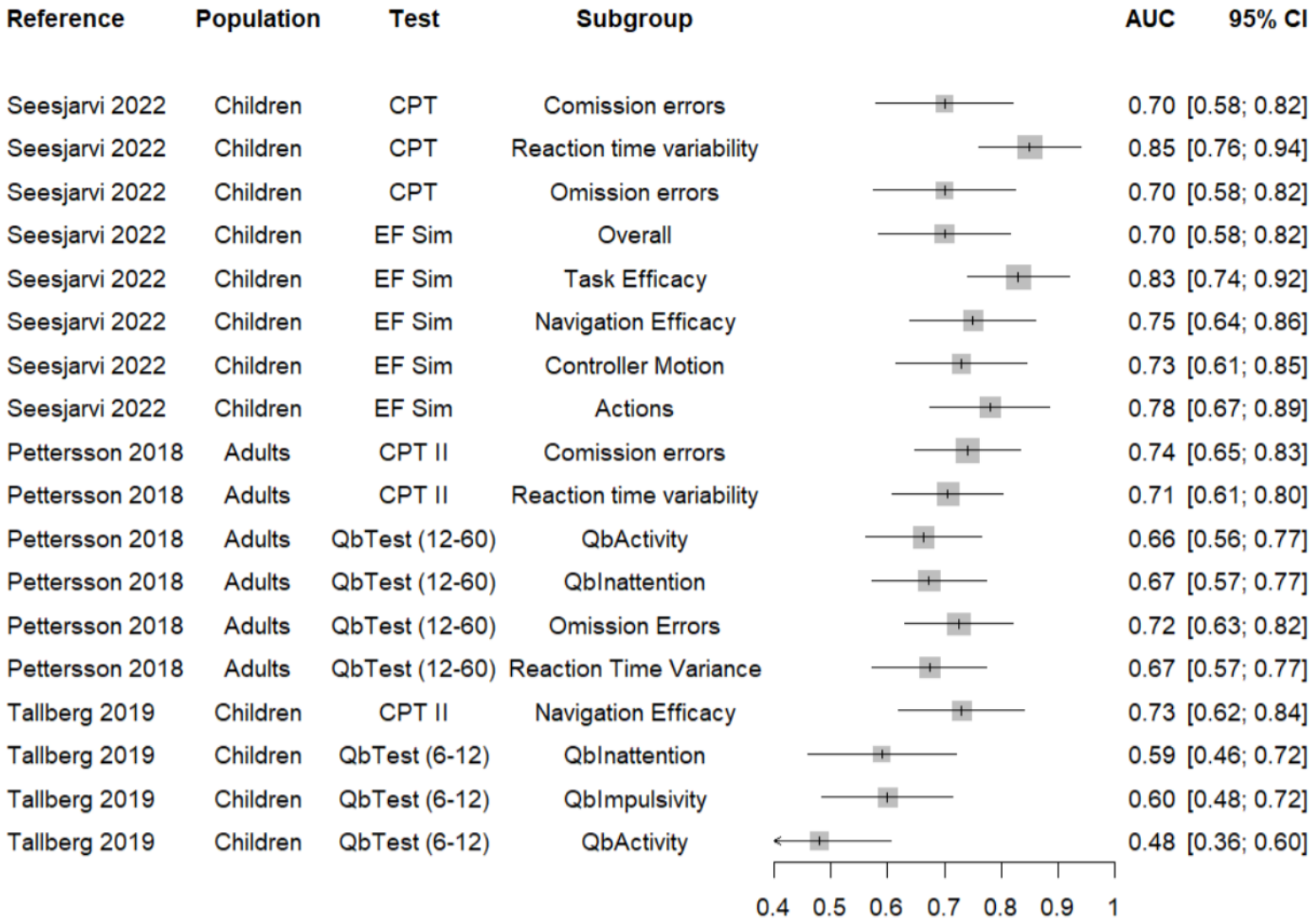


Table 8 Formal statistical comparisons of sensitivity and specificity within studies that compared multiple index tests

Test 1	Test 2	OR (95% CI) Sensitivity	p-value Sensitivity	OR (95% CI) Specificity	p-value Specificity
Seesjarvi, 2022 in Children					
CPT – commission errors	EF Sim - Overall	1.16 (0.34, 3.99)	1	0.81 (0.30, 2.19)	0.82
CPT – reaction time variability	EF Sim - Overall	2.03 (0.54, 8.64)	0.38	2.57 (0.88, 7.95)	0.09
CPT – omission errors	EF Sim - Overall	0.32 (0.10, 0.91)	**0.03**	2.99 (1.00, 9.61)	**0.05**
Pettersson, 2018 in Adults					
CPT – commission errors	QbActivity	0.15 (0.06, 0.36)	**<0.01**	13.71 (4.07, 60.83)	**<0.01**
CPT – commission errors	QbInattention	0.36 (0.16, 0.80)	**0.01**	5.41 (1.55, 24.34)	**<0.01**
CPT – commission errors	Omission Errors	0.18 (0.08, 0.43)	**<0.01**	8.36 (2.46, 37.13)	**<0.01**
CPT – commission errors	Qb Reaction Time Variance	0.66 (0.29, 1.46)	0.35	3.62 (0.99, 16.73)	**0.05**
CPT – reaction time variability	QbActivity	0.11 (0.04, 0.27)	**<0.01**	7.36 (2.59, 23.50)	**<0.01**
CPT – reaction time variability	QbInattention	0.26 (0.11, 0.60)	**<0.01**	7.36 (2.59, 23.50)	**<0.01**
CPT – reaction time variability	Omission Errors	0.13 (0.05, 0.32)	**<0.01**	2.90 (0.98, 9.38)	**0.05**
CPT – reaction time variability	Qb Reaction Time Variance	0.48 (0.20, 1.09)	0.08	1.94 (0.62, 6.48)	0.31
Tallberg, 2019 in Children					
CPT II	QbInattention	5.95 (2.58, 14.86)	**<0.01**	0.90 (0.33, 2.44)	1
CPT II	QbImpulsivity	7.63 (3.32, 19.04)	**<0.01**	0.46 (0.16, 1.29)	0.16
CPT II	QbActivity	5.39 (2.33, 13.46)	**<0.01**	1.23 (0.46, 3.34)	0.82
Hollis, 2018 in Children & Adolescents					
QbOpen	QbBlind	0.26 (0.02, 1.53)	0.14	1.16 (0.38, 3.71)	0.8
Bijlenga, 2019 in Older adults					
QbTest + Clinical	QbTest	7.70 (3.37, 19.43)	**<0.01**	2.08 (0.87, 5.27)	0.11

4.2.3 Impact of sensor CPTs for diagnosis of ADHD on process measures

Ten studies provided data on process measures (Table 9). This included the AQUA trial[18] and five studies conducted in England that compared results before and after implementation of QbTest (referred to as "before-after implementation studies").[31, 66, 71, 87, 88] Although our inclusion criteria specified that we would only consider before-after studies conducted in the UK, we did not find any studies conducted outside of the UK. Four of the studies that evaluated accuracy (section 4.2.2) also provided additional data on test failure rates.[77, 79, 80, 82] All studies were conducted in children and adolescents (age <18 years).

The AQUA trial compared usual care with QbTest (6-12 and 12-60 depending on age), with test results available to clinician ("QbOpen") to a control group where diagnosis was based on the usual diagnostic pathway. The QbTest was also performed in the control group but test results were withheld from the clinician (and so this arm was described as "QbBlind") and so did not form part of the diagnostic workup of patients. Participants received the QbTest during one of their first 3 appointments with 98.4% having received the test by their

second appointment. The primary outcome was the number of consultations until a diagnostic decision confirming or excluding the diagnosis of ADHD.

The five before-after implementation studies explored the impact of implementing the QbTest in addition to standard diagnostic assessment, by comparing data from clinical records, pre- and post- QbTest implementation in England. One study was restricted to cases with a diagnosis of ADHD, selecting 40 cases diagnosed without QbTest and 40 cases diagnosed with QbTest.[87] The other four studies all selected a group of patients that had been evaluated for suspected ADHD prior to the introduction of the QbTest and a group of patients evaluated for suspected ADHD who had received the QbTest as part of their diagnostic workup. Sample size ranged from 20 to 549 patients in each group, in one study the sample size was unclear, the authors only state that 20-30 children per site across 3 sites (so 60 to 90 total) were enrolled.

Table 9 Overview of studies that evaluated the impact of sensor CPTs for diagnosis of ADHD on process measures

Author, Design & Location	Group 1	Group 2	Population
Hall (2016)[87] UK; uncontrolled before-after implementation study	QbTest + standard ADHD assessment (n=40)	Standard ADHD assessment (Strengths and difficulties questionnaire (SDQ) and school information form to parents/ teachers; Conners' parent and teacher rating scales; child developmental history taken by clinician) (n=40)	**Children and adolescents** (4.5-14.6 years) with ADHD diagnosis confirmed in community paediatric clinic
Hollis (2018)[18] UK; RCT with embedded qualitative evaluation and accuracy data (DTA sub-study) AQUA trial	Usual care + QbTest (6-12 and 12-60), with test results available to clinician ("QbOpen") (n=123)	Usual care + (6-12 and 12-60), with test results withheld from clinician ("QbBlind") (n=127)	**Children and adolescents (**6-17 years) referred for first ADHD assessment in child and adolescent mental health services (CAMHS) or community paediatric clinics in England
Vogt (2011)[88] UK; uncontrolled before-after implementation study	QbTest + standard ADHD assessment (n=62)	Standard ADHD assessment (clinical interview by psychiatrists, medical examination, rating scales (e.g. SDQ; Conners) to parents/ teachers) (n=46)	**Children and adolescents** (Qb Group mean age 9; control mean age 10.5) referred for ADHD assessment in CAMHS
Sharma (2022)[66] UK; uncontrolled before-after implementation study	QbTest + standard ADHD assessment (n=20)	Standard ADHD assessment (no detail provided) (n=20)	**Children** (mean age 11.7yr, SD 2.4) referred for ADHD/ non-specific behavioural problems/ ASD who completed ADHD assessment in hospital paediatric clinic

Author, Design & Location	Group 1	Group 2	Population
Humphreys (2018)[71] UK; uncontrolled before-after implementation study (East Midlands AHSN) + survey	QbTest + standard assessment (unclear)	Standard assessment (no detail provided) (n=unclear)	**Children and adolescents** (5-16 years) referred for ADHD assessment in 8 community paediatric mental health settings in 3 NHS trusts
McKenzie (2022)[31] UK; uncontrolled before-after implementation study ("Focus ADHD") plus survey and qualitative study	QbTest + standard assessment (n=549)	Standard assessment (no detail provided) (n=549)	**Children** referred for ADHD assessment in 20 CAMHS and paediatric sites
Bijlenga (2019)[80] The Netherlands; Germany; Sweden; Two-gate DTA study	QbTest (12-60) (n=234)	N/A – only process measure data the study reported is test failure rate for the sensor CPT	**Adults** ADHD group: Adults (age 55+); DSM-4-TR ADHD diagnosis Healthy controls: Adults (age 55+) with score below cutoff on symptom severity measures, matched on age and gender
Groom (2016)[82] UK; Two-gate DTA study	QbTest (12-60) (n=84)		**Adults** ADHD group: DSM-5 diagnosis of ADHD. Autism (ASD) group: ICD10 diagnosis of Asperger's syndrome
Seesjarvi (2022)[77] Finland; Two-gate DTA study	EPELI (n=115)		**Children (age 9-12 years)** ADHD group: ADHD diagnosis by licensed physician using ICD-10 Non-ADHD group: No mental or behavioural disorder; matched to cases.
Ulberstadt (2020)[79] Germany; Sweden; USA; Two-gate DTA study	QbCheck (n=149)		**Adolescents and adults** (12-59 years) Cases: DSM-5 diagnostic criteria. Controls: Healthy controls; those with high levels of inattention/hyperactivity/ impulsivity according to DSM-5 excluded.

Risk of bias

The AQUA trial was judged as being at high risk of bias for outcomes involving time to event data (number of consultations to diagnostic decision, minutes spent at clinic appointments, number of clinic appointments, number of days to diagnostic decision), based on the RoB 2 assessment (Table 48).[18] This was due to a large proportion of participants being censored from the analysis as they dropped out or were discharged from the clinic and so did not

have a diagnosis at 6 months – 29/123 in the QbTest group and 51/127 in the control group. Reasons and numbers for drop-outs and discharge from clinic were not reported. The analysis for these outcomes assumed that participants were uninformatively censored and so had equivalent outcomes to those for whom full follow-up data were available. It was unclear how cost data were calculated, and how censored participants contributed to these data, and so the trial was judged at unclear risk of bias for this outcome. The trial was judged at low risk of bias for other outcomes (proportion of participants with a diagnostic decision, diagnostic status, diagnostic confidence and stability of diagnosis). Health-related quality of life (HRQoL) was pre-specified as an outcome in the study protocol and the data were not reported, therefore there is potential for selective reporting in the trial.

All five implementation studies that reported on process measures were judged as being at serious risk of bias based on the ROBINS-I tool assessment. Four were rated as serious risk of bias due to confounding.[31, 71, 87, 88] This was because important confounders (age at the point of seeking ADHD referral, sex, comorbidities, nature and severity of symptoms at presentation, socioeconomic status, and ethnicity) were not controlled for and there was potential for confounding of the effect of intervention. Additionally, one of these studies (Focus ADHD) was confounded by the COVID-19 pandemic, which coincided with the "post-Qb Implementation" group in the trial. The confounding domain was judged as "no information" for the other study, due to being a conference abstract with very limited detail.[66] This study was, however, rated at serious risk of bias due to the selection of participants, as participants were excluded if their assessment resulted in an inconclusive diagnosis or they did not have a diagnosis in the timeframe.[66]

Of the other four studies, one was rated at low risk due to random selection of cases,[87] and three were rated as no information.[87, 107] Three studies were rated at low risk for bias in deviations due to intended interventions,[31, 87, 88] one study was rated as no information due to being a conference abstract with limited detail,[66] and the other study was rated as moderate risk of bias due to there having been a full pathway redesign of the service in 2/3 sites after the introduction of the QbTest.[71] One study was rated as moderate risk of bias for missing data (people with a final diagnosis were selected, so we do not know the number of individuals referred who never received a diagnosis)[87] one as no information,[71] and three as low risk of bias.[31, 66, 108] All studies were rated at low risk for bias in the classification of interventions, as intervention groups were clearly defined. All studies were rated as moderate risk of bias for measurement of the outcomes (measurement of the outcome may have been influenced by knowledge of the intervention received) and for selection of the reported result (no protocol).

The four DTA studies that also reported process measures were judged as being high risk of bias, based on the QUADAS-2 assessment.[77, 79, 80, 82]

Results

Table 10 provides a summary of results from studies that evaluated the impact of introducing the QbTest as part of the diagnostic process for ADHD on process outcomes. Very few studies provided a formal statistical comparison of results between intervention groups.

Time to diagnostic decision

Five studies reported data on time to diagnostic decision. The AQUA trial reported that the number of appointments required to reach a consultation was less in the QbTest group compared to control (HR 1.44, 95% CI 1.04, 2.01; p=0.029). When results were stratified by QbTest version, only those using the QbTest (6-12) version were found to have fewer appointments (HR 1.84, 95% CI 1.23, 2.68; p=0.001), this was not seen in the QbTest (12-60) group (HR 0.82; 95% CI 0.37, 1.80; p=0.618). The AQUA trial also reported that the mean number of appointments to a diagnosis was slightly less in the QbTest arm compared to control (2.69 vs 2.72). [redacted] The time spent at clinic appointments until diagnosis was less in the QbTest group compared to the control group (median 150 mins vs 165 mins; time ratio 0.85; 95% CI 0.77, 0.93; p=0.001). There was also a suggestion that the number of days to diagnosis was less in the QbTest group, but the evidence for this was weak (median 96 vs 108 ; time ratio 0.90 (95% CI 0.73, 1.10; p=0.285). However, the HR and TR estimates should be interpreted with some caution due to the large proportion of participants who were censored ((i.e. dropped out of the study or were discharged from clinic). Estimates are based on an analysis of the full dataset where those without a diagnosis are censored after their last appointment, under the assumption that they would have similar hazard or time ratios as those that had a diagnosis.

Four of the before-after studies also reported on the number of consultation to reach a diagnosis – in all studies this was reported to be less following implementation of the QbTest, although only one study reported strong evidence for a difference between groups (p=0.02), another study reported no difference between groups (p>0.05) and the other two studies did not make a formal comparison between groups. Two of the before-after studies also reported that time to diagnosis was reduced following implementation of the QbTest, but did not provide a statistical comparison of results. The Focus ADHD reported that time from referral to diagnosis (p<0.01) and time to reach a diagnostic decision (p-value not reported) were increased in the period following implementation of the QbTest, but these data are likely to have been confounded by the Covid-19 pandemic.

Impact on clinical decision making

The AQUA trial reported improved diagnostic decision making (diagnostic decision was made for 76.4% (95%CI 68.9%, 83.9) in QbTest group compared to 59.8% (95%CI 51.3%, 68.4%) in the control group at 6 months); OR=2.43 (95% CI 1.34, 4.39) and greater confidence in the diagnostic decision (p=0.022). Clinician confidence in the diagnostic

decision was greater in the QbTest group compared to control (OR 1.77, 95% CI 1.09, 2.89). There was no difference in the stability of the diagnosis over time (change from when the diagnosis was first confirmed) (p=0.32). They also reported that ADHD could be ruled out in more cases within the QbTest group (RRR 2.14, 95% CI 1.00, 4.59). As highlighted above, these data should be interpreted with some caution due to the exclusion of those who dropped-out or who were discharged from clinic. The Focus ADHD study reported that fewer children were diagnosed with ADHD after the QbTest was implemented (76%) compared to the control period (81%). They also reported that fewer in school observations were used to help make the ADHD diagnosis in the post-QbTest group (9%) compared to the control group (22%), however, these data are likely to have been influenced by the Covid-19 pandemic.

Outcomes at 1 year follow-up

The Vogt (2011) study reported outcomes of patients at 1-year follow-up and found no difference between groups in the proportion of children in each of the following categories (p=0.24): ADHD diagnosis changed, medication trial, continuing on medication, discontinued medication and lost to follow-up. It reported that a higher proportion of children who had initially been diagnosed as not having ADHD receiving a revised diagnosis of ADHD at 1-year follow up in the control group (37%) compared to none in the QbTest group.

Cost

The AQUA trial reported that the cost of clinic appointments was slightly less in the QbTest group (£87.62) compared to control (£90.06). The study by Hall also reported that costs were lower following QbTest with an average cost per patient for a diagnosis of £265.90 following introduction of the QbTest and £329.40 prior to introduction of the QbTest. Neither study provided a formal statistical comparison between groups.

Test failure rate

Four DTA studies, all two-gate designs, provided data on test failure rate.[77, 79, 80, 82] Two studies reported test failure rate for the QbTest (12-60). One reported that 25/234 (11%; 9 ADHD, 16 controls) participants had an unavailable test result. Reasons for missing results included: not understanding the task, being an extreme outlier, not following instructions, technical errors, and aborted tests.[80] The other study reported that 4/84 (5%) had an unavailable test result, described as non-completion of the test (no further information provided).

The study that evaluated QbCheck reported that 7/149 (5%; 6 ADHD, 1 control) of participants had an unavailable test result. Reasons included failure to complete the test due to technical problems with the camera (2), participant ending test in the middle of the session for unknown reasons (4), and intentionally discontinuing the test (1).[79] The study that evaluated the EFSim (EPELI version) test reported that 22/115 (19%; 5 ADHD, 17 controls) had an unavailable test result, due to technical failures or human error (no further information provided).[77]

Table 10 Overview of results from studies that evaluated the impact of sensor CPTs for diagnosis of ADHD on process measures

Outcome category	Outcome details	Hollis AQUA trial[18]	Hall (2016)[87]	Vogt (2011)[88]	Sharma (2022)[66]	Humphreys (2018)[71]	McKenzie (2022)[31] Focus ADHD
Time to diagnostic decision	No. consultation to ADHD diagnosis	Diagnosis rate (appointment number units): HR 1.44, 95% CI 1.04, 2.01 (p=0.03); 1.84 (1.23, 2.68) 6-12y; 0.82 (0.37, 1.82) 12-17y Mean number of appointments to diagnosis: QbTest: 2.69 (SD=0.85) Control: 2.72 (SD=0.91)	IRR = 0.71 (95% CI 0.54, 0.94); p=0.02		Qb Test: Mean 2.4 (SD 0.8) Control: Mean 2.7 (SD 0.7); p>0.05	Qb Test: 0.24 to 1.04 less per child Control: range 3 to 8 appts	Qb Test: Mean 2.85 (Range 1-32) Control: Mean 3.22 (range 1-50)
	Time from referral to diagnosis				Qb Test: 5.5 (SD 1.8) months Control: Mean 6.5 (SD 3) months	*Qb Test:* Average ranged from 15-252 days *Control:* Average ranged from 161-453 days	Qb Test: Mean 507 (Range 43-1281) days Control: Mean 452 (Range 15-3276) days; p<0.01*
	Total consultation time	Median time to diagnosis: QbTest: 150 (95% CI 140, 155) Control: 165 (95% CI 150, 180) mins Time ratio 0.85 (95% CI 0.77, 0.93)					

Outcome category	Outcome details	Hollis AQUA trial[18]	Hall (2016)[87]	Vogt (2011)[88]	Sharma (2022)[66]	Humphreys (2018)[71]	McKenzie (2022)[31] Focus ADHD
	Days to reach diagnostic decision	QbTest: Median 96 (95% CI 85, 99) Control: Median 108 (95% CI 91, 140) Time ratio 0.90 (95% CI 0.73, 1.10)					Qb Test: Mean 129 (Range 0-1378) Control: Mean 117 (Range 0-1570)
Impact on clinical decision making	Proportion of patients with a diagnosis	OR=2.43 (95% CI 1.34, 4.39)					
	Stability of diagnosis	No difference, p=0.032					
	Number with ADHD diagnosis						Qb Test: 418/549 (76%) Control: 445/549 (81%)
	Confidence in diagnostic decision	OR 1.77 (95% CI 1.09, 2.89)					
	Number in whom ADHD diagnosis excluded	RRR 2.14 (95% CI, 1, 4.59)					
	Number of children in whom school observations utilised						Qb Test: 49/549 (9%) Control: 120/549 (22%)
Outcomes at 1 year follow-up	Outcomes for those with ADHD			No difference between groups (p=0.24)			
	Diagnosis of ADHD in those with			Qb Test: 0/19			

Outcome category	Outcome details	Hollis AQUA trial[18]	Hall (2016)[87]	Vogt (2011)[88]	Sharma (2022)[66]	Humphreys (2018)[71]	McKenzie (2022)[31] Focus ADHD
	diagnosis rejected at initial assessment			Control: 7/19 (37%) P<0.0035			
Cost	Cost of clinic appointments *(unclear how costed)*	Qb test: £87.62 Control: £90.06					
	Cost per patient to diagnosis		Qb Test: £265.90 Control: £329.40				

4.2.4 Clinician and patient views of sensor CPTs for diagnosis of ADHD

Eight studies evaluated clinician, patient or carer views of sensor CPTs for the diagnosis of ADHD, collected through surveys, qualitative interviews or focus groups.[31, 71, 74, 77, 79, 89, 90, 109] Five evaluated the QbTest, [31, 71, 74, 89, 109] one assessed the QbCheck,[79] and two assessed the EFSim test.[77, 90] An overview of these studies is provided in Table 11 and further details are outlined in

Appendix 3.

Of the five studies that evaluated the QbTest, two combined qualitative interviews and a survey. One was conducted as part of the FACT feasibility RCT (in the very specific population of young boys in a young offenders institute)[74] and the other as part of the AQUA trial.[109] Two studies were implementation studies included for section 4.2.3.[31, 71]. One reported survey data from patients, families and clinical staff who had used QbTest on their experience of using the test,[71] and one (Focus ADHD) reported both qualitative interview data from staff and survey data from patients, families and staff on their experiences of using the QbTest.[31] All four of these studies were conducted in England. The remaining study was a mixed methods study that reported focus group data and survey data concerning clinicians, young service users, and their families' experiences of using QbTest in addition to standard ADHD assessment in CAMHS.[89] This study, which was conducted in Ireland, only provided data on patient and/or clinicians views and so was only included for this section of the review.

The study that evaluated the QbCheck test (in Germany, Sweden and the USA),[79] and one of the studies that evaluated the EF Sim test (in Finland),[77] were DTA studies included in section 4.2.2 that reported survey data from patients on the ease of use/ acceptability of the tests. The other study of the EF Sim test, included in the manufacturer submission from Peili Vision, only reported survey data on views of the test and therefore was only included for this section of the review. This study was a pilot project in which 50 students in Finland completed the EF Sim test, and survey data were gathered from teachers [redacted] about their experience of using the test.[90]

Table 11 Overview of studies that evaluated clinician and/or patient views of sensor CPTs for diagnosis of ADHD

Author, Location, Design & Test	Study components
Studies with interview and survey data	
Chitsabesan (2022)[74, 110] England; Interview and survey components of FACT feasibility RCT; QbTest + standard assessment	1. Semi-structured interviews with 6 adolescent boys from the QbTest group of the FACT trial 2. Semi-structured interviews with 1 research assistant and 5 staff members who used QbTest in the FACT trial 3. Survey completed by 10 adolescent boys from the QbTest group of the FACT trial
Hollis (2018)[109] England; Qualitative sub-study of AQUA trial; Usual care + QbTest (6-12 and 12-60), with test results available to clinician ("QbOpen")	1. Semi-structured interviews with the 10 clinical leads of sites involved in the AQUA trial 2. Semi-structured interviews with 20 families from the AQUA trial "QbOpen" Group 3. Survey completed by the 10 clinical leads and 76 families involved in AQUA trial
McKenzie (2022)[31]	1. Interviews with 21 healthcare staff involved in implementation of QbTest at their site, or conducting the test/ interpreting test results, in the Focus ADHD study.

Author, Location, Design & Test	Study components
England; Qualitative interview and survey components of an uncontrolled before-after implementation study (Focus ADHD); QbTest (6-12) or QbTest (12-60) + standard ADHD assessment	2. Survey completed by 65 healthcare staff involved in the Focus ADHD study 3. Survey completed by 22 patients who had been assessed with the QbTest in the Focus ADHD study
Pellegrini (2020)[89] Ireland; Mixed methods study of real-world impact of test implementation; QbTest + standard ADHD assessment	1. Focus groups with 19 clinicians who were using the QbTest in one of the three CAMHS teams selected for this study in Ireland 2. Survey to 17 clinicians, 15 young people and their parents/guardians (n=18) who had used QbTest in one of the three CAMHS involved in this study
Studies with survey data only	
Humphreys (2018)[71] England; Survey component of an uncontrolled before-after implementation study; QbTest (6-12) or QbTest (12-60) + standard ADHD assessment	1. Survey completed by 48 patients (children who had ADHD assessment using QbTest in CAMHS in the before-after study) and their families 2. Survey to staff who had used QbTest in the study (n = unknown)
Peili Vision (NR)[90] Finland; Pilot cohort study; EF Sim test + psychologist evaluation	1. Survey completed by 21 teachers of participating schools that used EF Sim for students in the Health Service Pilot [redacted]
Seesjarvi (2022)[77] Finland; Survey data from two-gate DTA study; EF Sim (EPELI version)	1. Survey completed by children (some with ADHD; some healthy controls – n=not reported) who took part in the DTA study using EF Sim (EPELI version) test and completed the survey component
Ulberstadt (2020)[79] Germany, Sweden, USA; Survey data from two-gate DTA study; QbCheck	1. Survey completed by patients who used QbCheck in the DTA study and who completed the survey (n=125; 59 ADHD and 69 healthy controls)

Risk of bias

Qualitative study components

Two of the four studies that provided qualitative data on patient and carer views had no concerns regarding study quality based on the CASP checklist assessment. This was the qualitative component of the study by Pellegrini (2020),[89] which involved focus groups with 19 clinicians who had used the QbTest in CAMHS in Ireland, and the qualitative sub-study of the AQUA trial, which involved interviews with clinicians and families who had used the QbTest in the trial.[109]

The other two studies appeared to use appropriate methodology but they reported limited detail which made it difficult to judge certain items in the CASP checklist. In Chitsabesan (2022; reports interview data as a secondary outcome of the FACT feasibility RCT) and McKenzie (2022; reports on the interview component of the Focus ADHD study), there were

limited details on the relationship between researcher and participant and data analysis and so it was not possible to fully assess the quality of the approach taken.[31, 74]

Survey study components

Two of the eight studies that provided survey data on patient and carer views had very few concerns regarding study quality based on the Q-SSP assessment: the AQUA trial sub-study,[109] and Pellegrini (2020).[89] The other six studies were judged to have some concerns due to a lack of information about participants, methodology, and analysis.[31, 71, 74, 77, 79, 90]

Results

Below, we summarise our synthesis of findings from these studies. The full synthesis is presented in Appendix 4.

QbTest

We identified two broad themes from the findings concerning the QbTest: views around the helpfulness of the test and barriers to the implementation of the test. Conceptual categories that pertained to views around the helpfulness of the QbTest included contribution to ADHD diagnosis and communication with caregivers.

Findings from qualitative data suggested that healthcare staff felt that the QbTest increased their confidence in decision making,[31, 89, 109] helped to differentiate ADHD subtypes (particularly subtle presentation, common in girls),[31, 109] and supported diagnosis in the presence of comorbidities.[74, 109] Healthcare staff also felt that the test could decrease the time to diagnostic decision.[31, 74, 89, 109] For example, some sites in the Focus ADHD study commented that the QbTest implementation had resulted in fewer appointments by replacing the school observation, and that the faster assessment pathway supported the young person in getting educational support quickly.[31] Families also appeared to feel that the QbTest could have a positive impact on the diagnostic process. They recognised the role that the QbTest could have in shortening the emotionally overwhelming diagnostic procedure and they emphasised the need for a quick diagnostic decision.[109] However, they also felt that the process should not be rushed, and their child should not be "labelled" quickly.[109]

Clinicians valued the perceived objectivity of the test, which they felt added important information to clinical assessments and, in some cases, increased confidence in decision making and reduced the burden on clinician time.[31, 74, 89, 109] However, clinicians also reported a need to establish where the QbTest falls on the ADHD assessment pathway[31, 109] and expressed uncertainty about whether the clinical setting of the test is representative of what happens in other settings (e.g. school).[109]

Findings suggested that the QbTest helped to improve communication between clinicians and patients and their families,[31, 89, 109] between clinicians and schools,[109], between clinical colleagues,[89], and between patients and families.[109] In the AQUA trial, clinicians reported

that being able to show a comparison of the child's performance to a normative sample helped them to communicate the diagnostic decision to families, and they thought that this helped families to accept the decision.[109] However, some clinicians in the Focus ADHD study commented that families could still struggle to accept a diagnostic decision.[31] Some families interviewed in the AQUA trial were unclear about how the QbTest report was being used to inform decision making.[109] This was also reflected in survey responses, which suggested that some families did not think the QbTest helped them to understand how diagnoses were made.[31, 109] Furthermore, some families and young people felt that the results of the QbTest were not properly explained to them,[31] and did not help them to understand symptoms.[74, 109]

Barriers to the implementation of the QbTest

Conceptual categories that pertained to views around barriers to the implementation of the QbTest included practical barriers and acceptability to patients and caregivers. Interviews and focus groups with healthcare staff highlighted that staffing (i.e. the need for someone trained to administer the task), room requirements, and technology were barriers to QbTest implementation.[31, 74, 89, 109]

Concerning patient views on the acceptability of the test, some patients found the test boring, long and repetitive.[31, 74] In the Focus ADHD study,[31] interviews with healthcare staff highlighted that some individuals (particularly young people and people with Autism Spectrum Disorder) experienced sensory discomfort and struggled with wearing the tight headband. Staff commented that other young people struggled to follow the instructions, and felt anxious during the test, due to the test itself and/or being without their caregivers. Additionally, concerns were raised about the lack of representation of different ethnicities in the test explanation video, the requirement to choose biological sex before conducting the test, and the use of the word "test", which staff felt induced stress in participants.[31] The study of QbCheck reported that participants found it easy to use, however this was from a brief three question survey conducted as part of a DTA study.[79]

EF Sim Test

Two studies evaluated the EF Sim Test[77, 90]. One study, run by the test manufacturer, surveyed 21 teachers of participating schools that had implemented the EF Sim test for students in a pilot study. On average, the majority of the teachers found the test results usable and reported that they can support communication with guardians, and that they are helpful to identify executive functioning challenges in students that may otherwise go unnoticed.[90] [redacted] The other study was a DTA study of the EF Sim test (previous version named EPELI) in children (some with ADHD, some healthy controls, n=not reported). Answers to a

short survey suggested that, on average, children appeared to feel enthusiastic about the tasks, found them interesting, and they put effort into their performance on the test.[77]

4.3 Objective 2: Diagnostic accuracy and clinical-effectiveness of sensor CPTs for the diagnosis of ADHD in people referred with suspected ADHD for whom current assessment cannot reach a diagnosis

We did not identify any studies that met inclusion criteria for this objective.

4.4 Objective 3: Clinical- effectiveness of sensor CPTs in evaluating medication effectiveness during initial dose titration and treatment decisions for people with a diagnosis of ADHD

Six studies were included for objective 3 - three RCTs (FACT, QUOTA and AQUA)[74, 109, 111], one DTA study[68] and two implementation studies.[31, 71] All studies evaluated the QbTest. One RCT (the QUOTA trial), that included a qualitative sub-study, was only included for objective 3.[111] The other five studies also contributed to objective 1, one reported data on the accuracy of QbTest for medication dose titration,[70] the other four reported qualitative and survey data on the use of QbTest for medication management. [31, 68, 71, 74, 109]

4.4.1 Diagnostic accuracy of sensor CPTs during initial dose titration and treatment decisions for people with a diagnosis of ADHD

The DTA study by Tallberg (2019)[68] evaluated the accuracy of the QbTest for medication dose titration in children with ADHD (Table 12). The study enrolled a single group of patients with ADHD. They were assessed with the QbTest and a behaviour rating scale for ADHD (Swanson Nolan and Pelham Questionnaire (SNAP-IV)).[112] Before starting treatment with methylphenidate. Dose titration started at a low dose of 18 or 20mg and the dose was titrated in steps of 10 or 18 mg depending on the drug brand to a maximal dose of 60 mg (less in case of side effects). At each dose titration, children were tested with both the SNAP-IV behavioural test and the QbTest. To determine the accuracy of the QbTest for medical titration QbTest results at 1 year follow-up were cross-tabulated with “good” or “poor” outcome. A “good” outcome was defined as being on the optimal dose 1 year after titration as defined by EITHER a SNAP-IV score increase of at least 0.2 (equivalent to 0.4 standard deviations (SD) OR a QbTest score decrease of at least 0.4 SD. This is problematic as the QbTest formed part of the reference standard which is likely to overestimate the accuracy of the test. The study was therefore judged at high risk of bias. Accuracy was estimated separately for the QbInattention and QbActivity subcategories. Sensitivity was estimated at 82% (95% CI 69, 91%) and specificity at 60% (95% CI 26, 88%) for the QbInattention domain, and sensitivity was 76% (95% CI 62, 87%) and specificity 40% (95% CI 12, 74%) for the QbActivity domains.

4.4.2 Impact of sensor CPTs during initial dose titration and treatment decisions for people with a diagnosis of ADHD on patient and process outcomes

The QUOTA trial[111] was a feasibility trial conducted in England that explored the feasibility of conducting an RCT to evaluate the efficacy of the QbTest as part of medication management for children with ADHD. It compared the QbTest protocol in which participants completed

the QbTest at baseline and two follow-up points on medication (2-4 weeks and 8-10 weeks) and control where participants received treatment as usual, that included at least two follow-up consultations. Outcomes evaluated included: use of interventions, impact on clinical decision making, ease of use/ acceptability and confidence in healthcare professional (HCP) assessment. However, as this was a feasibility study it was designed and powered to assess the feasibility of conducting a full trial, not to formally evaluate the impact on outcomes. For this reason a formal risk of bias assessment was also not undertaken for this study. The number of participants was very small with 44 children randomised – 21 to the intervention arm and 23 to the control.

Results suggested that those in the QbTest arm were more likely to have had their medication changed (type of dose of ADHD medication) at the first follow up point (10/18 in intervention vs 7/21 in control), but figures were more similar at follow-up 2 (7/17 in intervention vs 9/19 in control). These findings should be interpreted with caution due to the feasibility design and small sample size it was not possible to draw conclusions regarding clinical effectiveness from this study.

Table 12 Details of studies that provide information on sensor CPTs in evaluating medication effectiveness during initial dose titration and treatment decisions for people with a diagnosis of ADHD

Study	Williams (2021)[111] (QUOTA trial)	Tallberg(2019)[68]
Design	Feasibility RCT	DTA study (one-gate)
Sample size	44 (44 analysed); 21 in intervention arm and 23 in control group	186 (56 analysed)
Population	Children aged 6-15yrs, diagnosed with ADHD and referred to CAMHS/ community pediatric clinic in the UK to commence ADHD medication	Children and adolescents aged 7-18, with ADHD, from a child and adolescent psychiatry clinic in Sweden
Group or Test	Intervention: QbTest(6-12 or 12-60) + usual care Control: Usual care	Index test: QbTest(6-12 or 12-60) + SNAP-IV behaviour rating scale Reference standard: SNAP-IV or QbTest score
Funding	Non-industry	Non-industry

4.4.3 Clinician and patient views of sensor CPTs during initial dose titration and treatment decisions for people with a diagnosis of ADHD

Five studies provided data on clinician and patients views of the QbTest for dose titration and treatment decision making. Three RCTs (FACT, QUOTA and AQUA trials) reported interview and survey data concerning patient and clinician views of the QbTest for medication management and dose titration,[74, 109,111] one implementation study reported patient and carer views of the test from survey data,[71] and one implementation study reported qualitative interview and survey data (the Focus ADHD study).[31]

Risk of bias

Qualitative study components

The AQUA trial had no concerns regarding study quality based on the CASP checklist assessment.[109] The QUOTA trial had very few concerns.[111] The FACT trial[74] and the Focus ADHD study[31] reported limited details on the relationship between researcher and participant and data analysis and so it was not possible to fully assess the quality of the approach taken.

Survey study components

The AQUA trial had very few concerns regarding study quality based on the Q-SSP assessment.[109] The other four studies that contributed survey data were judged to have some concerns due to a lack of information about participants, methodology, and analysis.[31, 71, 74, 111]

Results

Across the five studies that reported on clinician patient views of the QbTest for dose titration and treatment decision making,[31, 71, 74, 109, 111] healthcare staff and families mostly appeared to value the role of the test for dose titration, checking medication utility, and improving medication adherence.

Clinicians interviewed in the AQUA trial qualitative sub-study reported greater support from parents on initiating and continuing medication, and greater adherence to medication, as a result of being able to directly observe the effect of medication with a QbTest.[109] Additionally, families interviewed in the AQUA trial reported that seeing the QbTest results made them more confident that the medication would help their child.[109] This objectivity was also highlighted as a positive in interviews with clinicians in the QUOTA trial, who valued the objectivity of the QbTest in comparison to informant measures traditionally used to monitor medication.[111] Interviews with healthcare staff in the Focus ADHD study also identified that the QbTest could be helpful in dose titration and checking medication utility, and the staff felt that the QbTest helped young people/ caregivers to understand medication decisions and the effects of the medication. This study only involved interviews with staff, not patients/ carers.[31]

Survey data from two studies suggested that patients/ caregivers were not convinced that the results of the QbTest helped them to understand medication decisions.[74, 109] Less than half (20/52) of families surveyed in the AQUA trial felt that it helped them to understand the decisions made about medication, although it is notable that most participants did not commence medication, so the results are difficult to interpret.[109] Likewise, in the FACT RCT, there was no consensus among 10 adolescent boys assessed for ADHD as to whether the QbTest results helped them to understand how the decisions about medication had been made (the majority voted “neither agree/ disagree”).[74] In contrast, interviews with parents (six in the intervention and two in the control group) in the QUOTA trial provided mainly positive feedback. The QbTest was found to increase parents’ confidence in their child’s

treatment and ongoing medication decisions. Parents described how a visual representation of the child's symptoms helped them to better understand treatment impact, though the test was noted to be boring by some and it requires taking time out of school to have multiple appointments to monitor medication.

Some healthcare professionals in the Focus ADHD also felt that the QbTest helped them to decide how effective the medication is, and had increased their confidence in decision making about treatment.[31] In contrast, in a survey to clinicians in CAMHS (n=not reported), only half of the respondents agreed that the QbTest results aided treatment decisions (30% of respondents remained neutral).[71] In the QUOTA trial, the survey of clinicians showed that across both follow-ups 73% (24/33 responses) of clinicians reported that the QbTest was useful in determining treatment, 18% (6) were neutral, and 9% (3) stated it was not helpful. More clinicians found the QbTest helpful at follow-up 1 (76.5%; 13/17), than follow-up 2 (68.8%; 11/16). In interviews, clinicians also highlighted the potential role of the suggested that the QbTest appears to help parents to be more accepting of treatment recommendations, and they reported it increased their confidence in treatment, and helped to communication around treatment impact. However, they did also note that having more appointments for medication management can present logistical issues in scheduling appointments, and they reported a preference to only add additional QbTest appointments when it was perceived to add value.

4.5 Objective 4: Clinical-effectiveness of sensor CPTs for evaluating treatment effectiveness during long-term treatment monitoring for people with a diagnosis of ADHD

We did not identify any studies that met inclusion criteria for this objective.

5 Assessment of cost effectiveness

Sections of this Chapter have been reproduced from the review protocol, available at the NICE website.[1]

5.1 Review of cost-effectiveness models of diagnostic testing and treatment of ADHD

5.1.1 Review methods

We conducted a systematic review to identify previous cost-effectiveness studies of diagnostic tests for the assessment of ADHD and previous cost-effectiveness models of treatment for ADHD.

We searched the following databases:

- MEDLINE (MEDALL) via Ovid;
- Embase via Ovid;
- PsyCINFO via Ovid; and
- CINAHL via EbscoHOST.

The full search strategies are reported in Appendix 1b.

We also included any relevant papers on cost-effectiveness of sensor CPTs for the assessment of ADHD that were identified in the clinical effectiveness review, searched citations in relevant publications, and asked experts in the field. We also ran additional targeted searches to identify specific inputs required in the economic model.

We assessed the quality of cost-effectiveness studies of diagnostic tests for the assessment of ADHD using the Drummond checklist.[113]

5.1.2 Results of the cost-effectiveness review

Figure 22 shows the PRISMA flowchart showing the studies identified from the systematic review of cost-effectiveness models for diagnosis or treatment of ADHD, and Figure 23 of Appendix 6 shows the PRISMA flowchart for economic evaluations of sensor CPTs for the assessment of ADHD.[38]

Cost-effectiveness models of diagnosing ADHD

We did not find any studies reporting cost-effectiveness models of diagnostic tests for the assessment of ADHD.

Economic evaluations of sensor CPTs for diagnosing ADHD

We found 1 RCT that assessed the cost-effectiveness of diagnostic tests for the assessment of ADHD[18] and 1 implementation study (2 reports[71 114]). The quality assessment of the two economic evaluations using the Drummond check-list is given in Appendix .

AQUA trial (Hollis et al 2018)[18]

Hollis et al presents the results of the AQUA trial of ADHD diagnosis in children and adolescents, including a cost-effectiveness analysis. They use an NHS perspective and the cost analysis focuses on the staff time (number and length of appointments) required to reach a diagnosis confirming or excluding ADHD. The analysis compares QbTest plus usual care (QbOpen) to usual care, with the usual care arm including QbTest but the results were not provided to the diagnosing clinicians (QbBlind). In the costing analysis, they incorrectly exclude the cost of QbTest from both arms rather than including it for the QbOpen arm only. Whilst QbTest was used in both arms of their trial, the QbBlind arm reflects the situation where QbTest is not used, and so cost of the test should be applied for QbOpen and not for QbBlind.

EQ-5D-Y was used to calculate QALY weights for participants in each intervention group, relying on multiple imputation as only 43% of study participants completed the questionnaire. The EQ-5D-Y questionnaire is stated in the analysis plan to be measured at baseline, 4-8 weeks after medication titration, and 6 month follow up, however it is not stated how the repeated measures were combined within the multiple imputation analysis, or what value set was used to convert EQ-5D-Y to QALY weights, and the results are not given; only the incremental QALYs for the two arms are reported.

Cost-effectiveness is also reported in terms of incremental cost per incremental time to diagnosis, in which the time to diagnosis was reduced in the QbOpen arm.

For the purposes of this analysis, data presented on resource use, time to diagnosis, and the proportions with a diagnosis (ADHD or no ADHD) will be used to model the impact of QbTest.

East Midlands AHSN study, Kent Surrey Sussex AHSN report

Humphreys et al report a study by the East Midlands AHSN which collected data from three East Midland trusts (Derbyshire, Leicestershire and Lincolnshire).[71] The Kent Surrey Sussex AHSN conducted a cost-benefit analysis using the data collected by the East Midlands AHSN.[114]

The assessment uses a return on investment calculation which accounts for the costs of implementing QbTest and benefits to the NHS in terms of reduced number of appointments for clinical assessment and school nurses, and social benefit in terms of improved quality of life while on the waiting list.

Cost calculations are not shown explicitly and resource use units are not clearly described. All input costs are increased based on a bias scale and then total costs are increased 15% and benefits decreased 15% to give a more conservative result.

Three scenarios are presented, one based on data collected by the study authors at three East Midlands trusts, the second based on data provided by the QbTest manufacturer, and

the third using scenario one data and additional assumptions to estimate the return on investment of a national scale up of QbTest.

The cost-benefit analysis is presented in a report which does not appear to be peer reviewed. There is some lack of clarity in presentation of the methods, some of these are more clearly described in the results and discussion sections.

No decision model is used, rather, the net benefit is calculated within each scenario. In all cases, there is a positive return on investment result, which is primarily driven by the cost of implementing QbTest being lower than the NHS cost savings due to two fewer appointments being needed for each patient when QbTest is implemented.

Review results for cost-effectiveness models of treatment for ADHD

We found 24 studies describing cost-effectiveness models for treatment of ADHD. The cost-effectiveness models for treatment of ADHD are summarised in Table 13. All studies described either Markov models or decision tree models, and one study (Klein 2011)[115] also described a trajectory analysis model as an alternative to their Markov model. One report, the NICE guideline NG87,[16] included two separate studies; these were of parent training (Appendix 1 of NG87) and combination treatment (Appendix 2 of NG87).

13 studies described Markov models [115-128] 5 of these studies used or closely based their models on a previously published model: the Cottrell 2008 Markov model[116] was adapted by Hong 2009[120] and Prasad 2009[124]; the Faber 2008 Markov model[118] was adapted by Schawo 2015[125] and van der Schans 2015[128]; and the Sikirica 2012 Markov model[126] was adapted by Lachaine 2016.[121]

11 studies described decision tree models.[129-139]

The Zimovetz 2018[138] study used the same model as Zimovetz 2016,[137] but applied it to adults rather than children and adolescents.

Treatments modelled were either drug treatments, behavioural therapy, a combination of the two, or no treatment. Only 3 models[122, 127, 139] compared directly against no treatment (which is required for our diagnostic strategies models), but most models included treatment discontinuation with consequences of not being on treatment. Switching between treatments in sequence was conducted in 9 models, of which 5 were Markov models[115, 116, 120, 123, 124] and 4 were decision tree models.[131-133]

Only two models were on adults,[127, 138] with all other models were for children and/or adolescents.

Most studies took either a health system or payer perspective. 7 studies considered a societal perspective as their sole perspective or as an additional perspective.[118, 121, 123, 125, 128, 133, 135]

Most studies used a time horizon of one year, stating a lack of long-term data as the reason for this choice. 5 studies used a longer time horizon, with the most common choice being a 10-year time horizon.[118, 119, 122, 125, 128]

All studies were cost-effectiveness or cost-utility analyses, except for Klein 2011[115] which modelled treatment trajectories, Nagy 2017[123] which described a conceptual model, and Vanoverbeke 2003[136]which was a cost analysis only.

The majority of studies (22 studies) had target populations in Europe, the US or Canada, with eight study models in the UK.[116, 124, 129-131, 136-138] The other two studies were modelled children and adolescents in Brazil,[122] and Iran.[135]

The most common states or events used to structure the economic models were response or no response to treatment, and discontinuation of treatment due to non-tolerance of adverse events. Some studies used more detailed stratification to differentiate between patients' symptom levels. The Sikirica 2012 Markov model,[126] also used by Lachaine 2016,[121] consisted of four health states to stratify patients according to the severity of their ADHD symptoms. These four health states are normal, mild, moderate and severe, and are based on a clinician-completed ADHD rating scale. The Faber 2008 Markov model,[118] also used by Schawo 2015[125] and van der Schans 2015,[128] differentiated between optimal and suboptimal responses to treatment.

In most models which included drug titration periods, the titration periods were either each around four weeks long,[116, 117, 120, 124, 131-133, 135, 137, 138] or eight weeks long.[118, 121, 126, 128] Models which included utility decrements from adverse events leading to treatment discontinuation assumed that the decrements last for four weeks.[117, 121, 133]

Table 13 Overview of cost-effectiveness models for treatment of ADHD

Study	Model type	Target population	Treatments studied, inc. any treatment sequencing	Study perspective	States/events in model	Time horizon/ discounting	Key assumptions
Nice guideline NG87 (2018) Appendix 1[129]	Decision tree	Children in UK with ADHD	Parent training vs no parent training	NHS and PSS	Response or no response to parent training	1-year	A proportion of children will also be on drug treatment.
NICE guideline NG87 (2018) Appendix 2[130]	Decision tree	Children in UK with ADHD	Combination treatment vs medication alone or behavioural therapy alone	NHS and PSS	Response or no response to treatment, and stopping treatment due to adverse events	1-year	Patients may experience tolerable adverse events, which do not lead them to discontinue treatment, but do have associated disutilities.
Cottrell (2008)[116]	Markov model. Monthly cycles over period of 1 year.	Children with ADHD in UK. Split into subgroups based on stimulant history.	Atomoxetine, compared against MPH, dexamphetamine, and no treatment. Patients either start on ATX or a comparator, and then follow same treatment sequence if not successful.	NHS	18 health states, based on different combinations of treatment/response/side-effects	1-year	Model assumes that all non-drug healthcare costs and indirect costs are equivalent between the treatment groups.

Study	Model type	Target population	Treatments studied, inc. any treatment sequencing	Study perspective	States/events in model	Time horizon/ discounting	Key assumptions
Erder (2012)[117]	Markov model. Weekly cycles over period of 1 year. Split into 4-week drug titration period, and 48-week maintenance period.	Children and adolescents with ADHD in US.	Comparing GXR vs ATX	US third-party payer. Only considered direct costs (drug costs and direct medical costs).	Titration phase: response, non-response (on treatment), discontinuation. Maintenance phase: response, discontinuation, non-response (off treatment).	1-year	Patients who discontinued treatment had the same utility and medical costs as non-responders. Adverse events (AEs) reduced the patients' health utilities during the titration period.
Faber (2008)[118]	Markov model, with a primary 2-month titration phase, followed by a Markov phase of length 10 years, with 1-day cycles.	Youths with ADHD in Netherlands, who have suboptimal response to immediate-release (IR) methylphenidate	Long-acting methylphenidate OROS vs IR methylphenidate	Societal/ community	Non-response, optimal response, suboptimal response, treatment stopped, functional remission, non-compliance	10-year horizon, discounting at 4% per year	Costs of nonpharmacological interventions were incurred in the first and sixth year of treatment, when the child is aged 8 years and 13 years respectively.
Freriks (2019)[119]	Markov model	Children in Netherlands with ADHD	Medication, behavioural, or combination treatment.	Includes healthcare costs and criminal justice system costs.	No delinquency, minor to moderate delinquency, serious delinquency	10-year horizon, discounting at 4% per year	Serious delinquency is an absorbing health state.

Study	Model type	Target population	Treatments studied, inc. any treatment sequencing	Study perspective	States/events in model	Time horizon/ discounting	Key assumptions
Hong (2009)[120]	Cottrell 2008 Markov model adapted to Spain. Monthly cycles and 1-year time horizon.	Children and adolescents with ADHD in Spain	Patients start on Atomoxetine or methylphenidate, then move to other if drug unsuccessful, and finally stop medication if neither drug successful	National Health Service in Spain	10 health states, based on different combinations of treatment/response/side-effects	1-year	Model assumes that all non-drug healthcare costs and indirect costs are equivalent between the treatment groups.
King (2006)[131]	Decision tree	Children and adolescents with ADHD in UK	Treatment sequences of MPH, ATX, DEX in different orders, followed by 4th line of no treatment	NHS and PSS	Tolerate, or intolerable side-effects. Response or no response	1-year, with a secondary analysis extrapolating beyond 1 year	Drug titration period lasts one month, after which non-responders move to next drug in treatment sequence.
Klein (2011)[115]	Two approaches: Markov model and trajectory analysis. Considered 1-month and 1-year cycle lengths.	Youth with ADHD in US	Models different patient groups transitions between treatment modalities (out of treatment, medication only, services only, combination)	N/A (costs not reported)	Out of treatment, medication only, services only, combination	1-year	Time on treatment assumes that medication is taken daily to completion of prescription.

Study	Model type	Target population	Treatments studied, inc. any treatment sequencing	Study perspective	States/events in model	Time horizon/ discounting	Key assumptions
Lachaine (2016)[121]	Markov model (similar to Sikirica 2012) with two stages: weeks 0-8 where all patients remain on treatment, and weeks 9-52 where patients in moderate/severe state may discontinue as considered non-responsive. Length 1 year, with weekly cycles.	Children aged 6-12 years with ADHD in Canada, with a sub-optimal response to GXR.	GXR adjunctive to long-acting stimulants	Two perspectives: Canadian Ministry of Health, and societal	Mild, moderate, severe, or normal, assigned using clinician-reported CGI-S scores.	1-year	Annual medical costs for patients in normal health state are assumed to be the same as median medical costs for non-ADHD patients. Adverse events are assumed to result in a utility decrement lasting 4 weeks.
Maia (2016)[122]	Unclear. Appears to be a Markov model, but is also described as a decision tree.	Children and adolescents in Brazil with ADHD	Methylphenidate vs natural course	Brazilian Unified Health System	Treatment (not) maintained, (no) spontaneous improvement, (no) improvement maintained	6-year horizon, discounting at 5% per year	Patients who discontinue treatment do not later restart treatment.
Marchetti (2001)[132]	Decision tree, with up to 4 treatment evaluation periods, each lasting 4 weeks	Children in US with ADHD	Treatment adjustment and sequencing. Methylphenidate (immediate or extended release), Adderall.	Payer perspective	Success and failure of treatments. Followed by management by psychologist/psychiatrist if four failures.	1-year	Once a child responds to medication they continue on that dose for the remainder of the evaluation period.

Study	Model type	Target population	Treatments studied, inc. any treatment sequencing	Study perspective	States/events in model	Time horizon/ discounting	Key assumptions
Nagy (2017)[123]	4-layer conceptual model, including Markov	Childhood through to adulthood in patients with ADHD	Treatment sequencing of drugs	Includes societal perspective	Drug toleration, response, compliance and persistence.	Not stated	Provides an example of 3-layers of conceptual model making some strong assumptions on the links between short-term and long-term outcomes.
Narayan (2004)[133]	Decision tree	Children in US with ADHD	Treatment sequencing of methylphenidate or amphetamine/ dextroamphetamine, followed by the other treatment, then no treatment	Societal perspective (though some indirect costs not included)	Response, non-response, or discontinuation of treatment. Tolerance of side effects.	1-year	Side effects are assumed to result in a utility decrement lasting 1 month.
Prasad (2009)[124]	Uses Cottrell 2008 Markov model	Children and adolescents in UK with ADHD	Atomoxetine, compared against MPH, dexamphetamine, and no treatment. Patients either start on ATX or a comparator, and then follow same treatment sequence if not successful.	NHS	18 health states, based on different combinations of treatment/response/side-effects	1-year	Model assumes that all costs other than study drug costs are equivalent between treatment groups.

Study	Model type	Target population	Treatments studied, inc. any treatment sequencing	Study perspective	States/events in model	Time horizon/ discounting	Key assumptions
Schawo (2015)[125]	Markov model (similar to Faber 2008), with 1-day cycle length and 12 year horizon	Children and adolescents in Netherlands with ADHD	Methylphenidate OROS vs IR	Societal perspective	Sub-optimal medication intake, optimal medication intake, remission, treatment stopped	12-year horizon. Costs discounted at 4%, effects discounted at 1.5%.	Costs of nonpharmacological interventions were incurred at ages 6 and 12, around when children change schools.
Sikirica (2012)[126]	Markov model, length 1-year, and cycle length 1 week. The model has two stages: weeks 0-8 and weeks 9-52. Patients considered non-responsive at week 8 permanently discontinue treatment.	Children and adolescents in US with ADHD	Guanfacine extended release vs stimulant monotherapy	US third-party payer.	Mild, moderate, severe, or normal, assigned using CGI-S scores.	1-year time horizon	Patients who do not respond to the initial therapy by week 8 discontinue treatment and do not switch to a new treatment.
Sohn (2016)[134]	Decision tree, with several arms for adverse events	Children and adolescents in US with ADHD	Atypical antipsychotics vs other alternatives to stimulants	US third-party payer.	Drug effectiveness, and several side effects including weight gain and high blood pressure	1-year time horizon	Side effects seen within 6 weeks of initial treatment will persist for the entire year as treatment is continued.
Tajik (2023)[135]	Decision tree	Children and adolescents in Iran with ADHD	Lisdexamfetamine vs methylphenidate	Social perspective	Toleration or non-toleration of treatment. Response or no response.	1-year time horizon	Patients who discontinue treatment due to intolerance are assumed to have the same utilities and costs as non-

Study	Model type	Target population	Treatments studied, inc. any treatment sequencing	Study perspective	States/events in model	Time horizon/ discounting	Key assumptions
							responders for the remainder of the 1-year model time horizon.
Tockhorn (2015)[127]	Markov model with 1-month cycles and 1-year horizon	Adults in Spain with ADHD	Atomoxetine vs no treatment	Spanish National Healthcare System	Treatment initiation, response or no response.	1-year time horizon	During the first three months patients may only discontinue due to adverse events as atomoxetine has a prolonged onset of treatment response.
van der Schans (2015)[128]	Markov model, similar to Faber 2008, with a 2-month titration phase followed by a 10-year Markov phase with 1-day cycles	Children and adolescents in Netherlands with ADHD with a sub-optimal response to immediate-release methylphenidate	Immediate-release vs slow-release methylphenidate	Societal perspective	Optimal response, suboptimal response, natural remission, discontinuing treatment	10-year horizon, future costs discounted at 4% per year, and future outcomes discounted at 1.5% per year	Patients may restart treatment (unlike the Faber 2008 model).
Vanoverbeke (2003)[136]	Decision tree	Children and adolescents in UK with ADHD	Behavioural treatment, immediate- or slow-release methylphenidate, followed by an alternative or combination treatment if first treatment fails	NHS and PSS	Success and failure of treatments.	1-year time horizon	Assumes medication compliance is the same for slow- vs immediate release methylphenidate.

Study	Model type	Target population	Treatments studied, inc. any treatment sequencing	Study perspective	States/events in model	Time horizon/ discounting	Key assumptions
Zimovetz (2016)[137]	Decision tree	Children and adolescents in UK with ADHD, who have responded inadequately to methylphenidate	Lisdexamfetamine dimesylate vs atomoxetine	NHS	Toleration or non-toleration of treatment over a 28-day titration phase, followed by response or no response to treatment over a 48-week post-titration phase.	1-year time horizon	Patients who discontinue treatment due to intolerance are assumed to have the same utilities and costs as non-responders for the remainder of the 1-year model time horizon.
Zimovetz (2018)[138]	Decision tree	UK adults with ADHD	Lisdexamfetamine dimesylate as a first- or second-line treatment vs slow-release methylphenidate and atomoxetine	NHS	Toleration or non-toleration of treatment over a 28-day titration phase, followed by response or no response to treatment over a 48-week post-titration phase.	1-year time horizon. Also used a 5-year time horizon in a sensitivity analysis, discounting at 3.5% per year.	Patients who discontinue treatment due to intolerance have the same utilities and costs as non-responders for the remainder of the 1-year model time horizon. Patients who responded to and tolerated treatment are persistent over the 1-year model time horizon.
Zupancic (1998)[139]	Decision tree	Children in Canada with ADHD	Methylphenidate vs dextroamphetamine vs pemoline vs non-drug therapy vs combined therapy vs no treatment	Third party payer	Toxicity or no toxicity, compliance or non-compliance	1-year time horizon	Children on no treatment visit their family physician the same number of times per year as children on drug treatment.

Implications of cost-effectiveness review for this economic evaluation

The two cost-effectiveness evaluations of diagnostic assessment for ADHD provide information which we used to parameterise our model. The AQUA trial [18] is of direct relevance to objective 1, as it compares QbTest plus clinical assessment to clinical assessment alone, with information on the resource use required to reach a diagnosis in each arm. The East Midlands study and Kent economic evaluation provides some additional information on resource use needed to reach a diagnosis.[71, 114]

Neither of these evaluations contain an economic model, and no previous economic models of diagnosis of ADHD were identified, so we needed to develop *de novo* models for this assessment. However, there have been several previous economic models of treatment of ADHD, which are relevant for modelling the costs and outcomes of ADHD treatment following diagnosis, and for the evaluation of sensor CPTs in the assessment of dose-titration and long-term monitoring.

Most of the models of treatments for ADHD included treatment response, adverse effects of treatment and treatment discontinuation, all of which are relevant for our models. Some modelled different types of response (optimal or suboptimal),[118, 125, 128] which is particularly relevant for models of dose-titration and long-term treatment monitoring. Many models capture patients moving through several lines of treatment, and some included remission, both of which are relevant for a model of long-term monitoring. Only 3 models[122, 127, 139] compared an active treatment strategy against no treatment, and none of these were UK based. However, outcomes on "no treatment" were assumed in many of the models for patients who discontinue treatment, which can be used for patients not on treatment in our model. A limitation of many of the previous models of treatment for ADHD is that they restrict to a 1-year time-horizon. This may be appropriate for comparisons of different active treatments, as patients are monitored every 6 months or annually. For a model of diagnostic strategies however, the time-horizon needs to be long enough to capture the time period before a diagnosis is eventually reached in all patients with ADHD, which is likely to be longer than 1-year.

We considered studies which were conducted in the UK to be the most appropriate source of information for health-state costs and utility inputs to the model. Cottrell 2008[116] and Prasad 2009[124] only included drug costs, assuming all other costs were the same between their comparators, and therefore were not useful for our model. Studies which reported costs in terms of responders vs non-responders [129-131, 137, 138] were of most relevance to our model.

5.2 Model structure and methods of economic evaluation

We aimed to develop decision-analytic models to estimate the incremental costs and quality-adjusted life years (QALYs) for sensor CPTs in addition to current methods of assessment compared with current methods of assessment alone, for each of the following purposes:

i) assisting diagnosis of ADHD in people referred with suspected ADHD (Objective 1)
ii) assisting diagnosis of ADHD in people referred with suspected ADHD for whom current assessment cannot reach a diagnosis (Objective 2)
iii) to assist in dose titration and treatment decisions in people with a diagnosis of ADHD (Objective 3)
iv) to assess treatment effectiveness for long-term treatment monitoring for people with a diagnosis of ADHD (Objective 4)

However, the majority of the evidence on sensor CPTs identified in the clinical review (Section 0) was relevant for objective 1 only. We did not identify any evidence for objective 2, but we present a scenario analysis for objective 1 to give some speculative results relevant to objective 2, albeit with strong assumptions. There was insufficient evidence available to assess the cost-effectiveness of the use of sensor CPTs for dose titration and long-term treatment monitoring (objectives 3 and 4), and so we describe potential model structures only and do not populate the models or report results for these objectives.

5.2.1 Population

For objectives 1 and 2 the population are patients suspected of having ADHD who have been referred for assessment. For our scenario analysis to explore objective 2 we assume that the technology is only used in those where a diagnosis was not reached after 2 appointments using standard assessment, and the results of the diagnostic test would be available at the 3rd appointment.

For objectives 3 and 4 the population are patients diagnosed with ADHD who initiate pharmacological treatment. We did not identify sufficient evidence on sensor CPTs for this population to be able to conduct an economic evaluation.

Subgroups

The key source of evidence on effectiveness of sensor CPTs was the AQUA trial [18] which evaluated QbTest (6-12) (in children 7-12years) and QbTest (12-60) (for adolescents 12-17 year olds). We did not identify any studies in adults that reported information on time and number of appointments until diagnosis, and no studies with diagnostic accuracy data for sensor CPTs in combination with clinical assessment. Our main analyses are therefore only directly applicable for children and adolescents. We conducted scenario analyses using the hazard ratio for diagnosis in children and adolescents separately, but note that this is the only the only outcome reported separately for children and adolescents, and all other model inputs are assumed to be the same.

There was insufficient evidence to conduct subgroup analyses for: sex, ethnicity, people with mental health, behavioural and neurodevelopmental conditions, people with developmental trauma, looked-after children, or people in the Youth Justice System or Adult Criminal Justice System. There was a feasibility study conducted in the very specific population of boys with symptoms of possible ADHD aged 15 to 18 years in young offenders

institutions in England.[74] However, as noted in section 4.2.1 due to the feasibility design, small sample size, low numbers of appointments (only 14 decisions were made, and all were exclusions of ADHD), and impact of COVID-19, there was insufficient evidence to conduct a subgroup analysis for male young offenders aged 15-18 years.

5.2.2 ADHD assessment strategies

We included sensor CPTs identified in the clinical effectiveness review (Section 0) and for which there was sufficient evidence available for the model. This meant that the economic evaluation focussed on QbTest (6-12) and QbTest (12-60) (for adolescents aged 12-17 years), as we did not have sufficient evidence for other sensor CPTs. We refer to these tests collectively as "QbTest". We conducted scenario analyses changing the test cost to match that of other tests where we had information on test costs, but note that these assume all other inputs are as for QbTest, and have to be interpreted as such.

Assessment strategies for ADHD diagnosis

Current methods for diagnosing ADHD are assessment by a healthcare professional (without use of the sensor CPTs) using history taking, third-party observational reports, and questionnaires.[16] Children are usually assessed face-to-face in clinic, whilst assessment for adults is often done remotely.

We evaluated the following diagnostic assessment strategies (restricted to QbTest as the only test with sufficient data):

Standard: All patients receive standard clinical assessment using current methods for diagnosis of ADHD

QbTestAll: All patients are offered QbTest, the results of which are available to the healthcare professional making the assessment at the 2nd appointment along with all other evidence used for standard assessment

QbTestUnclear: All patients receive standard assessment, and those patients who do not receive a diagnosis after 2 appointments are offered Qbtest, the results of which are made available to the healthcare professional making the assessment at the 3rd appointment.

QbTestUnclear is only evaluated as a scenario analysis to explore objectives 2.

Assessment strategies for dose-titration

Following a diagnosis of ADHD symptoms are managed using a combination of non-pharmacological and pharmacological interventions (section 1.2.3). For patients where pharmacological treatment is indicated, medications licensed in the UK include stimulants (methylphenidate (MPH), lisdexamfetamine (LDX), dexamfetamine) and non-stimulants (atomoxetine (ATX), or guanfacine). Patients undergo a "dose titration" period during which they begin with a low-dose of first line treatment and then are assessed at 2-week intervals for efficacy and side-effects and where decisions to change the dose or treatment are made. NICE guidelines recommend patients start with methylphenidate (MPH) for 6 weeks, then if no response they recommend switching to lisdexamfetamine (LDX) for 6 weeks, then if no

response switch to atomoxetine (ATX),[16] although in practice treatment choice is based on individual circumstances, response, tolerability, and adherence.[28] The period of time before the treatment and dose are settled upon varies greatly across patients, but we heard that the majority reach a stable dose by 12 weeks (6 appointments).

Williams (2021)[111] conducted a feasibility study to compare the use of QbTest in addition to clinical assessment with clinical assessment alone for dose titration. Patients completed a QbTest prior to initiating medication, and two further QbTests whilst on medication (2–4 weeks and 8–10 weeks after initiating medication). The study found that to fit with clinical practice there needed to be flexibility on the timing of the pre-medication QbTest, and to allow the number and timing of subsequent QbTests post-medication to be determined by the healthcare professional making the assessments.

For a model to evaluate sensor CPTs for dose-titration we would therefore assume the sensor CPT is performed pre-medication (which could be during the diagnostic assessment) and either once or twice more whilst on medication during the dose-titration period. The cost of the pre-medication sensor CPT would only be incurred in the case where this is not part of routine diagnosis. The sensor CPTs conducted during the titration period would need to be conducted in a dedicated in-person appointment because dose-titration assessments are largely conducted remotely, which needs to be reflected in the costs.

Dose-titration assessment strategies relevant to be evaluated for objective 3 are:
Standard: All patients receive standard assessment using current methods for dose-titration with fortnightly appointments until a stable dose / treatment is reached
Sensor CPT: The sensor CPT is completed pre-medication and either once or twice post-medication, the results of which are available to the healthcare professional making the assessment at fortnightly appointments

Assessment strategies for long-term monitoring

Following the dose titration period, patients are monitored regularly (annually for adults and at least every 6-months for children), including an assessment of whether medication needs to be adjusted. Patients may also take a “drug holiday”, to see if they still need to take medication (our clinical advisors consider this every 3-5 years for adults and maybe during school holidays for children).

We did not find any studies of the use of sensor CPT for long-term monitoring of ADHD patients, and it is not clear what format such monitoring would take. For this reason we were unable to describe the assessment strategies to compare the cost-effectiveness of the use of sensor CPTs to assist treatment decisions in long-term management of patients (objective 4).

5.2.3 Setting

The AQUA trial, which provided the main source of data for our model, recruited participants who were referred for assessment for ADHD in child and adolescent mental health services (CAMHS) (48%) or community paediatric clinics (52%) in England.[18] The model is therefore applicable for patients referred through these routes based on a similar patient mix as seen in the AQUA trial. The East Midlands AHSN study gathered data from three trusts in Derbyshire, Leicestershire and Lincolnshire. [71] In addition, they used data provided by QbTest manufacturers from undisclosed clinical settings. Details are not given on where assessments take place within the three trusts. QbTest was used for ADHD diagnosis in children, but an age range is not specified.

5.2.4 Model structures

The model structures were developed to capture the short- and long-term costs and benefits of sensor CPTs for the assessment of ADHD, informed by the findings of our review of clinical and cost-effectiveness studies and discussions with our clinical advisors and patient representatives.

Model structure for diagnostic assessment (objectives 1 and 2)

A Markov model structure was used to capture the process of diagnosis of ADHD (Figure 10). Patients enter the model after a referral for assessment for ADHD, and join a waiting list for assessment. The time spent waiting for assessment is assumed to depend on whether a sensor CPT is used or not, because a potential benefit of the use of sensor CPTs is to reduce the time and resources required to reach a diagnosis and hence release clinician time which can be used to reduce waiting times for assessment. Patients then undergo diagnostic assessment for ADHD which consists of a series of appointments until a diagnosis is reached or assessment is discontinued.

The AQUA trial presents the proportion of patients for whom a diagnosis is reached against the number of appointments (Figure 2 in Hollis et al. [18]), and a corresponding survival analysis that accounts for censoring for the high proportions who were lost-to-clinic (Appendix S6 in Hollis et al. [18]). The survival analysis indicates that most diagnoses had been reached by 6 appointments, but note that this makes the strong assumption of non-informative censoring. This is unlikely to be the case, as those lost to clinic are unlikely to achieve a diagnosis at the same rate as those attending clinic, and we know they aren't diagnosed within 6 months. We therefore distinguish between those who attend clinic and diagnosis can be reached within 6 months (for whom the survival analysis results are applicable to) and those who do not receive a diagnosis within 6 months (a proportion of whom may have further assessments and eventual diagnosis beyond 6 months). We treat these as two distinct subgroups of patients, with the proportion in each group depending on the assessment strategy used (as can be seen from the differential proportion of patients for whom a diagnosis is reached within 6 months in Figure 2 in Hollis et al.[18]). Furthermore, the case-mix of those with a diagnosis within 6 months differs between assessment strategies, with Qbtest plus clinical assessment being more likely to make a diagnosis excluding ADHD

than clinical assessment alone.[18 31] We therefore assume that the prevalence of ADHD amongst those receiving diagnosis within 6 months depends on assessment strategy.

Patients who have a diagnosis within 6 months are either diagnosed as having ADHD and will go on to receive treatment for ADHD or are diagnosed as not having ADHD and do not receive further treatment or assessments for ADHD. We heard from our clinical advisors that the main impact of QbTest is likely to be on the time waiting for assessment, number and length of appointments, and make it easier to exclude ADHD without leading to appeal, rather than on diagnostic accuracy of the eventual diagnosis. Adding QbTest to clinical assessment was not expected to make clinical assessment any less accurate, and this is assumed in our base-case model, although note that we do include the proportion of diagnoses made within 6 months and the proportion of those diagnoses that are ADHD in the model, both of which depend on test. We also include diagnostic test accuracy in a scenario analysis where those with a positive diagnosis include those who do have ADHD (true positives) and those who do not have ADHD (false positives) and those with a negative diagnosis include those who do have ADHD (false negatives) and those who do not have ADHD (true negatives), as illustrated in Figure 10. False positives are assumed to incur costs of treatment during the dose-titration period but without any benefits in terms of response to treatment. We heard from our clinical advisors that treatment may continue into the long-term for many patients who do not have ADHD but initiate treatment, and so we include costs of non-responders beyond the titration period to capture these on-going costs. False negatives do not incur treatment costs, but do not gain any treatment benefits.

QbTest is administered early in the assessment period in our model (and in the AQUA trial), and the results from the AQUA trial show that there is little additional benefit of QbTest after 5 appointments. Based on this, we assume that the diagnoses after 6 months are no different than for clinical assessment alone, since the additional appointments beyond 6 months are likely to be based on additional reports other than QbTest (which has already been considered). However, because the prevalence of ADHD in those who receive a diagnosis within 6 months depends on assessment strategy, so too does the prevalence of ADHD in those who receive a diagnosis after 6 months (since the overall prevalence must be the same regardless of assessment strategy).

Patients who have not been diagnosed by 6 months are likely to be a mixture of those who have stopped attending assessments and do not have further assessment (where for those with ADHD their diagnosis will be “missed”), and those who will continue to have assessments and who get an eventual diagnosis. In other words there are the following 4 groups of patients:

- those who undergo further assessment for ADHD and receive a diagnosis of ADHD and go on to receive treatment for ADHD;
- those who undergo further assessment for ADHD and receive a diagnosis of not having ADHD and receive no further treatment or assessments for ADHD; or

- those who have ADHD but do not undergo further assessment and so do not receive appropriate treatment ("missed diagnosis")
- those who do not have ADHD and do not undergo further assessment for ADHD, so further treatment for ADHD is not received or required. These patients are captured in the "No Treatment with No ADHD (true negatives)" state, even though they do not actually receive a diagnosis, since the health states are equivalent.

To evaluate the diagnosis model we use an alternative (but equivalent) model structure illustrated in Figure 11. Here we evaluate the model separately for those who do and do not have a diagnosis within 6 months, and then form an average over the proportions in each subgroup which varies depending on whether QbTest is used or not. This makes it possible to have different model parameters for those who do not have a diagnosis within 6 months, and use tunnel states to ensure that the assessment period for those who have further assessments is longer than 6 months. For those who do not have further assessments we assume they have an average of 3 assessments before they stop attending assessments, which is based on data provided to us from the authors of the AQUA trial on the number of appointments for those patients who were censored. These patients will follow the same path in the model as those with further assessments, but do not incur the assessment costs.

We assume patients with an ADHD diagnosis initiate pharmacological treatment following NICE guidance,[16] starting with MPH for 2 monthly cycles, then if no response they switch to LDX for 2 monthly cycles, then if no response they switch to ATX. Note the guidance is to switch treatments for non-responders every 6 weeks, but we have approximated this with 2 months to align with the cycle length of our model. The treatment model is shown for ADHD patients who initiate treatment (true positives) in Figure 12(a), where costs and utilities depend on treatment and response status. Patients who discontinue treatment due to adverse effects are modelled as if they are non-responders. For ADHD patients not on treatment (false negatives and those who did not receive a diagnosis), we assume they are non-responders and incur costs and utilities for non-responders but without treatment costs (Figure 12(b)), although this may be an over-estimate as non-responders are likely to be monitored more closely. For patients who do not have ADHD but receive a diagnosis (false positives), we assume that they initiate treatment, but do not respond, but may continue to incur monitoring costs long-term (Figure 13(a)). In a scenario analysis we assume that the false-positives do not incur monitoring costs long-term. For patients who do not receive a diagnosis and do not have ADHD (true negatives) they are not on treatment and do not incur any additional costs (Figure 13(b)).

Whilst waiting for diagnosis (either on waiting list or under assessment) the proportion of patients with ADHD receive quality adjusted life years (QALYs) corresponding to those with ADHD but not on treatment. In our base-case we assume that there are no additional costs whilst waiting, but in a scenario explore this being the same as ADHD patients not on treatment. Whilst under assessment all patients incur appointment costs and QbTest costs as appropriate.

Figure 10 Markov model structure for the diagnosis of ADHD

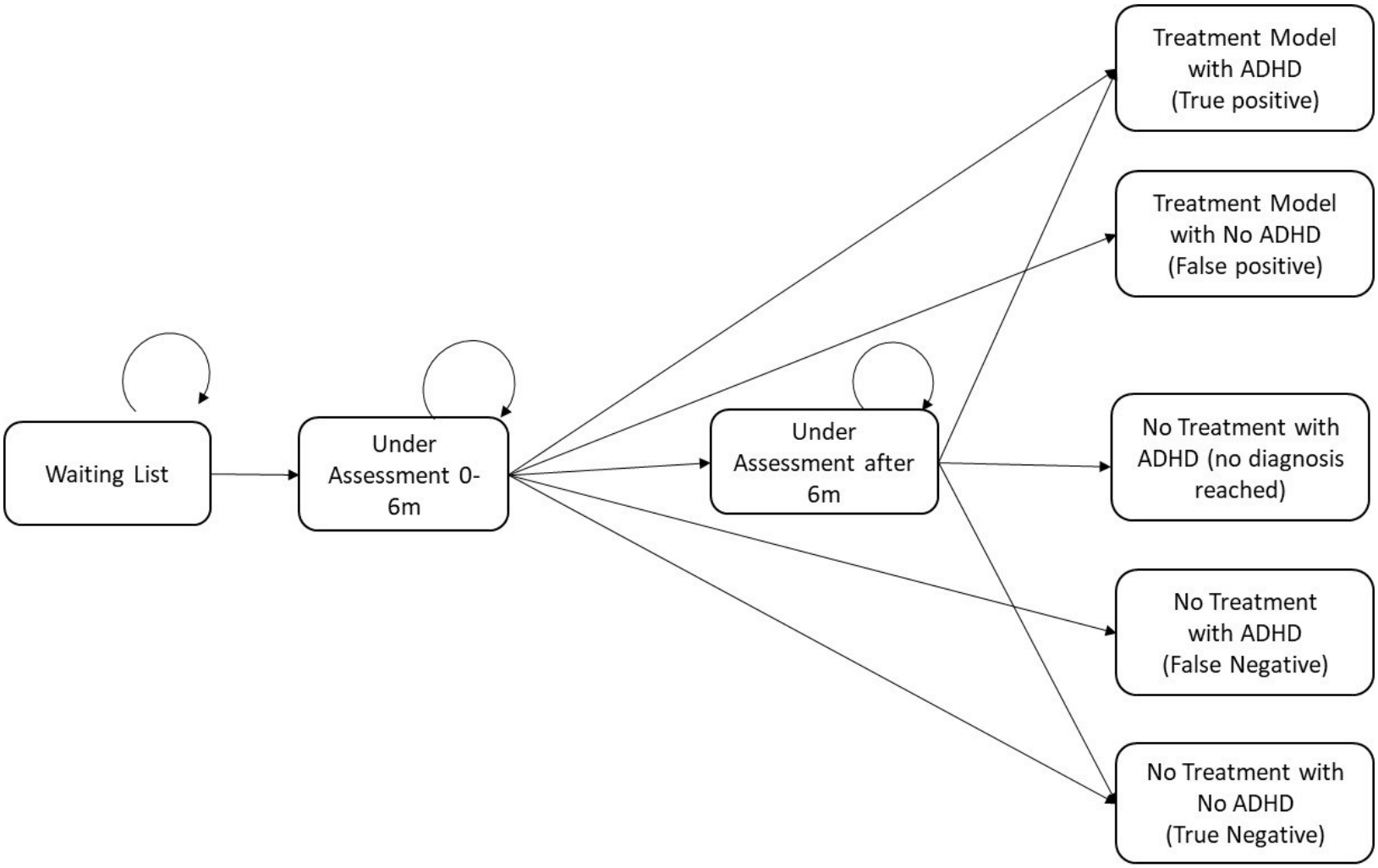


Figure 11 Markov model structure for the diagnosis of ADHD, restructured by subgroups with diagnosis before/after 6 months

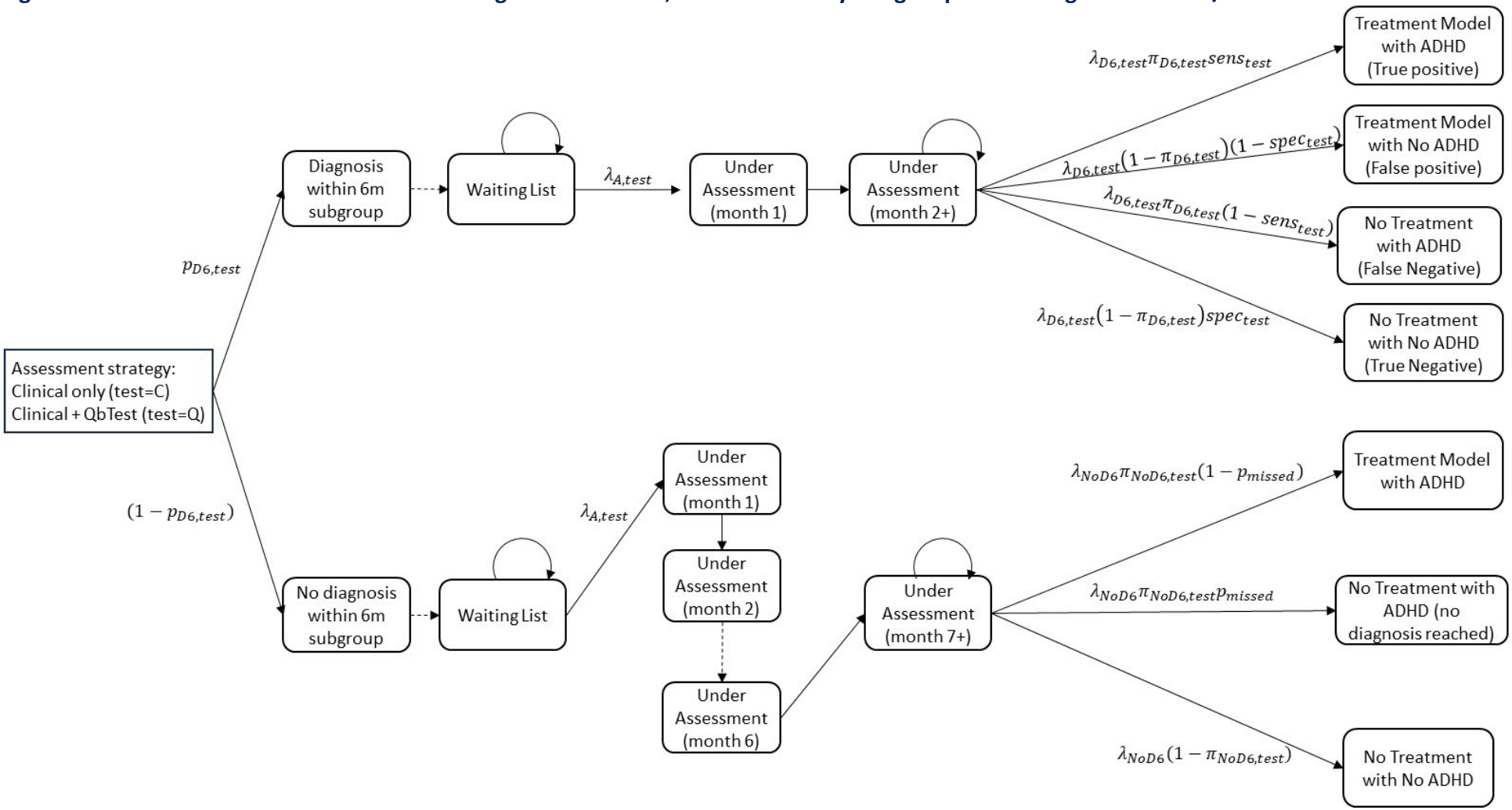


Figure 12 Markov model structure following diagnosis for patients with ADHD (a) for those diagnosed with ADHD (true positives) and (b) for those not diagnosed with ADHD (false negatives)

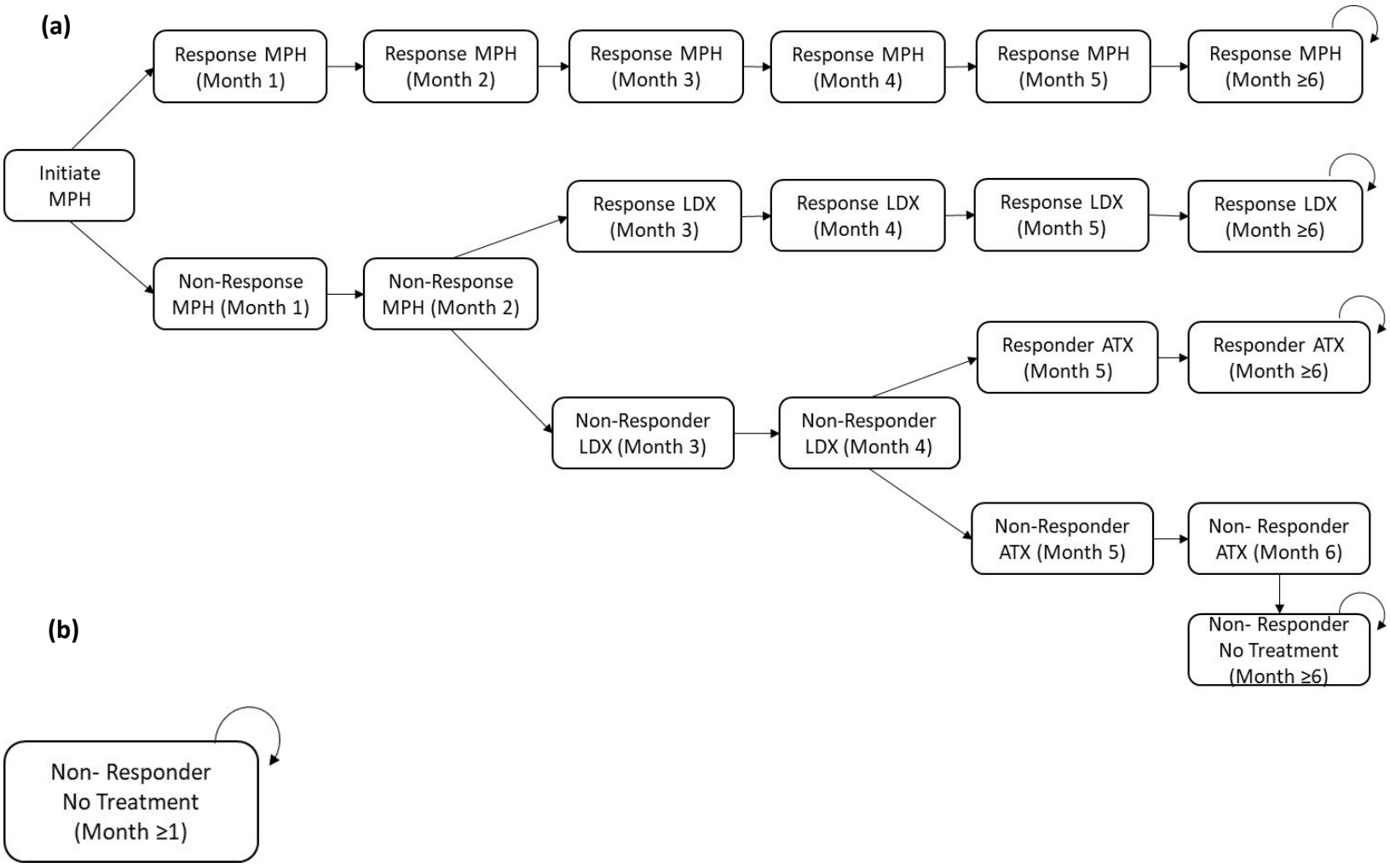
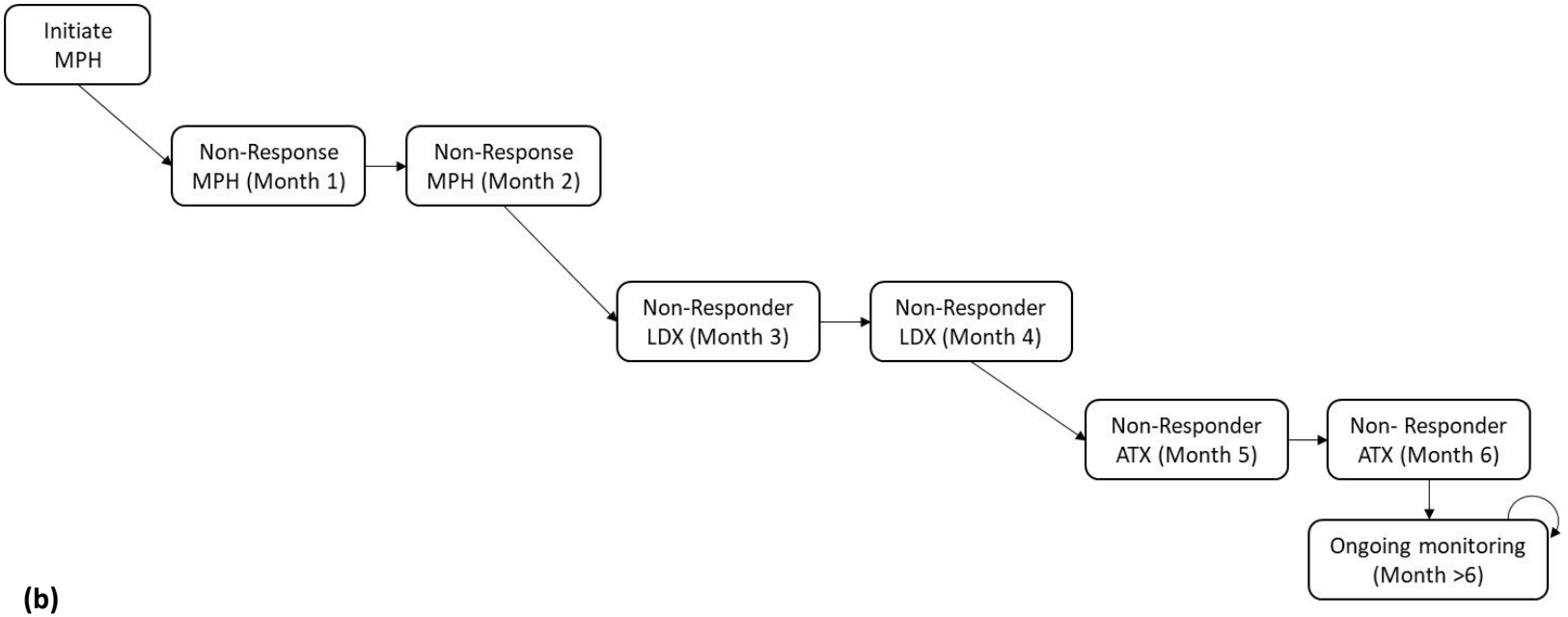
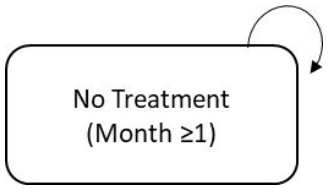


Figure 13 Markov model structure following diagnosis for patients without ADHD (a) for those diagnosed with ADHD (false positives) and (b) for those not diagnosed with ADHD (true negatives)

(a)



(b)



The transition parameters of the model in continuous patient-time are indicated in Figure 11 defined below where *test* indicates whether the assessment is made using standard clinical assessment only ($test=C$) or QbTest alongside clinical assessment ($test=Q$):

$p_{D6,test}$ is the proportion of patients with a diagnosis within 6months, and depends on assessment strategy

$\lambda_{A,test}$ is rate at which patients leave the waiting list for assessment, and depends on assessment strategy

$\lambda_{D6,test}$ is rate at which patients receive a diagnosis for the subgroup that receive a diagnosis within 6 months, and depends on assessment strategy

λ_{NoD6} is rate at which patients receive a diagnosis for the subgroup that do not receive a diagnosis within 6 months but go onto have further assessments, and does not depend on assessment strategy.

$\pi_{D6,test}$ is the proportion of patients with ADHD in the subgroup of patients that receive a diagnosis within 6 months, and depends on assessment strategy due to the difference in case-mix of those diagnosed by QbTest plus clinical assessment compared to clinical assessment alone

$\pi_{NoD6,test}$ is the proportion of patients with ADHD in the subgroup of patients that do not receive a diagnosis within 6 months, and depends on test because $\pi_{D6,test}$ depends on test and the overall prevalence of ADHD must be the same regardless of assessment strategy

$sens_{test}$ is the proportion with ADHD having a positive diagnosis (sensitivity) for each assessment strategy in those who are diagnosed within 6 months. In our base case the sensitivity of the assessment is assumed to be perfect ($sens_{test}=1$), and we run scenario and threshold analyses assuming a lower sensitivity for QbTest plus clinical assessment

$spec_{test}$ is the proportion without ADHD having a negative diagnosis (specificity) for each assessment strategy in those who are diagnosed within 6 months. In our base case the specificity of the assessment is assumed to be perfect ($spec_{test}=1$), and we vary this in scenario analyses.

p_{missed} is the proportion of patients without a diagnosis within 6 months who do not undergo further assessment and so do not receive a diagnosis. It is assumed that this does not depend on test, although the proportion without a diagnosis within 6 months does depend on test. This parameter is a key uncertainty which we vary in scenario analysis and threshold analysis.

To obtain transition probabilities from transition rates, we used the following relationships, where t is the cycle length in months.

The probability of moving from the waiting list to assessment in a cycle is the same regardless of patient subgroup:

$$p(wait \rightarrow assessment) = 1 - \exp(-\lambda_{A,test} t)$$

For those who receive a diagnosis within 6 months the proportion that receive an ADHD or No ADHD diagnosis in a cycle is:

$$p(assessment \rightarrow ADHD\ diagnosis(true + ve)) = \left(1 - \exp(-\lambda_{D6,test} t)\right) \pi_{D6,test} sens_{test}$$

$$p(assessment \rightarrow ADHD\ diagnosis(false + ve)) = \left(1 - \exp(-\lambda_{D6,test} t)\right)\left(1 - \pi_{D6,test}\right)(1 - spec_{test})$$

$$p(assessment \rightarrow No\ ADHD\ diagnosis(false - ve)) = \left(1 - \exp(-\lambda_{D6,test} t)\right) \pi_{D6,test} \left(1 - sens_{test}\right)$$

$$p(assessment \rightarrow No\ ADHD\ diagnosis(true - ve)) = \left(1 - \exp(-\lambda_{D6,test} t)\right)\left(1 - \pi_{D6,test}\right) spec_{test}$$

For those who do not receive a diagnosis within 6 months the proportion that receive an ADHD diagnosis, No ADHD diagnosis, or Missed ADHD diagnosis in a cycle (after 6 months) is:

$$p(assessment \rightarrow ADHD\ diagnosis) = \left(1 - \exp(-\lambda_{NoD6} t)\right) \pi_{NoD6,test} \left(1 - p_{missed}\right)$$

$$p(assessment \rightarrow Missed\ ADHD\ diagnosis) = \left(1 - \exp(-\lambda_{NoD6} t)\right) \pi_{NoD6,test} p_{missed}$$

$$p(assessment \rightarrow No\ ADHD\ diagnosis) = \left(1 - \exp(-\lambda_{NoD6} t)\right)\left(1 - \pi_{NoD6,test}\right)$$

In the AQUA trial there were up-to 6 appointments over a 6 month period, and so we assume that appointments are scheduled approximately every month and so use a monthly cycle for the model.

Evaluating strategy QbTestUnclear (Objective 2)

We did not find any evidence on the use of sensor CPTs in those for whom a diagnosis could not be reached using standard assessment (objective 2) and so we need to make some assumptions, which it is important to note are speculative and only presented as a scenario analysis. The AQUA trial evaluated the use of QbTest in all patients referred for assessment, and not in those with an unclear diagnosis, but we use some of the findings to support our assumptions for objective 2. In the AQUA trial QbTest was administered after the 1st appointment and before the 2nd appointment, and showed that there was no difference in the proportion of patients receiving a diagnosis after 2 appointments (Figure 2 in Hollis et al.[18]), and no difference in the appointment time until diagnosis for the first 120 minutes appointment time, which also corresponds to 2 appointments. (Supplementary Figure S7 in Hollis et al. 2018[18]) There was an increase in the proportions diagnosed and a reduction in appointment time to reach a diagnosis for QbTest from the 3rd appointment onwards (ie the 2nd appointment after administering QbTest). This suggests that it may be reasonable to assume that there is a proportion of patients (approximately 20% from Fig 2 of Hollis et al 2018) for whom diagnosis is relatively straightforward and can be achieved after 2 appointments (1 appointment after QbTest is administered) regardless of whether QbTest results were used. This view agrees with our clinical advisers experience who uses QbTest only if a diagnosis is not reached after 1 assessment appointment (following the initial appointment).

To assess the QbTestUnclear strategy (objective 2) we ran a scenario analysis where it is assumed that QbTest is not administered until after 2 appointments, and then only in those where a diagnosis has not yet been reached. We assume that 20% of patients reach a diagnosis after 2 appointments without QbTest, after which QbTest is administered to the remaining 80% of patients whose diagnosis is less clear. We vary this proportion in a scenario and threshold analysis. We assumed that the only difference between strategy QbTestUnclear compared with strategy QbTestAll was the proportion of patients incurring the cost of QbTest, under the assumption that the diagnosis for the straightforward diagnoses does not depend on whether QbTest is used or not.

Model structure for dose-titration (objective 3)

We developed a conceptual model to capture the impact of Sensor CPT compared with Standard assessment for dose-titration in patients initiating pharmacotherapy for ADHD if sufficient data were available to populate it. The model captures the time period from initiating treatment until the first long-term monitoring assessment (assumed 6 months from the end of the titration period for children and 12 months for adults). Figure 14 shows a Markov model structure for the titration period, including sequences of treatments following the recommendations in NICE Guidelines NG87. It is assumed that patients undergo a period of dose-titration until they reach a stable dose and treatment, which may either be an optimal or sub-optimal dose / treatment. This is followed by a period on treatment until their first long-term monitoring assessment when their medication will be reviewed. During this time it is assumed patients remain on the stable treatment / dose, but that an optimal dose may become sub-optimal over time and patients move from the "optimal response" state to the "sub-optimal response" state. Also, patients may discontinue treatment due to adverse effects, lack of adherence, or lack of response. During the dose titration period patients are monitored every 2 weeks, when they incur appointment costs (likely remote appointments) and depending on assessment strategy the costs of the Sensor CPT. Patients accrue costs and QALYs depending on whether they are have optimal response, sub-optimal response or have discontinued treatment. The cycle length is 2 weeks to reflect the titration process, and the time-horizon reflects the time from initiation of treatment until the first long-term monitoring appointment.

Model structure for long-term monitoring (objective 4)

We did not identify any studies on the use of Sensor CPT for long-term treatment monitoring of patients with ADHD, and so it is unclear how Sensor CPT would be used in this context. However, we have developed a conceptual model setting which could potentially be used if sufficient evidence on use of Senso rCPTs in this context were available to populate it. Figure 15 shows a model which cycles between two phases, with the first phase modelling the routine long-term monitoring assessment where those patients with optimal response continue on medication until the next monitoring appointment, those with sub-optimal response or not on treatment have their medication adjusted with dose titration if required, and a proportion of patients may be deemed to be in remission following a

treatment holiday. Patients on treatment then enter into the response model until their next monitoring assessment, which is identical to that used for objective 3 post-titration. Patients in remission are assumed to stay in remission until their next monitoring assessment, when they may have relapsed. Routine monitoring is assumed to occur annually for adults and between 6 – 12 monthly for children.

5.2.5 Perspective and time-horizon

An NHS and personal social services (PSS) perspective was taken where costs and QALYs were discounted at an annual rate of 3.5%. Because longer waiting times lead to lower test costs under discounting, we also run a scenario where discounting is not applied. For the diagnostic assessment model we used a 10-year time-horizon, which was considered long enough to capture the time waiting for assessment, time to reach a diagnosis, and consequences of treatment in children before they enter adult services, by which time we assume all have been appropriately diagnosed and treated. We run sensitivity analyses to the time horizon. The model included health effects for both patients and carers, but run a scenario analyses to inclusion of carer dis-utility.

We did not evaluate the dose-titration and long-term monitoring models, due to insufficient evidence. For the dose-titration model the time-horizon should reflect the time until the first long-term monitoring appointment (6months for children / adolescents, and 12months for adults), and so discounting is not necessary. The long-term monitoring model should use a life-time horizon, or until the cohort of patients have all stopped treatment.

5.2.6 Uncertainty

To reflect uncertainty in model inputs, we conducted probabilistic sensitivity analysis (PSA), where parameter uncertainty is captured with probability distributions and simulation used to estimate expected (mean) costs, expected QALYs, incremental cost-effectiveness ratios (ICERs), and expected incremental net benefit (INB) at willingness to pay of £20,000 and £30,000 per QALY. The impact of uncertainty is presented using cost-effectiveness planes and the probability that QbTest is cost-effective at willingness to pay of £20,000 and £30,000 per QALY. One way sensitivity analyses were performed for all key parameters.

5.2.7 Model Implementation and Validation

The model is implemented in the R programming language.[54] All files to run the model are provided, including a guide to running the model. The model underwent internal validation by two members of the team not involved in the building of the model, following Büyükkaramikli et al.[140] The validation included face validity tests, checks of model calculations, and examination of the model outputs.

Figure 14 Markov model structure for dose-titration in the pharmacological treatment of ADHD. Dotted arrows indicate starting state in maintenance period model on the right-hand side.

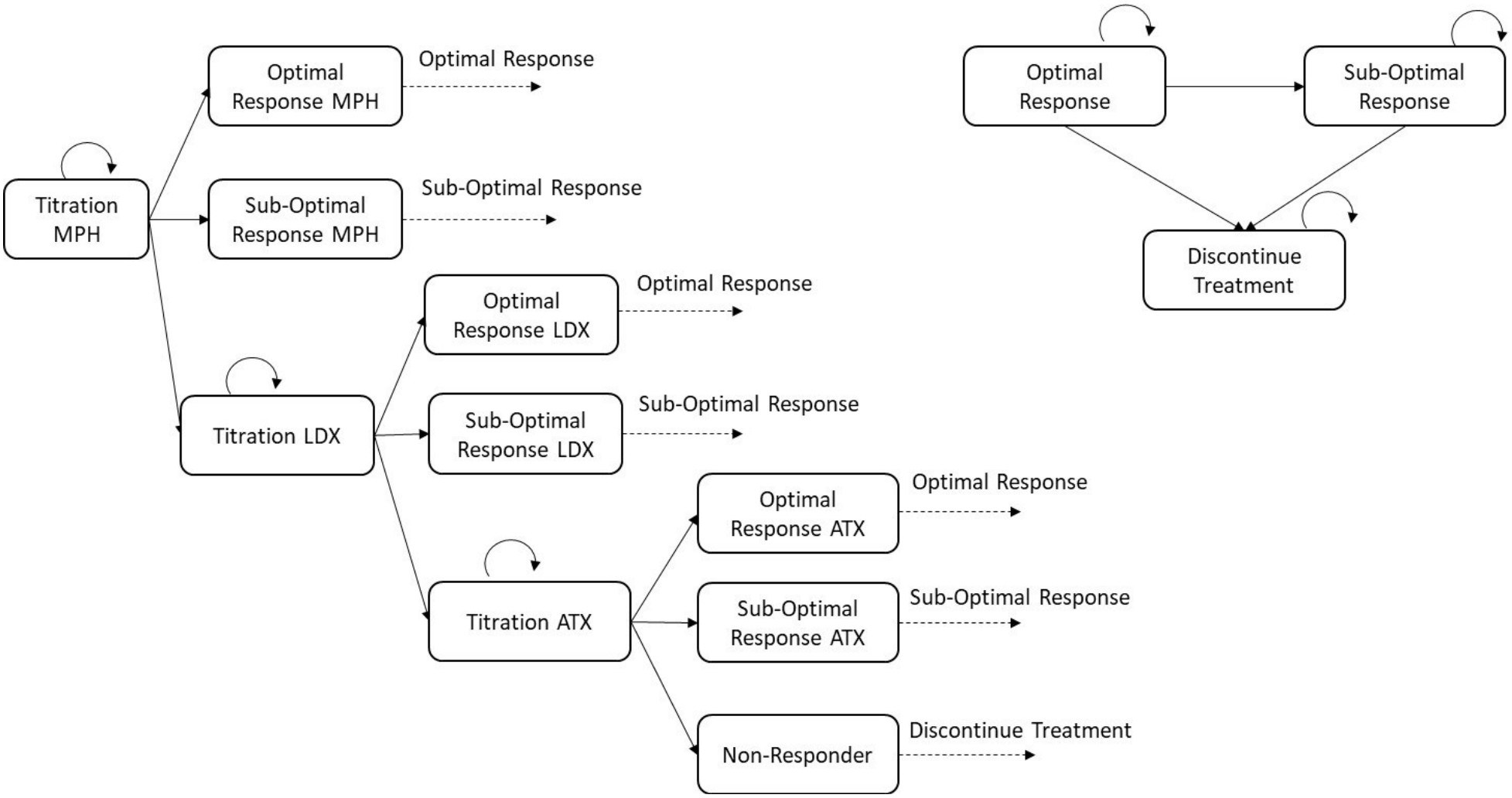
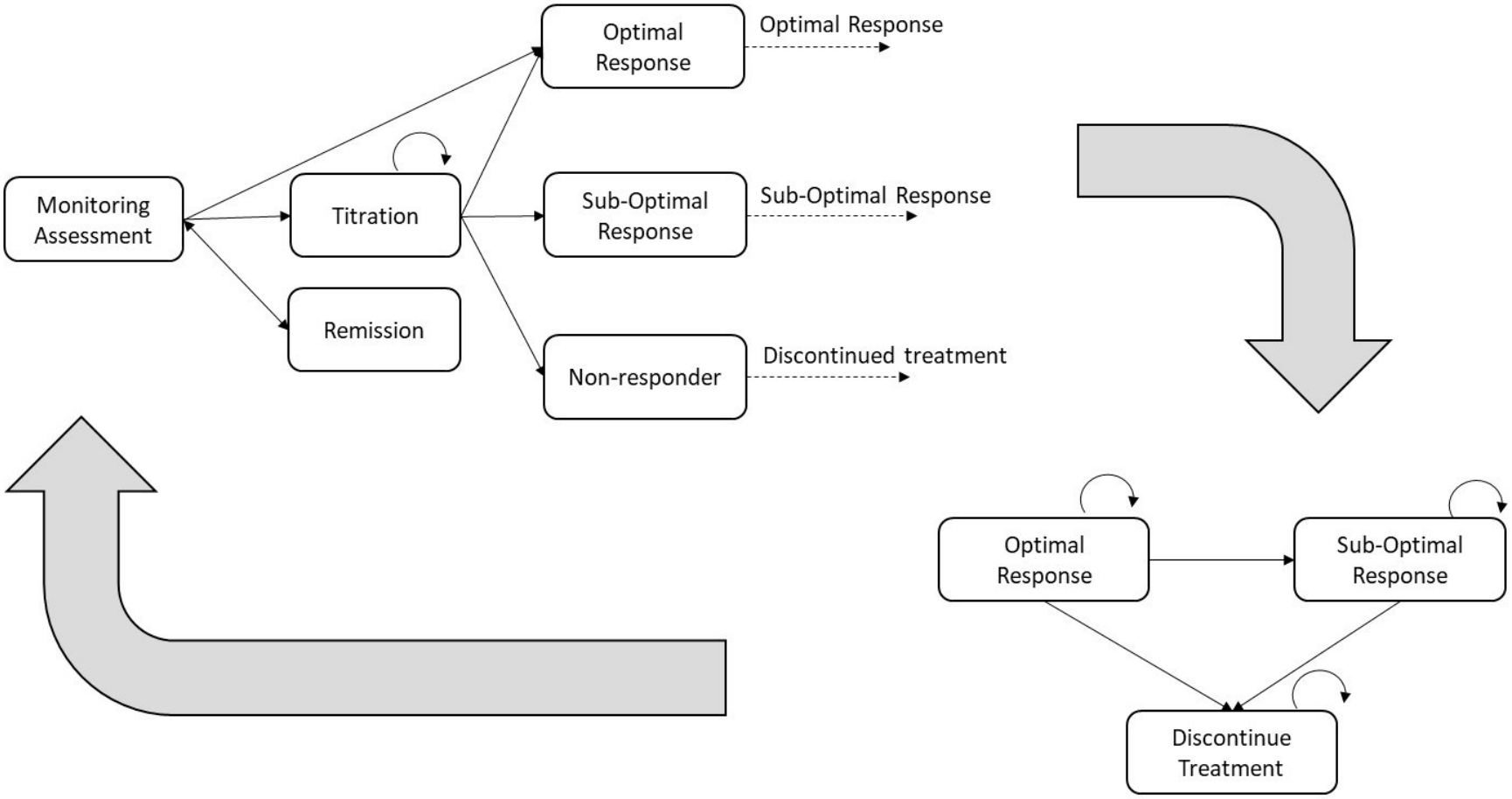


Figure 15 Markov model structure for long-term monitoring in the pharmacological treatment of ADHD



5.3 Model parameters and inputs

Model inputs for the diagnostic assessment model (Figure 11) are described below. These were derived from the clinical and cost-effectiveness reviews where possible, mostly from the AQUA trial, supplemented by targeted literature searches. Where there was insufficient evidence available we based parameters on expert opinion and conducted scenario analyses to explore the impact of these assumptions on the results. A summary of all model inputs, assumed values, assumed distributions, and evidence source is provided in Table 26.

5.3.1 Proportion receiving a diagnosis within 6 months after initiating assessment

In the AQUA trial 94/123 = 76.4% (95%CI 68.9%, 83.9) of patients received a diagnosis within 6 months after initiating assessment in the QbTest group (which corresponds to our strategy QbTestAll), whereas 76/127 = 59.8% (95%CI 51.3%, 68.4%) received a diagnosis within 6 months after initiating assessment in the control group (which corresponds to our strategy Standard).[18] We used these figures to inform the proportion receiving a diagnosis within 6 months, $p_{D6,test}$, in the model.

5.3.2 Waiting time for assessment

Under standard clinical assessment only

Studies providing information on waiting time for assessment under clinical assessment inform the rate that patients leave the waiting list for assessment for test=C, $\lambda_{A,C}$, which is the reciprocal of the mean waiting time (for an exponential waiting time distribution). Table 14 shows the results from a survey on waiting times for children conducted by the Petitions Committee of those who had signed petitions for improvements to ADHD assessment.[20] Applying the proportions to the range mid-points gives a mean waiting time of 368.65 days, although this may be an over-estimate due to selection bias (the sample being those who had signed a petition). The Focus ADHD study reports the mean time from referral to diagnosis and the mean time from assessment to diagnosis, from which we can calculate the mean time from referral to assessment, which was 335 days (with an approximation to the standard error of 25.0).[31] We prefer this estimate because it is based on data from 20 different sites, including a mix of CAMHS and paediatric services. We only use the data from the clinical assessment group (pre-QbTest) from the Focus ADHD study because the data post-QbTest was impacted significantly by the covid-19 pandemic.

Table 14 Studies with information on waiting time for assessment

Waiting time for clinical assessment	
Petitions committee survey [20]	
1-6m	18%
6m-1y	22%
1-2y	30%
2-3y	14%
Approximate mean time (days)	368.65
Focus ADHD,[31] Clinical Assessment Group (pre-QbTest)	

Waiting time for clinical assessment	
referral -> diagnosis (days)	Mean 452; range 15-3276; approx. SE* 22.5
assessment -> diagnosis (days)	Mean 117; range 0-1570; approx. SE* 10.8
referral -> assessment (days)	Mean 335; approx. SE* 25.0

*approximate standard error (SE) obtained by assuming range represents a 99.9% confidence interval

Under QbTestAll and QbTestUnclear assessment strategies

The only study that directly provides evidence on the time from referral to assessment when using QbTest is the Focus ADHD study.[31] As noted in the Focus ADHD report however, the estimates of number of days until assessment and until diagnosis for the post-QbTest group were significantly impacted by the covid-19 pandemic, and as such are not usable in our model. We therefore need a different approach.

The AQUA trial provides an estimated time-ratio (TR =0.85 95%CI 0.77, 0.93) for clinical appointment time for QbTest in addition to clinical assessment vs clinical assessment alone.[18] This estimate is based on an analysis of the full dataset where those without at diagnosis are censored after their last appointment, under the assumption that they would have similar time ratios as those that had a diagnosis. We therefore consider this time-ratio to be most applicable to those with a diagnosis within 6 months. The time-ratio can be interpreted as a proportional reduction in number of months (appointments) to reach a diagnosis. Assuming that those appointments could be offered to those on the waiting list, it may be reasonable to assume a similar proportional reduction in the number of months waiting for an appointment (assuming that there are no changes in the referral rate). So for a mean waiting time of 12*335/365 = 11.01 months under clinical assessment alone (Table 14), this would imply an adjusted mean waiting time of 0.85*11.01 = 9.36 months for QbTest in those with a diagnosis within 6 months of initiating assessment. We use a weighted average of an adjusted and non-adjusted transition rate according to the proportions who have a diagnosis within 6 months of initiating assessment:

$$\lambda_{A,Q} = \frac{p_{D6,Q}\lambda_{A,C}}{TR} + \left(1 - p_{D6,Q}\right)\lambda_{A,C}$$

Based on our assumed point estimates for ,

this gives a rate of 0.103, which corresponds to a mean waiting time of 9.70 months with QbTest compared with 11.01 months without it, ie a reduction in mean waiting time of 1.31 months.

The transition rate from waiting to assessment is applied to all patients regardless of whether they are in the subgroup of patients with diagnosis within 6 months or not, because that is unknown whilst the patient is on the waiting list. We vary both the mean waiting time under standard assessment and the time-ratio in sensitivity analyses to see the impact of assumptions around waiting list reduction on model results.

For the scenario where we explore the QbTestUnclear strategy, the waiting time is the same as for the QbTestAll strategy because the number of consultations for the patients with straightforward diagnoses is assumed to be unaffected by using QbTest.

5.3.3 Time from initiating assessment until a diagnosis is reached

Studies identified in the clinical review that report information on time from initial assessment to diagnosis are summarised in Table 10. The mean number of appointments roughly corresponds to mean time if it is assumed that appointments are scheduled at monthly intervals until a diagnosis is reached. We use data on the number of appointments, assumed monthly, to obtain estimates of mean time until diagnosis.

The pre-QbTest group in the Focus ADHD study[31] provides the largest and most representative evidence on the number of appointments until diagnosis under standard clinical assessment. We scanned and digitised data from the histogram for the number of appointments until diagnosis for pre-QbTest (Figure 6 in Appendix 2 of Focus ADHD study[31]) which enabled us to estimate the mean number of appointments separately in those who have a diagnosis within 6 months (appointments) and those who have further assessments after 6 appointments, presented in Table 15.

In our model we assume everyone has an initial appointment, after which the QbTest is administered and results made available in time for the next clinical appointment. The rate at which a diagnosis is reached for those who receive a diagnosis within 6 months under standard clinical assessment is estimated as the reciprocal of the mean (minus 1 for initial appointment), giving an estimate of the rate $\lambda_{D6,C}$ of 0.76 95%CI (0.706, 0.831), which we use in the model.

We then apply the hazard ratio reported in the AQUA trial to obtain the diagnosis rate (after the 1st clinical appointment) under the QbTest assessment strategy:

$$\lambda_{D6,Q} = \lambda_{D6,C} * HR$$

In a scenario analysis we use the HR for children and adolescents separately (Table 10).

We assume the diagnosis rate for those without a diagnosis within 6 months who continue to undergo further assessment is the same regardless of test, and estimated from the mean number of additional appointments (above 6) from the Focus ADHD study (Table 15), which gives a monthly rate of 0.12 95%CI (0.080, 0.189), which we use in the model.

Table 15 Mean number of appointments until diagnosis in the Focus ADHD study in those who have a diagnosis

Assessment -> Diagnosis	Clinical Assessment	QbTest plus clinical assessment
Focus ADHD[31] (n=549 per group)		
Mean (range) appointments	3.22 (1 to 50)	2.85 (1 to 32)†
Mean (se) appointments in those with ≤ 6 appointments (n=508)	2.3 (0.054) ‡	
Mean (se) additional (above 6) appointments in those with > 6 appointments (n=40)	8.9 (1.858) ‡	
† Note these figures were impacted by the Covid-19 pandemic ‡ Computed using reconstructed data from scanning the histogram in McKenzie et al Appendix 2[31]		

5.3.4 Prevalence of ADHD in those referred for assessment

Estimates of prevalence of ADHD in children range from 2% to 7%.[3] However, our model requires the prevalence of ADHD in those who have been referred for assessment for ADHD, which will be much higher due to the reasons for referral. We model prevalence of ADHD separately for those who have a diagnosis within 6 months, $\pi_{D6,test}$, and those who do not have a diagnosis within 6 months, $\pi_{NoD6,test}$.

Prevalence in those who have a diagnosis within 6 months

Studies providing information on the proportion whose diagnosis was ADHD in those who obtained a diagnosis (within 6 months in AQUA) are shown in Table 16. In the AQUA trial and Focus ADHD before-after study, there was a higher proportion of ADHD diagnoses (in those with a diagnosis) in the clinical assessment group compared to QbTest plus clinical assessment. We prefer to use the results from the AQUA trial which was an RCT and not influenced by the Covid-19 pandemic (which unfortunately impacted on the results from Focus ADHD). However, we note that the patterns seen are similar to those seen in Focus ADHD.

Table 16 Studies with the prevalence of ADHD diagnosis conditional on those with a diagnosis (within 6 months in the AQUA trial)

Prevalence of ADHD diagnosis (95%CI)	Clinical Assessment	QbTest plus clinical assessment
AQUA[18]	65/76 = 85.5% (77.6%, 93.4%)	69/94 = 73.4% (64.5%, 82.3%)
Focus ADHD[31]	445/549=81.1% (77.8%,84.3%)	418/549=76.1% (72.6%, 79.7%)

In our base-case we assume that there is perfect sensitivity and specificity, and so the estimates from the AQUA trial from Table 16 can be used directly to inform $\pi_{D6,C}$ and $\pi_{D6,Q}$.

In a scenario analyses we explore alternative values for sensitivity and specificity. To do this we assume that the results from the AQUA trial inform the prevalence of a positive diagnosis of ADHD from Table 16 (which includes both true and false positives), $\pi_{AQUA,test}$:

We can then rearrange to write the prevalence of ADHD in those with a diagnosis within 6 months as a function of $\pi_{AQUA,test}$, $sens_{test}$, and $spec_{test}$:

$$\pi_{D6,test} = \frac{\pi_{AQUA,test} - (1 - spec_{test})}{sens_{test} - (1 - spec_{test})}$$

Prevalence in those who do not have a diagnosis within 6 months

For those that did not receive a diagnosis within 6 months, the proportion of patients with ADHD is expected to be lower than in those who had a diagnosis within 6 months. We did not identify any studies proving information on this directly. Vogt et al 2011 [88] reported that 7/19=36.8% 95%CI (15.2%,58.5%) of patients who did not receive an ADHD under clinical assessment alone subsequently received an ADHD diagnosis after 1-year follow-up. We use this estimate for $\pi_{NoD6,C}$ in the model, and vary it in a sensitivity analysis.

To estimate the prevalence of ADHD in those who did not get a diagnosis by 6 months for the QbTest strategy, we note that the total prevalence of ADHD must be the same regardless of test. The means that:

$$\pi_{D6,C} p_{D6,C} + \pi_{NoD6,C}(1 - p_{D6,C}) = \pi_{D6,Q} p_{D6,Q} + \pi_{NoD6,Q}(1 - p_{D6,Q})$$

Re-arranging we obtain:

$$\pi_{NoD6,Q} = \frac{\pi_{D6,C} p_{D6,C} + \pi_{NoD6,C}(1 - p_{D6,C}) - \pi_{D6,Q} p_{D6,Q}}{(1 - p_{D6,Q})}$$

5.3.5 Sensitivity, and specificity

We did not find any suitable evidence to estimate sensitivity and specificity for QbTest in addition to clinical assessment in our clinical review due to issues with the reference standard used in the AQUA trial (see section 4.2.2). In our base-case we make an assumption that the sensitivity and specificity of QbTest plus clinical assessment is the same as that for clinical assessment alone (which is assumed a gold standard). The rationale for this is that adding additional information on which to base the assessment is not expected

to lead to a less accurate diagnosis in those where a diagnosis is reached. This is to some extent supported by the ROC analysis conducted by Hollis et al,[18] which found there was no evidence of a difference in diagnostic accuracy between QbTest plus clinical assessment and clinical assessment alone.

We conduct scenario and threshold analyses to explore the impact of changing sensitivity and specificity. The ratio (QbTest plus clinical assessment vs clinical assessment alone) of sensitivity against the imperfect reference standard from the AQUA trial was 0.86/0.96= 0.895. The corresponding ratio for specificity was 39.5/36.0=1.097, ie QbTest was more specific than clinical assessment alone, so specificity of Standard relative to QbTest is 0.9116. We therefore conduct a range of scenarios with alternative sensitivity and specificity assumptions.

5.3.6 Missed diagnosis (ADHD or No ADHD)

There were a high proportion of patients who did not receive a diagnosis in the AQUA trial, and this proportion was higher under Standard clinical assessment. The median number of appointments for those that did not receive a diagnosis in the AQUA trial was 3 appointments (calculated from data provided by the AQUA authors), however we do not know if they attended further assessment after the trial and eventually received a diagnosis (whether that was for ADHD or to Exclude ADHD). To get an understanding of the proportion of patients who have assessments beyond 6 appointments, the Focus ADHD study provides a histogram of the number of appointments until diagnosis in those who received a diagnosis (Figure 6 in Appendix 2 of Focus ADHD study[31]). Based on this we estimated that 7.25% of patients who eventually receive diagnoses (whether for ADHD or excluding ADHD) had more than 6 appointments. Applying this to the 40.2% of cases that did not receive a diagnosis in the standard clinical assessment arm of the AQUA trial, suggests that (100-7.25/40.2)=82% of those who do not have a diagnosis within 6 appointments will not attend for further assessment and their diagnosis is missed. If their diagnosis would have been for ADHD then they will not receive treatment benefits or costs as for false-negatives. If their diagnosis would have been to exclude ADHD then they will appropriately not receive treatment as for the true-negatives. In our base-case we assume the proportion who do not have further assessment p_{missed} =0.82. This is an important assumption in the model, due to the large and different proportions who do not receive a diagnosis in the AQUA trial, and so we vary this in scenario and threshold analyses.

5.3.7 Proportion of patients with a less clear diagnosis

We conducted a scenario analysis to evaluate the QbTestUnclear strategy (objective 2), as explained in section 5.2.4. We assume that everyone has 2 appointments, after which 20% of patients are diagnosed. QbTest is administered to the remaining 80% prior to the 3rd appointment. We base this estimate on the proportion without a diagnosis after 2 appointments in the AQUA trial, 80% 95%CI (75.0%. 85.0%), noting that the AQUA trial was

not designed to evaluate the QbTestUnclear strategy, and so these assumptions are speculative. We vary this proportion in sensitivity analysis.

5.3.8 Resource use and costs

Costs were obtained from routine NHS sources to represent costs in 2023/24 financial year values. For staff and unit costs related to administration of the sensor CPT and ADHD treatment, we use the latest NHS cost collection available from 2021/22,[141] and for costs from Personal Social Services Research Unit (PSSRU), we used the Unit Costs of Health and Social Care 2023 Manual for 2022/23 costs.[142] For 2023/24 NHS reference costs we also referred to the NHS payment scheme for 2023/24 published in August 2023,[143] however, none of the required unit costs were reported there. We inflated NHS cost collection 2021/22 and PSSRU 2022/23 to 2023/24 costs using the CPI index 06.2.1/3 (Medical services and paramedical services) using the ratio March 2024 to March 2023 (122.9 / 118.8 = 3.45% inflation)[141, 144] or March 2022 (122.9/114.4 = 7.43% inflation). For drug costs we use the British National Formulary (BNF) updated 26 March 2024,[145]. Resource use was estimated from our reviews of previous cost-effectiveness models, targeted literature searches, and through discussions with the manufacturers and clinical advisors. Unit costs of the sensor CPT were provided by the manufacturers. We did not include costs that are incurred regardless of assessment strategy, such as long-term treatment costs incurred for patients without ADHD.

Staff costs

Nurse time to administer QbTest

QbTest takes 15-20mins to complete, but the appointment to administer the test will need to be longer to conduct administrative tasks and set the test up. Hall et al. found a 30min nurse led appointment was required to administer the test,[87] whereas a previous economic evaluation assumed that a 1 hour appointment was required (based on assumption).[114] The economic evaluation[114] of the East Midlands AHSN study[71] noted that band 4 nurses were used in 2 trusts and band 2 in the other, whereas the manufacturer submission suggests a band 3 healthcare assistant. We assume a one-off 30min band 4 nurse-led appointment to administer the test (Table 17), based on an hourly cost of £38 inflated to £39.31.[142]

Consultant paediatrician time for assessment

We assume that each assessment appointment (with or without QbTest) is at a community paediatric service or CAMHS service. No costs for these services are available in the 2023 PSSRU so we take the mean of the costs of CAMHS Outpatient Attendance (£383.46) and Community Paediatric Service [Outpatient Attendance – code 290] (£350) from 2021/22 NHS reference costs [141]. Each appointment cost is therefore £366.73.[141] inflated to £393.98.

Costs related to using the technologies

A laptop computer, camera, tripod, and headband with reflective spot are required to conduct QbTest. A plastic sleeve is replaced on the headband each time the test is conducted, this is the only consumable used. When the test is completed, the results are

automatically uploaded to QbTest's central server in order to generate the report comparing the patient's results to the normative data. The device equipment is all provided as part of QbTest, as well as clinical advisor support, and training material, and this is included in the cost. Manufacturer advised that the cost per test ranges from £23-£96 per test depending on volume used, and most NHS trusts pay £31.20 per test. We vary this in a sensitivity analysis.

To administer the QbTest, a private and quiet room with a computer, desk and chair is needed. A hard stool with no back or arms is required for ages 6-12 and a hard chair with a back but no arms is required for ages 12-60. The room must be free of visual distractions for the patient or reflective areas, so windows must be able to be darkened. As staff time estimates account for overhead / space costs in PSSRU, we do not include additional costs for space, but note that appropriate space will need to be available, which may be an issue for implementation.

Trained healthcare assistants or nurses can oversee the test, and a trained clinician interprets the results. According to training material available on the QbTest website, there are three training modules, administration (2-3 hours), interpretation (2-3 hours), and intermediate interpretation (2-3 hours). The healthcare assistant or nurse (band 4) administering the test would only need to complete the administration portion of the training, while clinicians interpreting the results would complete all three portions. We assume the clinicians are medical or psychiatric consultants with an hourly cost of £109/hour [142] inflated to £112.76. The cost of training is likely to be approximately £118 per (band 4) nurse trained, and £1,015 per consultant trained, but we do not account for this in our model as it is a start-up cost that isn't allocated per patient treated.

The clinical review found that some patients (between 5%-11%, section 4.2.3 on test-failure) were unable to complete the QbTest assessment, however the test administration costs will still be incurred, and so test costs are incurred for all patients in the model. For patients for whom the test is not appropriate (for example those with IQ < 70)(manufacturers submission) QbTest would not be used under any assessment strategy, and so those patients are not included in our model. We run scenario analyses where 5% or 11% incur the test administration cost, but the outcomes are as for Standard assessment rather than QbTest.

Table 17 Cost of QbTest administration

Item	Cost
Band 4 nurse 30 minutes (£39.31 per hour*)	£19.66
QbTest unit cost per test	£31.20 (range £23-£96)
Total	£50.86
*Band 4 nurse per hour [excluding qualifications](PSSRU 2023)[142]	

QbTest is the only sensor CPT for which we found effectiveness data, however we do have cost information for Nesplora AULA (suitable for paediatrics) and EFSim.

Nesplora AULA costs £21.03 for a single use (plus a one-off registration fee of £84.12), £75.70 for 7 uses (monthly), £227.11 for 22 uses (quarterly) or £1345.85 per year for unlimited use on a single VR device. The actual price paid will therefore depend on the volume of tests required and the plan chosen. For the purposes of illustration we run a scenario with all inputs as for QbTest, but the test costs of £21.03 (for a single use), a scenario with the test cost of £10.32 (based on 22 uses per quarter), and a scenario with test cost of £2.80 (based on the annual professional plan with 40 assessments per month as estimated by Nesplora in their response to the EAG report). The cost of the nurse time to administer the test is as in Table 17 and added to the test cost.

Peili Vision Oy (ARVO) propose a different delivery model where a dedicated healthcare assistant travels to each practice one day per month to provide EFSim assessments to all patients with suspected ADHD based on initial screening. They estimate a cost per practise 7.5 hour working day of £197.05. Based on an assumed 30min slot for each test, 15 tests would be conducted per day at a cost of 197.03/15 = £13.14 per test. This includes the healthcare assistant cost. We include an illustrative scenario using this cost with all other inputs as for QbTest.

We stress that the scenarios using the costs for Nesplora AULA and EFSim should not be interpreted as cost-effectiveness analyses of those technologies, since there is no effectiveness data for these tests, and in the case of EFSim the delivery model is quite different.

Health-state costs for ADHD patients who do and do not respond to treatment

We identified health-state costs from analyses within our review of cost-effectiveness of ADHD treatment which were conducted in the UK, of which we considered the King HTA,[131, 137] and NICE guideline NG87[16], in particular Appendix 2 [130] to be the most appropriate sources for health state costs in paediatrics (see Section 5.1.2).

Zimovetz 2016[137] was the most recent UK-based study and it updates the health-state costs for the items from the King et al 2006 HTA report [131] using a survey of 21 UK specialists. However the NICE NG87 Guideline highlights concerns about potential bias in Zimovetz 2016 due to industry funding. Using the resource use and unit costs presented in Zimovetz 2016 Table 2, and in King 2006 Table 88, we updated the costs for responders and non-responders using PSSRU 2023[142] and National Schedule of Reference Costs 2021/2022.[141] inflated to 2024. The resulting costs are shown in Table 18 and Table 19.

The Appendix 2 of the NICE NG87 guideline [130] presents the resource use during dose titration and maintenance, and for non-responders to other treatments. Unit costs of psychiatrist time and band 7 nurse are updated to costs from PSSRU 2023. We assume a

ratio of 1:0.95 for contact hours for consultants, while the ratio for band 7 nurse is 1:0.33 [142]. The hourly cost for a consultant psychiatrist is £109 and for a band 7 nurse is £68 (excluding qualifications)[142] with inflated unit costs accounting for time ratios of £228.34 and £97.16 per contact hour, respectively. The resource use and costs per month on treatment are shown in Table 20.

We used resource use values for dose titration and responders and non-responders to apply to the states in the treatment models (Figure 12 and Figure 13). False-positives are assumed to incur the cost of a non-responder post-titration reflecting that patients are likely to continue to be monitored and treated, but we run a scenario analysis where no further costs are incurred post-titration for false-positive cases. We use the updated NICE NG87 appendix 2 values in the base case (Table 20 £38.06 and £76.11 for responder and non-responder costs per month after dose titration). In a scenario analysis we used the higher values for responder and non-responder costs after dose titration from Zimovetz 2016 (£170.52 and £325.90) and King 2006 (£398.86 and £573.13).

Table 18 Annual health-state costs of paediatric responder vs non-responder to ADHD treatment updated from Zimovetz 2016 Table 2[137]

Item	Responder Resource Use	Non-responder Resource Use	2022 Unit Cost	Responder Cost	Non-Responder Cost
Psychiatrist[1]	2.48	5.19	411.95	1021.64	2138.03
Pediatrician[2]	2.33	4.1	306.18	713.39	1255.32
GP[3]	2.62	4.24	50.69	132.81	214.93
Nurse[4]	2.71	4.48	60.00	162.60	268.81
Blood test[5]	0.42	0.72	3.18	1.34	2.29
ECG[6]	0.18	0.39	80.48	14.49	31.39
Total Annual				2046.27	3910.76
Monthly				**170.52**	**325.90**

Unit costs updated to 2023/24 values with sources matched as closely as possible unit costs used in Zimovetz 2016[137]

1. CAMHS outpatient attendances [141]
2. Paediatric outpatient attendance 420[141]
3. Table 9.4.2. Per consultation lasting 10 minutes, including direct care staff costs, excluding qualification costs (PSSRU 2023 unit cost manual)[142]
4. Table 9.2.1 Band 6 cost per hour excluding qualifications (PSSRU 2023 unit cost manual)[142]
5. DAPS05 – Haematology [141]
6. DADS EY51Z Electrocardiogram Monitoring or Stress Testing [141]

Table 19 Annual health-state costs of paediatric responder vs non-responder to ADHD treatment updated from King Table 88 [131]

Item	Responder Resource Use	Non-responder Resource Use	Unit Cost	Responder Cost	Non-Responder Cost
Psychiatrist[1]	3.5	5.75	411.95	1441.83	2368.72
Pediatrician[2]	2.25	2.5	306.18	688.90	765.44
GP[3]	3	2.75	50.69	152.07	139.40
Blood test[4]	0.05	0.35	3.18	0.16	1.11
ECG[5]	0.18	0.33	80.48	14.49	26.56
EEG[6]	0	0.43	286.53	0.00	123.21
Allergy test[7]	0	0.5	8.18	0.00	4.09
Total Annual				2297.44	3428.52
Monthly				191.45	285.71

Unit costs updated to 2023/24 values

1. CAMHS outpatient attendances [141]
2. Paediatric outpatient attendance 420 [141]
3. Table 9.4.2. Per consultation lasting 10 minutes, including direct care staff costs, excluding qualification costs (PSSRU 2023 unit cost manual)[142]
4. DAPS05 – Haematology [141]
5. DADS EY51Z Electrocardiogram Monitoring or Stress Testing [141]
6. DADS AA33D Conventional EEG, EMG or Nerve Conduction Studies, 18 years and under [141]
7. DAPS06 Immunology [141]

Table 20 Monthly health-state costs of paediatric responder vs non-responder to ADHD treatment updated from NG87 appendix 2 and applied to model structure shown in Figure 12 and Figure 13

State	Month	Resource use psychiatrist (minutes)	Resource use nurse (minutes)	Total cost
Response MPH	1	60	20	260.73
	2	100	0	380.57
	3	10	0	38.06
	4	10	0	38.06
	5	10	0	38.06
	6+	10	0	38.06
Non-response MPH	1	60	40	293.12
	2	0	0	0.00
Response LDX	3	60	20	260.73
	4	100	0	380.57
	5	10	0	38.06
	6+	10	0	38.06
Non-response LDX	3	60	40	293.12
	4	0	0	0.00
Response ATX	5	60	20	260.73
	6	100	0	380.57
	7+	10	0	38.06
Non-response ATX	5	60	40	293.12
	6	0	0	0.00
	7+	20	0	76.11
No treatment with ADHD	1+	0	0	0.00

Unit cost for psychiatrist £228.34 per hour and unit cost nurse £97.16 per hour, accounting for ratios of contact time. Following two months of dose titration, responders are assumed to have two hours of psychiatrist contact per year (averaged to 10 minutes per month) and for non-responders are assumed to have four hours of psychiatrist contact per year (averaged to 20 minutes per month). All resource use adapted from [130] and unit costs from PSSRU 2022 unit cost manual.[142]

Drug costs

MPH is available in modified-release (12h tablets or 8h capsules) and immediate release formulations. The NHS Specialist Pharmacy Service notes that modified release may be preferred in general (unless flexible dosing is required)[146]. We therefore identified costs for modified release formulations based on the average doses (Table 21) during titration and after titration used in the King HTA[131] using the nearest actual dose available. There is a variation in monthly costs across the different formulations available (Table 22), and in the absence of information on the market share of the different formulations, we used an average cost across formulations in our model.

LDX is available as an oral capsule. Dittmann et al 2013[147] found that starting with a 30mg daily dose, the mean dose after optimisation was 52.5mg (Table 21), which is close to the 50mg capsule. We assume the average dose during titration, is 40mg (the mid-point between starting and optimised dose). The estimated monthly costs are shown in Table 22.

Mean dose for ATX after titration in the King HTA was 45mg,[131] whereas it was 40.2mg in the Dittman trial.[147] The Dittmann trial was specifically on patients who have not responded after a trial of MPH, which is most relevant to our model, and so we use a dose of 40mg for ATX after titration. We use the estimate from the King HTA which is close to the 25mg available dose. There were 12 different products listed on the BNF, all with similar costs, and so we present an average cost for ATX in Table 22.

Table 21 Average drug dosage

Drug	Average dose during titration	Av dose after titration	Source
MPH Modified-Release12	27mg	35mg	King HTA[131]
MPH Modified-Release 8	25mg	41mg	King HTA[131]
LDX	-	52.5mg	Dittmann trial[147]
 ATX	28mg -	45mg 40.2mg	King HTA[131] Dittmann trial[147]

Table 22 Drug costs

Item	Pack price/ size	Monthly cost	Source
Methylphenidate hydrochloride			
Dose-titration average dose			
Concerta XL 27mg	£36.81 / 30	£36.81	BNF
Affenid XL 27mg*	£12.87 /30	£12.87	BNF
Delmosart 27mg*	£15.57 / 30	£15.57	BNF
Matoride XL 27mg*	£15.58 / 30	£15.58	BNF
Xaggitin XL 27mg*	£15.58 / 30	£15.58	BNF
Xenidate XL 27mg*	£15.57 / 30	£15.57	BNF
Equasym XL 20mg	£30.00/30	£30.00	BNF
Medikinet XL 20mg	£28.86/30	£28.86	BNF
Metyrol XL 20mg	£20.43/30	£20.43	BNF
	Average	**£21.25**	
Average dose after titration			
Concerta XL 36mg	£42.45 / 30	£42.45	BNF
Affenid XL 36mg*	£14.85 /30	£14.85	BNF
Delmosart 36mg*	£21.21 /30	£21.21	BNF
Matoride XL 36mg*	£21.22/30	£21.22	BNF

Item	Pack price/ size	Monthly cost	Source
Xaggitin XL 36mg*	£21.22/30	£21.22	BNF
Xenidate XL 36mg*	£21.21 /30	£21.21	BNF
Equasym XL 40mg	£60.00/30	£60.00	BNF
Medikinet XL 40mg	£57.72/30	£57.72	BNF
Metyrol XL 40mg	£39.88/30	£39.88	BNF
	Average	**£33.31**	
Lisdexamfetamine mesilate			
Average dose during titration			
Elvanse 40mg	£62.82 / 28	£67.31	BNF
Average dose after titration			
Elvanse 50mg	£68.60 /28	£73.50	BNF
Atomoxetine			
Dose-titration average dose			
Atomoxetine 25mg (average)†	£49.43 / 28	£52.96	BNF
Average dose after titration			
Atomoxetine 40mg (average)†	£50.79 / 28	£54.42	BNF
*bio-similar to Concerta; †average over 12 available products;			

5.3.9 Treatment effects

Adverse events

Adverse events rates were estimated using the NG87 NICE guideline review (summary forest plots for children aged 5-18 displayed in section E2 of document D).[16] There was no evidence of differences between the treatments in the total number of adverse events with risk ratio for MPH vs ATX RR=0.99 95%CI (0.87, 1.13), and risk-difference for ATX vs LDX RD=-0.01 95%CI (-0.12, 0.10). For the purpose of our model, which focuses on diagnosis decisions, rather than treatment decisions, we consider it reasonable to assume that the overall adverse event rate is the same for each treatment. To estimate the adverse event rate attributable to treatment, we estimate the risk difference compared with placebo. We pool the results from the studies of ATX, LDX, or MPH vs placebo to get a pooled risk-difference of 0.1435 95%CI (0.0734, 0.2186) (Table 23). We assume that this proportion of patients will experience adverse events whilst on treatment and there will be a dis-utility associated with this.

Table 23 Proportions with adverse events, and pooled risk difference for active treatment compared with placebo

AE/n (prop.) Study	Placebo	ATX	LDX	MPH
Hervas 2014[148]	73/111 (0.658)	76/112 (0.679)		
Martenyi 2010[149]	11/33 (0.333)	44/72 (0.611)		
Newcorn 2008[150]	40/74 (0.541)	149/221 (0.674)		146/219 (0.667)
Takahasi 2009[151]	43/62 (0.694)	144/183 (0.789)		
Wehmeier 2012[152]	27/62 (0.435)	32/63 (0.508)		
Montoya 2009[153]	19/51 (0.373)	65/100 (0.650)		
Childress 2014[154]	34/72 (0.472)		162/218 (0.743)	
Findling 2011[155]	45/77 (0.584)		160/233 (0.687)	
Random Effects Meta-Analysis: **Pooled risk difference treatment vs placebo: 0.1435 95%CI (0.0734,0.2186)**				

Some patients will discontinue treatment due to adverse effects, which we obtained from studies in the NG87 NICE guideline review of pharmacological studies (Document C). For MPH as a first line treatment there was no evidence of heterogeneity and so we used a fixed effect meta-analysis to give a pooled estimate for discontinuation for adverse effects of 0.0244 95%CrI (0.0127, 0.0396) (Table 24).

LDX and ATX are used for patients who have not responded to MPH. The NG87 NICE guideline review of pharmacological sequencing (Figure 274 of Document C)[16] identified 1 study with information for LDX and ATX in the population of those who have not responded to MPH, which we use as inputs to our model (Table 24).

Table 24 Treatment discontinuation due to adverse effects

Study	Discontinue	Total	Proportion discontinue	Standard Error
MPH				
Coghill 2013[156]	2	112	0.017857	0.012514
Findling 2008[157]	2	91	0.021978	0.015369
Wolraich 2001[158]	1	94	0.010638	0.010582
Palumbo 2008[159]	1	29	0.034483	0.033883
Wang 2007[160]	6	166	0.036145	0.014487
Fixed Effect Meta-Analysis: **Pooled proportion discontinuing 0.0244 95%CrI (0.0127, 0.0396)**				
LDX (in those who have not responded to MPH)				
Dittmann 2013[147]	8	128	0.0625	0.0214
ATX (in those who have not responded to MPH)				
Dittmann 2013[147]	10	134	0.0746	0.0227

Response to treatment

Response rate for MPH as a first line treatment was based on the studies with modified-release MPH in the NG87 NICE guideline review of pharmacological studies (Figure 42 of Document C).[16] We pooled these in a fixed effect meta-analysis which gave a pooled estimate of 0.502 95%CI (0.434, 0.571) (Table 25).

LDX and ATX are used for patients who have not responded to MPH. The NG87 NICE guideline review of pharmacological sequencing (Figures 268 and 273 of Document C) [16] identified 2 studies of LDX and 1 study of ATX in the population of those who have not responded to MPH. We pool the 2 studies of LDX in a fixed effect meta-analysis, and use the single study for ATX[147] as inputs to our model (Table 25).

Table 25 Proportion responding for MPH, LDX and ATX

Study	Responders	Total	Proportion responders	Standard Error
MPH				
Coghill 2013[156]	57	107	0.53271	0.048233
Wolraich 2001[158]	44	94	0.468085	0.051466
Fixed Effects Meta-Analysis: **Pooled proportion responders 0.502 95%CI (0.434, 0.571)**				
LDX (in those who have not responded to MPH)				
Dittmann 2013[147]	103	126	0.81746	0.034413
Jain 2011[161]	15	19	0.789474	0.093529
Fixed Effects Meta-Analysis: **Pooled proportion responders 0.672 95%CI (0.409, 0.872)**				
ATX (in those who have not responded to MPH)				
Dittmann 2013[147]	84	132	0.636	0.04187

5.3.10 Health state utilities

Utilities on waiting list and under assessment

Whilst patients are waiting for assessment and diagnosis, we assume that the proportion with ADHD have the same health-related quality of life as an ADHD patient who is not on treatment or not responding to treatment. For the proportion of patients without ADHD we assume they have the same health-related quality of life as an ADHD patient who is responding to treatment, which we consider to be more appropriate than using values from the general population, since they have been referred for ADHD assessment and likely have another condition which affects their quality of life. So, the average utility for a patient waiting for assessment and diagnosis is

$$utility = \left(u_{non-responder} - u_{carer-dis}\right)prev + u_{responder}(1 - prev)$$

where $u_{carer-dis}$ is the disutility (utility decrement) for a carer of an untreated ADHD patient (see below) and where the prevalence of ADHD can be estimated from the model prevalence parameters (section 5.3.4) as:

$$prev = \pi_{D6,C} p_{D6,C} + \pi_{NoD6,C}(1 - p_{D6,C})$$

Utilities for ADHD patients who do and do not respond to treatment

For the model we need utilities for those who do and do not respond to treatment ($u_{responder}$ and $u_{non-responder}$ resp.). Our review of previous treatment models found that typically it was assumed that utilities for patients not on treatment were the same as non-responders to treatment, and we also make this assumption. We reviewed previous models for utility values, and identified recent systematic reviews of quality of life in people with ADHD, and searched the references for UK studies or studies using EQ-5D.[162-167] We considered the most appropriate source to be the van der Kolk et al study[168] which was used in the NICE Guideline NG87 models,[16] was reasonably large and although conducted in the Netherlands, used a UK value set. The estimated utilities were 0.83 and 0.74 for responders and non-responders respectively which we use in the model. In sensitivity analyses we use the three sets of utilities that were used in sensitivity analyses by Zimovetz et al 2016. [137]

Utility decrement for adverse events of treatment

We assume a utility decrement due to adverse events of treatment based on Secnik 2005[169] which was used in the NICE Guideline NG87 models,[16] and who report a reduction in utility (using adjusted standard gamble) for with vs without adverse events of 0.01, which we use in the model.

Carer utilities

The quality of life for carers of patients with ADHD was based on Peasgood et al 2021[170] which was the most relevant study identified for a recent UK population, and reports results for EQ-5D. Peasgood et al compared the EQ-5D for carers of a child with ADHD with a matched control group, and we assume that this difference is a proxy for the difference in EQ-5D for carers of ADHD patients who are responding to treatment compared with non-responders. They report a difference in EQ-5D for carers of a child with ADHD vs matched controls of -0.071 when matching on standard covariates, -0.05 when also matching on results of ADHD screening for the carer, and -0.018 when also matching on employment and relationship factors.[170] We use a value of 0.018 for carer disutility, $u_{carer-dis}$, in our base-case model, and vary it to 0.071 in a sensitivity analysis, as well as running a sensitivity analysis with no carer disutility.

Table 26 Summary of model inputs, values and distribution assumed in base-case analysis, and source of evidence

Model parameter	Value in base-case	Distribution for PSA	Evidence source
Waiting time parameters			
Mean waiting time, Standard	335 days (SE 25) 11.01 months (SE 0.8217)	Normal(mean=11.01,sd= 0.8217)	Focus ADHD [31]
Rate waiting -> assessment, Standard	1/mean waiting time		Assumption
Time-ratio for clinical appointment time, QbTest vs Standard, TR	0.85 95%CI (0.77, 0.93)	LogNormal(meanlog=-0.163, sdlog=0.0482)	AQUA[18]
Rate waiting -> assessment, QbTest	$\lambda_{A,Q} = \frac{p_{D6,Q}\lambda_{A,C}}{TR} + \left(1 - p_{D6,Q}\right)\lambda_{A,C}$		Assumption
Prevalence of ADHD parameters			
Prevalence of ADHD in those who have a diagnosis within 6 months, Standard	65/76 = 85.5% (77.6%, 93.4%)	Beta (mean=0.855, var=0.0404^2)	AQUA[18]
Prevalence of ADHD in those who have a diagnosis within 6 months, QbTest	69/94 = 73.4% (64.5%, 82.3%)	Beta(mean=0.734,var=0.0456^2)	AQUA[18]
Prevalence of ADHD for those with no diagnosis within 6m, Standard	36.8% 95%CI (15.2%,58.5%)	Beta(mean=0.368,var=0.1107^2)	Vogt 2011 [88]

Model parameter	Value in base-case	Distribution for PSA	Evidence source
Prevalence of ADHD diagnosis given no diagnosis after 6m, QbTest	$\pi_{NoD6,Q} = \frac{\pi_{D6,C} p_{D6,C} + \pi_{NoD6,C}(1 - p_{D6,C}) - \pi_{D6,Q} p_{D6,Q}}{(1 - p_{D6,Q})}$	N/A	Derived from the requirement that total prevalence of ADHD does not depend on assessment strategy
Subgroups			
Proportion with diagnosis within 6 months, Standard	59.8% 95%CI (51.3%, 68.4%)	Beta(mean=0.598, var=0.0435^2)	AQUA[18]
Proportion with diagnosis within 6 months, QbTest	76.4% 95%CI (68.9%, 83.9%)	Beta(mean=0.764, var=0.0383^2)	AQUA[18]
Diagnosis rates			
Monthly diagnosis rate in those with diagnosis within 6m, Standard	0.76 95%CI (0.706, 0.831)	Log-Normal(meanlog=-0.269, sdlog=0.041)	Focus ADHD[31]
Hazard ratio for diagnosis QbTest vs Standard (in those with diagnosis within 6m)	1.44 (1.04, 2.01)	Log-Normal(meanlog=0.365, sdlog=0.168)	AQUA[18]
Monthly diagnosis rate in those with diagnosis within 6m, QbTest	$\lambda_{D6,Q} = \lambda_{D6,C} * HR$		Assumption
Diagnosis rate (in those with no diagnosis after 6m)	0.12 (0.080, 0.189)	Log-Normal(meanlog=-2.164, sdlog=0.222)	Focus ADHD[31]

Model parameter	Value in base-case	Distribution for PSA	Evidence source
Diagnostic accuracy			
Sensitivity of QbTest	1.0	N/A	Assumption
Specificity of QbTest	1.0	N/A	Assumption
Sensitivity standard clinical assessment	1.0	N/A	Assumed gold standard
Specificity standard clinical assessment	1.0	N/A	Assumed gold standard
Proportion of those without diagnosis at 6months who do not have further assessment	0.82	N/A	Assumption based on Focus ADHD[31] and AQUA[18]
Costs			
QbTest cost including nurse time to administer the test	£50.86 per test	N/A	Manufacturer submission, PSSRU 2023[142]
Consultant paediatrician out-patient appointment	1 appointment £393.98	N/A	NHS Reference costs 2021/22 [141] Average of CAHMS and community services
Monthly average costs for responders	During titration month 1 £260.73, month 2 £380.57, post-titration £38.06	N/A	NG87 appendix 2, PSSRU 2023.[130, 142]
Monthly average costs for non-responders	During titration month 1 £293.12, post-titration £76.11	N/A	NG87 appendix 2, PSSRU 2023.[130, 142]

Model parameter	Value in base-case	Distribution for PSA	Evidence source
Drug costs MPH	During titration £21.25 per month After titration £33.31 per month	N/A	BNF
Drug costs LDX	During titration £67.31 per month After titration £73.50 per month	N/A	BNF
Drug costs ATX	During titration £52.96 per month After titration £54.42 per month	N/A	BNF
Treatment Effects			
Proportion of responders on MPH	0.502 95%CI (0.434, 0.571)	Beta(alpha=100.9,beta=99.9)	Meta-Analysis of studies from NICE NG87
Proportion of responders on LDX	0.814 95%CI (0.751, 0.877)	Beta(alpha=118,beta=27)	Meta-analysis of LDX studies from NG87
Proportion of responders on ATX	0.636 95%CI (0.554, 0.718)	Beta(alpha=84,beta=48)	Dittman 2013[147]
Proportion with adverse events on treatment	0.1435 95%CI (0.0734, 0.2186)	Beta(alpha=13.2, beta=78.7)	Meta-Analysis of studies from NICE NG87
Proportion discontinuing due to adverse effects	MPH: 0.0244 95%CrI (0.0127, 0.0396) LDX: 0.0625 95%CrI (0.0206, 0.1044) ATX: 0.0746 95%CrI (0.0301, 0.1191)	Beta(alpha=12.0, b=481.7) Beta(alpha=8,beta=120) Beta(alpha=10,beta=124)	Meta-Analysis of studies from NICE NG87
Utilities			
Utility for patients waiting for assessment and diagnosis	$(u_{non-responder}$-$u_{carer-dis})$*prev + $u_{responder}$*(1-prev) where	See distribution for utilities for responders and non-responders below	Van der Kolk 2014[168]

Model parameter	Value in base-case	Distribution for PSA	Evidence source
	$prev = \pi_{D6,C} p_{D6,C} + \pi_{NoD6,C}(1 - p_{D6,C})$		
Utility for ADHD patients responding to treatment, $u_{responder}$	0.83	Beta(alpha=489.7, beta=100.3)	Van der Kolk 2014[168]
Utility for ADHD patients not on treatment or not responding to treatment, $u_{non-responder}$	0.74	Beta(alpha = 436.6, beta=153.4)	
Disutility for adverse events from treatment	0.01	N/A	Secnik 2005[169]
Carer disutility for ADHD patients not on treatment, and for patients not responding to treatment, $u_{carer-dis}$	0.018	N/A	Peasgood 2021[170]

5.4 Scenario and sensitivity analyses

A summary of the sensitivity and scenario analyses is given in Table 27 together with a rationale for each scenario.

Table 27 List of scenario analyses included

Scenario	Description	Base-case	Sensitivity Analysis	Rationale for analysis
1	Proportion of patients with less clear diagnoses	N/A	A threshold analysis for different values for the proportion of patients that the test is used for: varied from 0.5, up to 1	To explore objective 2 where sensor CPT is used in those with less clear diagnoses. We assume the only difference is in the cost of the test.
2	Hazard ratio for diagnosis rate, QbTest plus clinical assessment vs clinical assessment alone	1.44 (1.04, 2.01)	(a) 1.84 (1.23, 2.68) Subgroup analysis from AQUA for children 6-12y (b) 0.82 (0.37, 1.82) Subgroup analysis from AQUA for adolescents 12+y (c) 1 In all of above, the time ratio (TR) is assumed to vary linearly on a log-scale (passing through the base-case values and where TR=1 when HR=1) giving: $TR = \exp(-0.445 * \ln(HR))$	The hazard ratio for diagnosis rate from the AQUA trial differed in young children and adolescents
3	Mean waiting time under standard assessment	11.01 months (SE 0.8217)	3 months, 6 months, and 18 months	There is wide variation in waiting times across regions.
4	Sensor CPT cost (including nurse time)	£50.86	(a) £42.66 (QbTest lower range) (b) £115.66 (QbTest upper range) (c) £40.69 (Nesplora AULA single use) (d) £29.98 (Nesplora AULA quarterly plan for 22 uses)	We do not have effectiveness data for sensor CPTs other than QbTest. To explore the impact of different test costs, we vary the price using the range of costs provided by the manufacturers of QbTest, Nesplora AULA, and

Scenario	Description	Base-case	Sensitivity Analysis	Rationale for analysis
			(e) £22.46 (Nesplora AULA annual professional plan, 40 assessments per month) (f) £13.14 (EFSim assuming delivery model and costs proposed by company and 15 tests per monthly practice visit)	EFSim, which vary according to volume of use.
5	Higher response/non-response cost after dose-titration period	Responders: £260.73 m1, £380.57 m2, £38.06 m3+ Non-Responders £293.12 m1, £0 m2, £76.11 m3+	Zimovetz: Responders: £260.73 m1, £380.57 m2, £170.52 m3+ Non-Responders £293.12 m1, £0 m2, £325.90 m3+ King: Responders: £260.73 m1, £380.57 m2, £191.45 m3+ Non-Responders £293.12 m1, £0 m2, £285.71 m3+	We use the NG87 appendix 2 values in the base case and for post dose-titration (month 3+) responder and non-responder costs we use the higher Zimovetz or King values as a scenario analysis
6	Proportion with no further assessment after no diagnosis within 6m, p_{missed}	0.82	0, 0.25, 0.5 A threshold analysis for different values for the proportion of patients that have no further assessments: varied from 0 up to 1	We have no evidence to inform the proportion without a diagnosis within 6 months who go on for further assessments, but model results are likely

Scenario	Description	Base-case	Sensitivity Analysis	Rationale for analysis
				sensitive to assumptions on this parameter.
7	Time horizon	10 years	15 years and 20 years	The 10-year time-horizon is in line with the longest time-horizons of previous treatment models, but is somewhat arbitrary. We therefore explore sensitivity of results to longer time-horizons.
8	Discount rate	3.5%	0%	Longer waiting times lead to lower test costs under discounting, which may benefit longer waiting times. We therefore run a scenario where discounting is not applied.
9	Time-ratio (TR)	0.85	0.9, 0.95, 1	The time ratio is used to determine the impact of QbTest on waiting times, but this is based on assumption that the proportional effect in TR for number of appointments can be applied to waiting times. To explore the impact of this assumption we vary the TR to reflect a smaller proportional effect on waiting times.

Scenario	Description	Base-case	Sensitivity Analysis	Rationale for analysis
10	Diagnostic accuracy	$sens$=1 $spec$=1	(a)$sens_Q$ =0.9, $spec_C$=1 (b) $sens_Q$ =1, $spec_C$=0.9 (c) $sens_Q$=0.9, $spec_C$=0.9 (d) $sens_Q$ =0.9, $spec_C$=0.9 $\pi_{D6,test} = \frac{\pi_{AQUA,test} - (1 - spec_{test})}{sens_{test} - (1 - spec_{test})}$	There was no evidence comparing test accuracy of QbTest plus clinical assessment vs clinical assessment alone. We assumed that there is perfect diagnostic accuracy in our base-case, but relax this in this scenario.
11	Prevalence of ADHD in those without a diagnosis within 6months under clinical assessment, $\pi_{NoD6,C}$	36.8% 95%CI (15.2%,58.5%)	20%, 50% Threshold analysis varying this from 0% to 100%	We did not find any studies reporting this directly, so made an assumption based on Vogt 2011 [88]
12	Carer disutility, $u_{carer-dis}$	0.018	0, 0.071	Peasgood 2021[170] report different estimates depending on what they match for. We run a sensitivity analysis using 0.071 rather than 0.018. We also run a sensitivity analysis that does not include a carer disutility.
13	Waiting list costs	0	Waiting list costs for those with ADHD assumed equal to those for non-responding ADHD patients	Patients with ADHD may use additional NHS resource whilst waiting for assessment. For illustration we set this to the resource costs for ADHD patients not responding to treatment,

Scenario	Description	Base-case	Sensitivity Analysis	Rationale for analysis
				although acknowledge this may be an upper bound as these patients will be monitored more closely.
14	False-positive costs post dose-titration	Non-responder health state cost	0	Ideally those without ADHD who initiate treatment (false-positives) would stop treatment after a dose-titration period due to lack of response. In practise this does not happen and so we include a monitoring cost in our base-case, but set this to 0 in a scenario.
15	Proportion with diagnosis within 6 months, QbTest	0.764 95%CI (0.689, 0.839)	0.689, 0.598	To explore the impact of a lower proportion diagnoses within 6m on QbTest, at the lower CI from AQUA, and at the extreme with no difference between QbTestAll and Standard
16	Test-failure	Costs and QALYs unchanged	Test failure rate 5%, 11% who incur test administration cost, but all other costs and QALYs as for Standard	Those who do not complete the QbTest are likely to have costs and QALYs similar to those under standard assessment
17	Utility for ADHD patients responding to treatment; and	0.83 and 0.74	(a) 0.827 and 0.773 (b) 0.82 and 0.70 (c) 0.926 and 0.905	There is limited data on utilities. These scenarios cover those used in Zimovetz et al 2016 [137]

Scenario	Description	Base-case	Sensitivity Analysis	Rationale for analysis
	not on treatment / not responding to treatment			and cover assumptions made in previous models of treatment of ADHD

5.5 Model Results

5.5.1 Base-case results for strategy QbTestAll for diagnostic assessment

Under the base case scenario, QbTestAll has higher costs and QALYs gained compared to standard assessment, with incremental costs of £238.35 and incremental QALYs of 0.0385 per person evaluated for ADHD (Table 28). The resulting ICER is £6183.71 per QALY gained, which is cost-effective at a willingness to pay (WTP) threshold of £20,000 per QALY. The mean incremental net benefit (INB) is £532.55 and £918 at WTP of £20,000 and £30,000 per QALY, respectively. Exploring the impact of uncertainty in the input parameters, the QbTestAll intervention is cost-effective under 92% and 84% of model runs with a £20,000 and £30,000 WTP threshold respectively (Table 28 and). It may appear counter-intuitive that the probability that QbTestAll is cost-effective falls for higher WTP (Figure 17), however the reason for this is due to uncertainty as to whether QbTestAll has higher or lower incremental costs, as can be seen from the cost-effectiveness plane (Figure 16). Some model runs fall within the bottom-left quadrant (lower costs and lower QALYs), and so a higher proportion of model runs lie under the WTP threshold line at £20,000 compared with £30,000 WTP per threshold. Most model runs (71%) fall in the top right quadrant (higher costs and higher QALYs), with 17% in the bottom left quadrant (lower costs and lower QALYs), and 12% in the bottom right quadrant (lower costs and higher QALYs, ie dominant).

Table 29 shows the breakdown of costs and QALYs accrued while on the waiting list, under assessment, and post-assessment (for those that do or do not initiate treatment). In terms of costs, the QbTestAll strategy reduces the cost of assessment but increases the cost of treatment within the time horizon evaluated. This is due to diagnosis being reached sooner with QbTestAll, leading to patients being on treatment for a longer duration, and also due to a higher proportion initiating treatment (Table 30), due to more patients receiving a diagnosis with QbTestAll. In terms of QALYs, fewer QALYs are accrued on the waiting list and under assessment with the QbTestAll strategy, again due to faster diagnosis. More total QALYs are accrued for those on treatment, while fewer are accrued for those who do not have ADHD and do not receive treatment. Note that in the base case sensitivity and specificity of both tests are 1, so there are no false positives or false negatives. However, the proportion who do not receive a diagnosis is lower with QbTestAll which is why there are fewer QALYs accrued in the no-treatment group under QbTestAll. Overall, QALYs gained under QbTestAll are due to patients diagnosed with ADHD getting on treatment sooner, and a higher proportion receiving a diagnosis.

Table 28 Cost-effectiveness results comparing the QbTestAll strategy with Standard for diagnostic assessment (probabilistic analysis)

Strategy	Total Costs (discounted)	Total QALYs (discounted)	Incremental Costs	Incremental QALYs	ICER	(£20,000 WTP) Mean INB	(£20,000 WTP) Prob(CE)	(£30,000 WTP) Mean INB	(£30,000 WTP) Prob(CE)
Standard	£6,004.78	6.9083	-	-	-	-	-	-	-
QbTestAll	£6,243.14	6.9469	£238.35	0.0385	£6183.71	£532.55	0.922	£918.00	0.884

ICER=Incremental Cost Effectiveness Ratio; INB=Incremental Net Benefit; WTP=Willingness-to-pay; Prob(CE)=Probability of being most cost-effective

Table 29 Costs and QALYs accrued whilst waiting for assessment, under assessment, and post-assessment for those who initiated treatment (true and false positives) and those who did not on initiate treatment (true and false negatives). Probabilistic analysis

Strategy	Total Costs (discounted)				Total QALYs (discounted)			
	Waiting	Assessment	Post-assessment: those who initiated treatment	Post assessment: those who did not initiate treatment	Waiting	Assessment	Post-assessment: those who initiated treatment	Post assessment: those who did not initiate treatment
Standard	£0.00	£1,462.02	£4,542.76	£0.00	0.7150	0.4930	3.2551	2.4453
QbTestAll	£0.00	£1,263.55	£4,979.59	£0.00	0.6361	0.3457	3.5718	2.3933

Table 30 Proportion entering the post-assessment states, base-case

Strategy	QbTestAll	Standard
Proportion Initiating Treatment	0.579	0.538
Proportion Not Initiating Treatment with ADHD	0.081	0.121
Proportion Not Initiating Treatment with No ADHD	0.340	0.340

Figure 16 Cost-effectiveness plane for base-case model QbTestAll vs Standard (probabilistic analysis), with dashed line showing WTP threshold of £20,000 / QALY and dotted line showing WTP threshold of £30,000 / QALY.

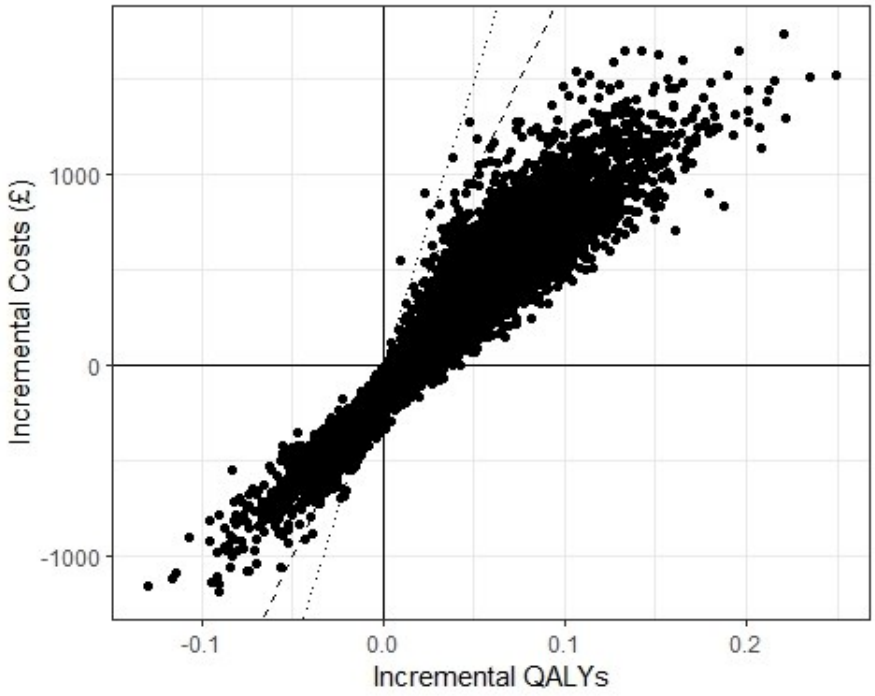
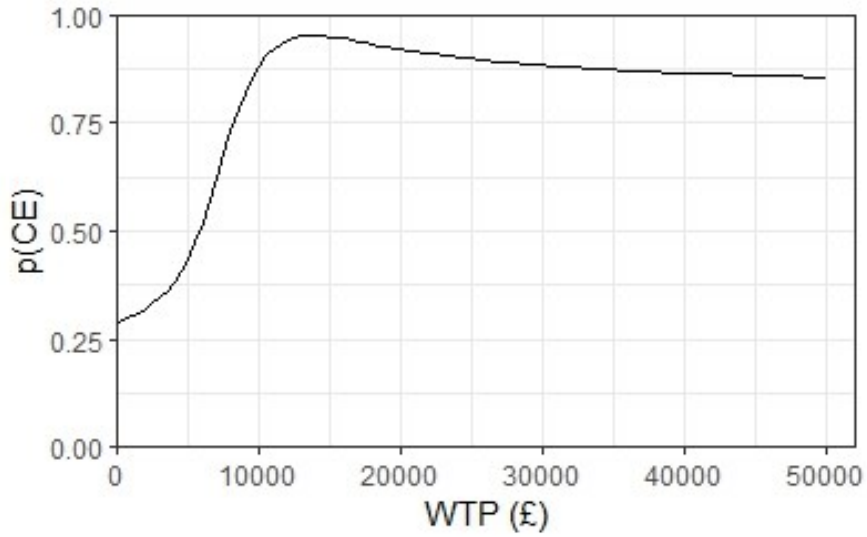


Figure 17 Cost-effectiveness acceptability curve for base-case model. Probability QbTestAll is cost-effective compared to Standard



5.5.2 Scenario and sensitivity analyses for diagnostic assessment

The main scenario analysis results are shown in Table 31, which we describe below. For the majority of scenarios examined, the QbTestAll scenario remains cost-effective.

Scenarios relating to parameters for time waiting for assessment

Varying the mean time on the waiting list under standard assessment (scenario 3) has little impact on the cost-effectiveness of QbTestAll, with the ICERs changing by <8% under the changes in waiting list time examined. Increasing the time-ratio parameter for the impact of increased rate of diagnosis due to QbTest on time spent on the waiting list (scenario 9) reduces both incremental costs and incremental QALYs, slightly reducing the ICER and the INB estimates, but QbTestAll remains cost-effective.

Scenarios relating to parameters for time from assessment to diagnosis

In scenario 2, we explore the impact of varying the hazard ratios for rate of diagnosis for QbTestAll compared to standard assessment. For the hazard ratio from children aged 6-12y (scenario 2a), the cost-effectiveness of QbTestAll is improved, with slightly higher incremental costs and higher incremental QALYs due to patients accessing treatment more quickly on average. When the hazard ratio is lower and highly uncertain as in children age 12+ (scenario 2b), costs are increased and QALYs reduced, compared to the base case. The mean INB is positive, but there is more uncertainty with only 65.9% or 68.9% of runs cost effective at £20,000 or £30,000 per QALY WTP thresholds, respectively. We also included a scenario in which we assume the hazard ratio is 1 (scenario 2c), such that QbTestAll does not increase the rate of diagnosis compared to standard of care. In this case, incremental costs are higher and incremental QALYs are lower than the base case, however the mean INB is still positive with probability of being cost-effective of 84.1% or 81.4% at £20,000 or £30,000 per QALY, respectively. This is because it is still assumed that a higher proportion receive a diagnosis within 6 months for QbTestAll.

Decreasing the proportion with diagnosis within 6 months (scenario 15) under QbTestAll results in negative incremental costs (cost-saving) for both parameter values tested. When $p_{D6,Q}$ =0.689 (the lower confidence interval from AQUA, scenario 15a) the incremental QALYs are positive and so QbTestAll dominates Standard assessment, with positive INB but only 71% or 62% of model runs cost-effective. When $p_{D6,Q}$ =0.598 (scenario 15b) there is no difference between the proportion with diagnosis within 6 months, and the mean incremental QALYs are negative and so the results represent the south-west quadrant, where we require the ICER to be less than -WTP thresholds, which is not the case indicating that QbTestAll is not cost-effective in this scenario. We also see that the INB is negative at both WTP thresholds, and there is only a 20% or 14% probability of being cost-effective at WTP £20,000 and £30,000 resp.

Scenarios relating to diagnostic test accuracy

In scenario 10 we explored different sensitivity and specificity assumptions. Reduced sensitivity of QbTestAll (scenario 10a) to 0.9 slightly reduces the ICER and the INB values for QbTestAll but does not affect the overall results (90% or 85% of runs are cost-effective). Reducing the specificity of QbTest to 0.9 increases the mean ICER to £10,296/QALY while decreasing the INB such that 71 or 72% of runs are cost effective. When both sensitivity and

specificity of QbTestAll are 0.9, the ICER is £7,584 and 75% or 73% of runs are cost-effective. When sensitivity of QbTestAll is 0.9 and specificity of standard assessment is 0.9, QbTestAll becomes more cost-effective than the base case with 94% or 90% of runs cost-effective and a mean ICER of £4,131. We conducted a threshold analysis varying the sensitivity of QbTestAll, which shows that INB is positive and increases with sensitivity (Figure 18). A breakdown of the costs and QALYs accrued while on the waiting list, under assessment, and post-assessment (for those that do or do not initiate treatment) shows that as sensitivity decreases lower treatment costs are accrued but also lower QALYs on treatment, as the proportion of false negatives increases (
Table 32).

Reducing the proportion with no further assessment after no diagnosis within 6m p_{missed} (scenario 6) drastically impacts the results for the values explored, with incremental costs becoming negative (cost-saving) so that QbTestAll dominates Standard assessment. All three values in scenarios 6a-6c make the QbTestAll cost-saving, with 95%-100% of model runs cost-effective. This occurs because there are more patients who do not have a diagnosis after 6m under Standard assessment, and if p_{missed} is small most of these patients will incur the costs of further assessment, leading to higher further assessment costs under Standard assessment compared with QbTestAll. The incremental QALYs decrease for QbTestAll compared with Standard when p_{missed} is small due to a higher number of ADHD cases being diagnosed after 6m for Standard compared with QbTestAll. A threshold analysis varying this parameter shows that while INB decreases as p_{missed} increases, it remains positive indicating that the conclusion that QbTestAll is cost-effective is robust to changes in this parameter (Figure 19).

The cost-effectiveness results are not sensitive to changes in the prevalence of ADHD in those without a diagnosis within 6 months (scenario 11), also shown by the threshold analysis (Figure 20). Increasing the proportion who fail to complete the test slightly increases the ICER and reduced INB, but overall conclusions do not change (scenarios 16a-b).

Scenarios relating to costs

Results were robust to varying the sensor CPT cost using values that represent the range of costs for QbTest or Nesplora (scenario 4).

Using the higher response and non-response costs for patients on ADHD treatment (scenario 5) has a large impact on the results. For scenario 5a using the costs based on resource use reported in Zimovetz 2016,[137] the ICER increased to £22,109/QALY with 48% of runs cost-effective at £20,000/QALY (85% at £30,000/QALY). For scenario 5b using the King HTA resource use costs,[131] the ICER increased to £24,472/QALY with 37% of runs cost effective at £20,000/QALY (80% at £30,000/QALY). The reason results are so sensitive to

these costs is because a higher proportion of patients initiate treatment and start treatment more quickly under QbTestAll and incur these costs.

If patients on the waiting list with ADHD are assumed to have resource use and costs equivalent to non-responding ADHD patients (scenario 13), then the cost-effectiveness is increased slightly with 94% or 90% of runs cost-effective. The results were also not sensitive to the removal of false-positive costs after dose titration (scenario 14), with this changing the ICER by no more than 1%.

Increasing the time horizon to 15 or 20 years (scenario 7) increases both incremental costs and incremental QALYs, but QbTestAll remains cost-effective. Using a discount rate of 0% slightly increases the ICER by 4% (scenario 8).

Scenarios relating to utilities

Results were robust to varying the utilities for responders and non-responders/not on treatment (scenario 17). When the difference in utility between responders and non-responders was small (scenario 17c) QbTestAll had a small increase in mean INB of £33.08 and the probability of being cost-effective was only 0.59 at the £20,000 willingness-to-pay threshold. Scenario 17c was a scenario used by Zimovetz 2016,[137] representing the values from a trial of LDX versus atomoxetine in patients who had an inadequate response to methylphenidate, and calculated using the Health Utilities Index Mark 2, whereas our base-case uses utilities were calculated using EQ-5D, did not restrict to those with an inadequate response to methylphenidate, and were based on a larger sample size with more precise estimates.

Removing the carer disutility (scenario 12a) reduces the QALYs gained and increases the mean ICER to £7,485, while increasing the carer disutility to 0.071 increases the QALYs gained and the mean ICER is reduced to £4,166 (scenario 12b). In both cases the overall result is similar to the base case.

Scenario for Objective 2 - QbTestUnclear

Scenario 1 examines the QbTestUnclear scenario to address objective 2, in which only a proportion of patients with unclear diagnosis receive QbTest. Due to QbTest being used for only a subset of patients, the QbTestUnclear scenario is slightly more cost-effective (lower ICER, higher INB) than the base case QbTestAll scenario. For example if only 50% of people receive QbTest the mean INB at £20,000/QALY increases to 556.41 with 93.3% of model runs cost-effective. As the proportion of patients who receive the QbTest decreases, the INB increases (Figure 21). Note however, that this scenario assumes no impact on diagnosis rates or other parameters than test cost, and so needs to be interpreted accordingly.

Table 31 Incremental cost-effectiveness results for QbTestAll vs Standard clinical assessment for the sensitivity and scenario analyses (probabilistic analysis)

QbTestAll (or QbTestUnclear) vs Standard				£20,000 WTP		£30,000 WTP	
Scenario	**Incremental Costs**	**Incremental QALYs**	**ICER**	**Mean INB**	**Prob CE**	**Mean INB**	**Prob CE**
BASE-CASE	£238.35	0.0385	£6,183.71	£532.55	0.922	£918.00	0.884
1a. Proportion with less clear diagnoses: 0.5	£212.71	0.0385	£5,531.25	£556.41	0.933	£940.97	0.895
1b. Proportion with less clear diagnoses: 0.6	£217.35	0.0384	£5,655.30	£551.32	0.926	£935.66	0.889
1c. Proportion with less clear diagnoses: 0.7	£222.75	0.0384	£5,807.51	£544.36	0.923	£927.92	0.885
1d. Proportion with less clear diagnoses: 0.8	£229.30	0.0388	£5,912.07	£546.41	0.924	£934.27	0.887
1e. Proportion with less clear diagnoses: 0.9	£236.91	0.0387	£6,114.70	£537.97	0.926	£925.42	0.890
2a. Hazard ratio for diagnosis rate, QbTestAll vs Standard: 1.84 (1.23, 2.68) Subgroup analysis from AQUA for children 6-12y	£241.84	0.0432	£5,593.45	£622.89	0.947	£1,055.26	0.915
2b. Hazard ratio for diagnosis rate, QbTestAll vs Standard: 0.82 (0.37, 1.82) Subgroup analysis from AQUA for adolescents 12+y	£312.42	0.0248	£12,604.07	£183.32	0.651	£431.19	0.689
2c. Hazard ratio for diagnosis rate, QbTestAll vs Standard: 1	£256.05	0.0306	£8,356.34	£356.78	0.841	£663.20	0.814
3a. Mean waiting time under standard assessment: 3 months	£208.89	0.0367	£5,692.11	£525.09	0.903	£892.08	0.860
3b. Mean waiting time under standard assessment: 6 months	££222.91	0.0375	£5,947.33	£526.71	0.911	£901.52	0.874
3c. Mean waiting time under standard assessment: 18 months	£259.36	0.0398	£6,511.20	£537.31	0.933	£935.64	0.903

QbTestAll (or QbTestUnclear) vs Standard				£20,000 WTP		£30,000 WTP	
Scenario	**Incremental Costs**	**Incremental QALYs**	**ICER**	**Mean INB**	**Prob CE**	**Mean INB**	**Prob CE**
4a. Sensor CPT cost (including nurse time): £42.66 (QbTest lower range)	£236.95	0.0390	£6,083.24	£542.08	0.924	£931.59	0.887
4b. Sensor CPT cost (including nurse time): £115.66 (QbTest upper range)	£304.57	0.0387	£7,862.25	£470.19	0.887	£857.58	0.863
4c. Sensor CPT cost (including nurse time): £40.69 (Nesplora AULA single use)	£217.52	0.0374	£5,812.26	£530.97	0.921	£905.22	0.880
4d. Sensor CPT cost (including nurse time): £29.98 (Nesplora AULA quarterly plan for 22 uses)	£220.28	0.0386	£5,705.75	£551.85	0.927	£937.91	0.889
4e. Sensor CPT cost (including nurse time): £22.46 (Nesplora AULA annual professional plan, 40 assessments per month)	£210.11	0.0387	£5,433.40	£563.29	0.931	£950.00	0.895
4f. Sensor CPT cost (including nurse time): £13.14 (EFSim assuming delivery model and costs proposed by company and 15 tests per monthly practice visit)	£204.74	0.0386	£5,302.40	£567.52	0.936	£953.65	0.900
5a. Higher response/non-response cost after dose-titration period from Zimovetz 2016: responder £170.52; non-responder £325.90	£845.24	0.0382	£22,109.05	-£80.63	0.481	£301.67	0.853
5b. Higher response/non-response cost after dose-titration period from King 2006:	£959.50	0.0392	£24,471.75	-£175.33	0.37	-£216.76	0.80

QbTestAll (or QbTestUnclear) vs Standard				£20,000 WTP		£30,000 WTP	
Scenario	**Incremental Costs**	**Incremental QALYs**	**ICER**	**Mean INB**	**Prob CE**	**Mean INB**	**Prob CE**
responder £191.45; non-responder £285.71							
6a. Proportion with no further assessment after no diagnosis within 6m , p_{missed} =0	-£676.47	0.0132	-£51,211.14 (**Dominates**)	£940.66	0.998	£1,072.76	0.998
6b. Proportion with no further assessment after no diagnosis within 6m , p_{missed} 0.25	-£401.94	0.0209	-£19,193.86 (**Dominates**)	£820.76	0.991	£1,030.16	0.980
6c. Proportion with no further assessment after no diagnosis within 6m , p_{missed} 0.5	-£120.77	0.0289	-£4,176.33 (**Dominates**)	£699.11	0.978	£988.28	0.948
7a. Time horizon 15 years	£385.65	0.0526	£7,326.94	£667.04	0.891	£1,193.39	0.856
7b. Time horizon 20 years	£483.85	0.0623	£7,771.24	£761.39	0.872	£1,384.01	0.839
8. Discount rate 0%	£290.25	0.0451	£6,440.65	£611.05	0.910	£1,061.69	0.875
9a. Time-ratio 0.9	£216.46	0.0365	£5,929.82	£513.60	0.914	£878.63	0.873
9b. Time-ratio 0.95	£193.33	0.0346	£5,591.57	£498.16	0.909	£843.91	0.866
9c. Time-ratio 1.0	£174.75	0.0331	£5,282.59	£486.85	0.904	£817.65	0.860
10a. Diagnostic accuracy =0.9, =1	£157.18	0.0316	£4,969.54	£475.41	0.898	£791.70	0.851
10b. Diagnostic accuracy =1, =0.9	£246.32	0.0239	£10,296.31	£232.15	0.713	£471.38	0.721
10c. Diagnostic accuracy =0.9, =0.9	£167.06	0.0220	£7,583.93	£273.51	0.749	£493.79	0.726
10d. Diagnostic accuracy =0.9, =0.9	£157.54	0.0381	£4,131.62	£605.08	0.943	£986.39	0.901
11a. Prevalence of ADHD in those without a diagnosis within 6months under clinical assessment, $\pi_{NoD6,C}$ =0.2	£229.47	0.0375	£6,115.25	£521.01	0.913	£896.24	0.877

QbTestAll (or QbTestUnclear) vs Standard				£20,000 WTP		£30,000 WTP	
Scenario	**Incremental Costs**	**Incremental QALYs**	**ICER**	**Mean INB**	**Prob CE**	**Mean INB**	**Prob CE**
11b. Prevalence of ADHD in those without a diagnosis within 6months under clinical assessment, $\pi_{NoD6,C}$ =0.5	£241.51	0.0389	£6,215.75	£535.57	0.925	£924.11	0.887
12a. Carer disutility, $u_{carer-dis}$=0	£241.48	0.0323	£7,485.01	£403.76	0.934	£726.39	0.903
12b. Carer disutility, $u_{carer-dis}$=0.071	£241.50	0.0580	£4,165.87	£917.93	0.881	£1,497.65	0.861
13. Waiting list costs for those with ADHD assumed equal to those for non-responding ADHD patients	£177.88	0.0390	£4,565.72	£601.33	0.943	£990.94	0.898
14. False-positive costs post dose-titration = £0	£244.20	0.0391	£6,253.25	£536.83	0.921	£927.34	0.882
15a. Proportion with diagnosis within 6 months, QbTest, $p_{D6,Q}$ =0.689	-£86.52	0.0035	-£24,709.03 (**Dominates**)	£156.56	0.710	£191.57	0.624
15b. Proportion with diagnosis within 6 months, QbTest, $p_{D6,Q}$ =0.598	-£497.18	-0.0408	£12,198.13 (**South-West Quadrant**)	-£317.99	0.201	-£725.58	0.138
16a. Test failure rate 5% who incur test administration cost, but all other costs and QALYs as for Standard	£237.49	0.0364	£6,520.86	£490.91	0.905	£855.10	0.867
16b. Test failure rate 11% who incur test administration cost, but all other costs and QALYs as for Standard	£235.09	0.0338	£6,938.35	£442.57	0.878	£781.40	0.846
17a. Utilities for responders and non-responders/not on treatment: 0.827 and 0.773	£237.34	0.0254	£9336.56	£271.07	0.984	£525.28	0.916

QbTestAll (or QbTestUnclear) vs Standard				£20,000 WTP		£30,000 WTP	
Scenario	**Incremental Costs**	**Incremental QALYs**	**ICER**	**Mean INB**	**Prob CE**	**Mean INB**	**Prob CE**
17b. Utilities for responders and non-responders/not on treatment: 0.82 and 0.70	£235.61	0.0489	£4814.03	£743.25	0.887	£1232.68	0.862
17c. Utilities for responders and non-responders/not on treatment: 0.926 and 0.905	£239.20	0.0136	£17570.07	£33.08	0.591	£169.22	0.997

Table 32 Costs and QALYs accrued whilst waiting for assessment, under assessment, and post-assessment for those who initiated treatment (true and false positives) and those who did not on initiate treatment (true and false negatives). Probabilistic an alysis

Strategy	Total Costs (discounted)				Total QALYs (discounted)			
QbTestAll sensitivity	Waiting	Assessment	Post-assessment: those who initiated treatment	Post assessment: those who did not initiate treatment	Waiting	Assessment	Post-assessment: those who initiated treatment	Post assessment: those who did not initiate treatment
0.6	£0	£1,263.73	£4,468.91	£0	0.6357	0.3874	3.2090	2.6716
0.65	£0	£1,263.73	£4,566.18	£0	0.6357	0.3794	3.2782	2.6188
0.7	£0	£1,263.73	£4,649.55	£0	0.6357	0.3726	3.3375	2.5736
0.75	£0	£1,263.73	£4,721.81	£0	0.6357	0.3666	3.3890	2.5343
0.8	£0	£1,263.73	£4,785.03	£0	0.6357	0.3614	3.4340	2.5000
0.85	£0	£1,263.73	£4,840.82	£0	0.6357	0.3568	3.4737	2.4697
0.9	£0	£1,263.73	£4,890.41	£0	0.6357	0.3528	3.5090	2.4428
0.95	£0	£1,263.73	£4,934.78	£0	0.6357	0.3491	3.5406	2.4187
1	£0	£1,263.73	£4,974.71	£0	0.6357	0.3459	3.5690	2.3971

Figure 18 Threshold analysis for sensitivity of QbTest plus clinical assessment vs clinical assessment alone

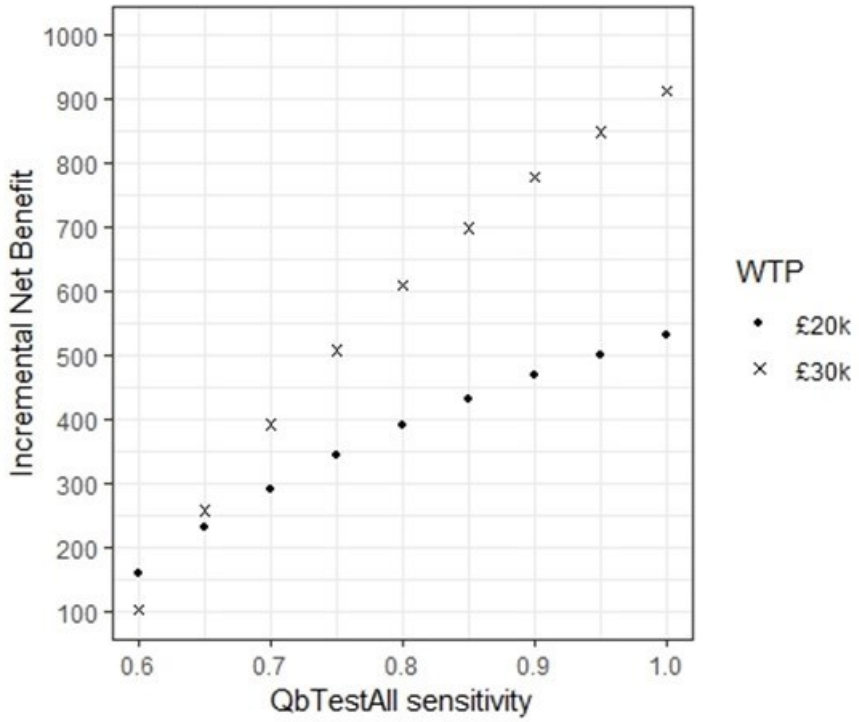


Figure 19 Threshold analysis for the proportion with no further assessment after no diagnosis within 6m. QbTestAll vs Standard for willingness-to-pay thresholds £20,000 and £30,000

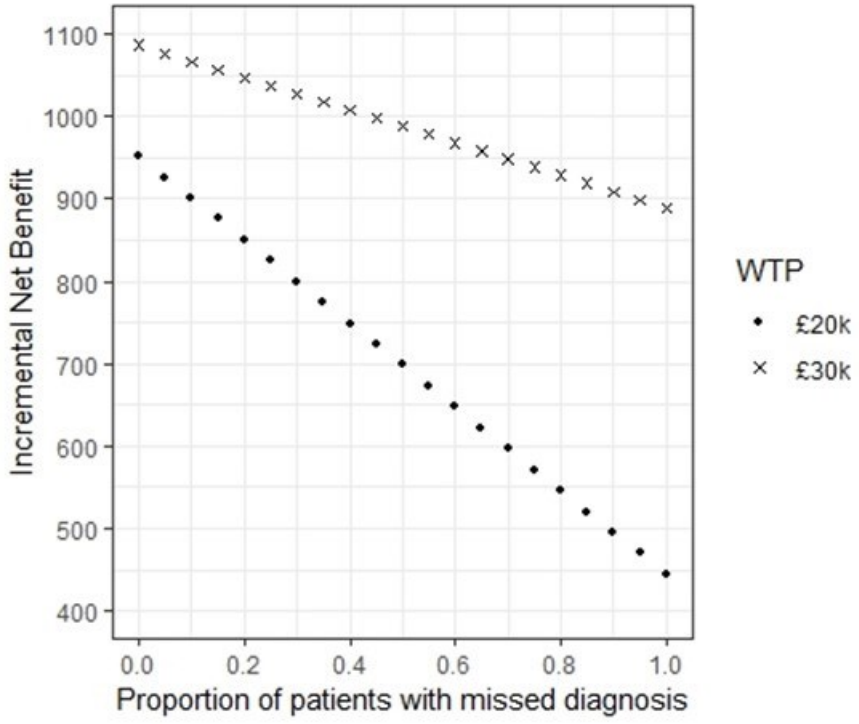


Figure 20 Threshold analysis for the prevalence of ADHD in those who do not have a diagnosis within 6 months. QbTestAll vs Standard for willingness-to-pay thresholds £20,000 and £30,000

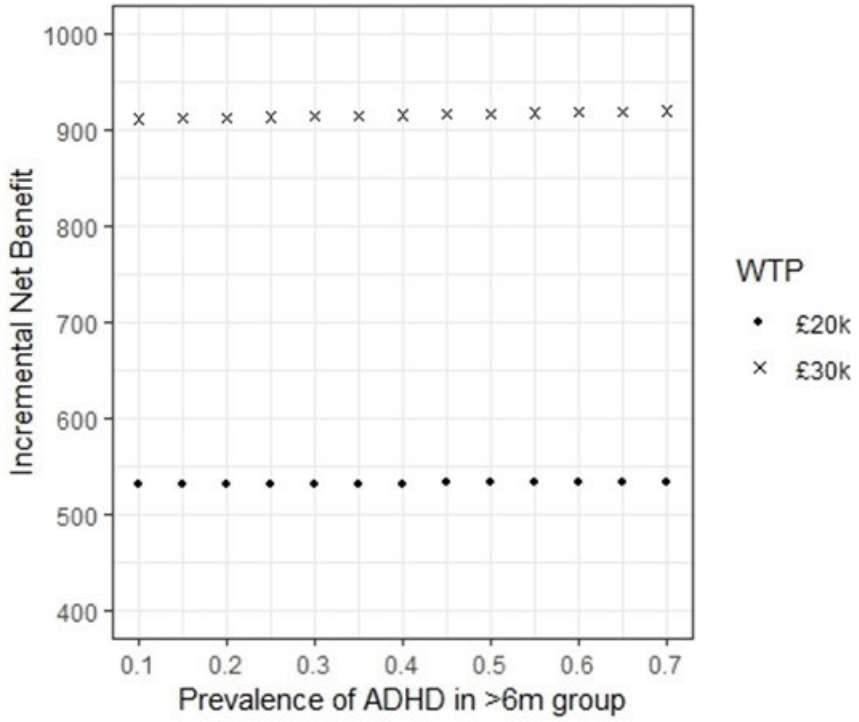
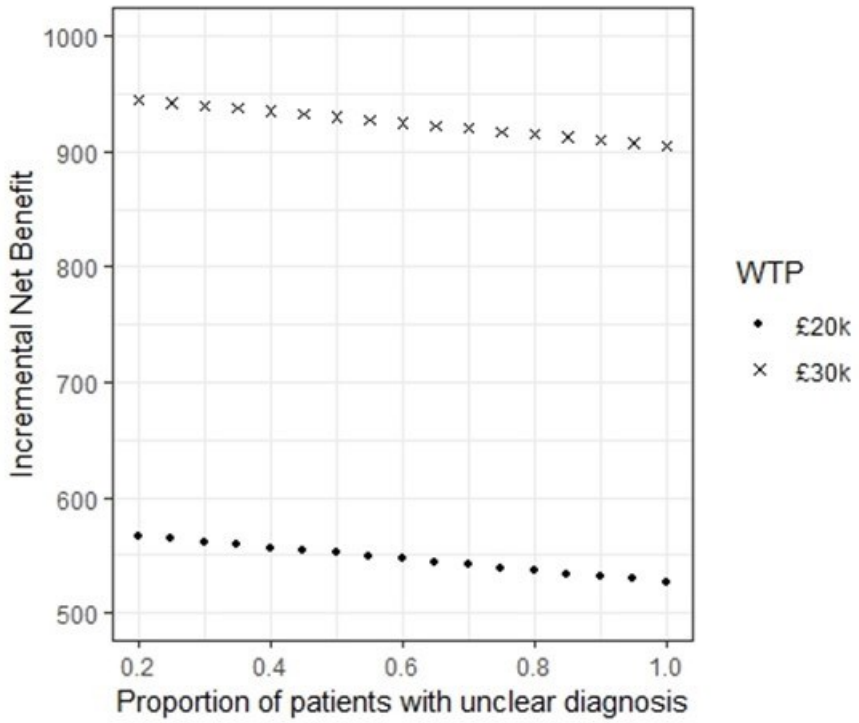


Figure 21 Threshold analysis for proportion with less clear diagnoses in whom QbTest is administered for objective 2. QbTestUnclear vs Standard for willingness-to-pay thresholds £20,000 and £30,000



6 Assessment of factors relevant to the NHS and other parties

Due to the subjective nature of diagnosis for ADHD, there may be concerns regarding the reliability and consistency of the diagnosis [17], which can lead to appeals which are time-consuming for all involved. A potential benefit of sensor CPTs is that they may lead to a lower proportion of cases being appealed. This potential benefit has not been directly captured in the economic modelling in this report.

The economic model estimates that there would be a higher proportion of those referred for assessment who initiate treatment when sensor CPTs are used, due to lower numbers without any diagnosis. This may have implications for availability of pharmacological medication.

To administer the sensor CPTs, a private and quiet room with a computer, desk and chair would need to be provided and staff would need to undergo training in order to be able to administer sensor CPTs.

If sensor CPTs were to be used for dose-titration and long-term monitoring of treatment where appointments are held remotely, administration of the sensor CPT would need to be held in-person in advance of the remote appointment, so that the results are in place to inform the assessment. Similarly for use in diagnosis for adults where assessments are typically conducted remotely.

Qualitative data suggested some concerns with the length and repetitive content of the QbTest, it may be that other tests are more interactive and engaging for patients. This should be explored further when making a decision regarding which sensor CPT to recommend.

7 DISCUSSION

7.1 Statement of principal findings

There were limited data on the clinical effectiveness of sensor CPTs for diagnosing ADHD. The majority of the evidence was focused on objective 1 (diagnostic accuracy and clinical- and cost-effectiveness of technologies that combine measures of cognition and motor activity for the diagnosis of ADHD in people referred with suspected ADHD), with some evidence for objective 3, but no data to address objectives 2 or 4. Most evidence was for the QbTest, mostly the in-person versions (6-12 and 12-60) with single studies on QbMini (the version for children aged 4 to 5) and the online QbCheck. There were two studies of EF Sim and two of Nesplora Kids – there were no studies of EF Sim web or of Nesplora Adults. Overall the limited data suggest that diagnosis with QbTest is likely to have similar accuracy compared to diagnosis based on clinical information alone, with some evidence of improvements in the number of consultations required to make a diagnosis. These findings are based primarily on the AQUA trial, which had some methodological limitations. There is insufficient data on the EF Sim or Nesplora tests.

Only one small feasibility study provided information on the impact of the QbTest on clinical outcomes. However, due to the feasibility design, small size and very low follow-up, impacted by the Covid-19 pandemic, it was not possible to draw conclusions regarding clinical effectiveness from this study.

Data on the accuracy of the tests was also very limited, particularly in combination with clinical assessment, which is how the test is intended to be used in practice. Overall, the populations enrolled in DTA studies varied, with nine studies conducted in adults (one of these focused on older adults), eight in children (five studies 6-12 years; one 5 years; one 5-15 years and one in children but age not specified). Two studies enrolled children and adolescents (12-18 years), one adolescents, and one adolescents and adults. Most studies included more male than female participants, particularly in the ADHD groups, although five studies included slightly higher proportions of female participants. Studies were conducted almost exclusively in Europe. Most studies reported baseline data on at least one PROGRESS-Plus characteristic, most commonly sex (18 studies), neurodevelopmental/ learning disorders (13 studies), and mental health disorders (11 studies). Some studies also reported on education (8), occupation (4), socioeconomic status (3), features of relationships (3 studies), place of residence (2), and ethnicity (1). However, we have highlighted that the reported data were not stratified by these characteristics, so we could not explore test accuracy within specific population subgroups.

Only five studies evaluated the accuracy of the QbTest in combination with clinical information, and only one of these (the AQUA trial) evaluated the accuracy in combination with clinical judgement. All others used prediction models to combine data from specific clinical measures with QbTest results – this is unlikely to reflect how the test would be used in practice. Data from the AQUA trial were limited as the diagnostic sub-study was restricted to children in whom a diagnosis was made at 6 months, resulting in exclusion of

80/250 children. It is likely that the restricted population may have represented a more "easy to diagnose" population as more complex cases may have been more like to withdraw from the study or to have been discharged without a diagnosis. However, as there was no information available on these participants this is difficult to judge. There were also limitations in the reference standard. This consisted of independent consensus criteria based on the DAWBA criteria, which is considered an accepted reference standard. However, in 123/241 participants DAWBAs were missing from one informant (i.e. either parent or teacher) meaning the independent assessors did not have access to this information when making a diagnosis. This is likely to have resulted in an underestimate of specificity and possible overestimate of sensitivity as the reference standard will have failed to diagnose some cases, these may have been more likely to be complex cases. This is supported by the results, as estimated specificity was very low (40%, 95% CI 25, 56%) for this study. There is therefore no reliable data on the accuracy of any of the sensor CPTs when used in combination with clinical judgement.

Estimates of the accuracy of the sensor CPTs alone were heterogeneous, and so results should be interpreted with caution. Summary estimates of the accuracy of the QBTest suggested that sensitivity was highest when the sub-components were combined into an overall measure (summary sensitivity 79%, 95% CI 69, 86%) but specificity was lower (summary specificity 59%, 95% CI 42, 74%) than when sub-categories were assessed individually. There was little evidence of a difference between the accuracy of the three sub-categories of activity, impulsivity and inattention. The single study of the QbMini suggested that this test had very poor discriminatory ability, but this is based on a single study which was judged at high risk of bias. The single study that evaluated the QbCheck suggested that this was at least as accurate as the in-person version of the test, but this was study was judged at high risk of bias and so results should be interpreted with caution. The single studies of Neslora Kids and EF Sim also suggested that accuracy was similar to that of the QbTest, but this was based on very limited information from studies at high risk of bias and no direct comparisons between tests was available.

Three studies provided a direct comparison between non-sensor CPT and sensor CPTs (two of QbTest and one of EF Sim), one study (the AQUA trial) provided a direct comparison between clinical diagnosis combined with QbTest with the accuracy of clinical diagnosis alone, and one compared the accuracy of the QbTest alone to the accuracy of QbTest plus clinical information. There were no consistent results to suggest that the accuracy of QbTest or EF Sim differed from that of standard CPT. One study reported that an overall measure from EF-Sim was more sensitive than the non-sensor CPT omission errors measure ($p=0.03$), but was less specific ($p=0.07$). There was no difference between the overall EF Sim measure and the other two CPT measures. One study reported that Qb measures were more sensitive ($p \leqslant 0.01$) but less specific than the two Connors' CPT measures, whilst the other reported that the QbTest was less sensitive ($p<0.01$) with no difference in specificity. The AQUA trial compared QbTest plus clinical judgement to a control group using the standard diagnostic process. The two groups had very similar specificity ($p=0.80$) but

sensitivity was slightly higher in the clinical diagnosis alone group compared to the group where diagnosis incorporated the QbTest (96% vs 86%), but there was no statistical evidence of a difference between groups (p = 0.14). A study in older adults presented a comparison between models based on the QbTest alone and a model that incorporated a clinical measure of ADHD symptoms. The model that incorporated the clinical information was much more sensitive than the QbTest alone (91% vs 56% p<0.01)). There was no evidence for a difference in specificity (p=0.11).

Five studies evaluated the impact of the QbTest on process measures. The AQUA trial randomised children to be assessed for ADHD with or without the QbTest as part of the diagnostic process. This study was judged at high risk of bias for time-to-event outcomes as a large proportion of participants (80/250) were uninformatively censored from the analysis as they dropped out or were discharged from the clinic and so did not have a diagnosis at 6 months. It was at low risk of bias for other outcomes, except cost of clinic appointments, where risk of bias was judged unclear.

It is likely that this reflective of what would happen in practice, but no details were available of the proportion of those that were censored who dropped out and what proportion was discharged without a diagnosis. It is also unclear why participants were discharged without a diagnosis and what the next steps would be for these children. The other four studies were retrospective record reviews, where data for those evaluated for ADHD prior to implementation of the QbTest were compared to data for those evaluated after the implementation of the QbTest. The largest of these studies, Focus ADHD, was affected by the Covid-19 pandemic as the Qb-Test was implemented over the same period as the pandemic. All four studies were judged at serious risk of bias as none adjusted for potential confounding factors. These studies also had other methodological limitations including lack of detail on how children were selected for inclusion in the assessments and very limited numerical and statistical data. Results from these studies should therefore be interpreted with extreme caution.

The AQUA trial reported a number of benefits associated with adding QbTest to the diagnostic process including fewer appointments to reach a diagnosis, reduced consultation time, increased proportion of patients with a diagnosis, greater clinician confidence in the diagnostic decision, and exclusion of the diagnosis in a greater proportion of children. They also reported that cost of clinic appointments were less in the QbTest arm compared to the control arm. The AQUA trial findings were supported by the limited data from the before-after studies which found that following implementation of the QbTest that fewer consultations were required to reach a diagnosis. These studies also reported other benefits included reduced time to reach a diagnosis (two studies), and reduced costs of testing. Focus ADHD reported increased time to make a diagnosis, fewer children having school observations as part of the diagnostic process, and fewer patients with an ADHD diagnosis, but these data are likely to have heavily confounded by the Covid-19 pandemic and so are unlikely to be reliable.

Eight studies provided data on clinician and/or patient and carer views of sensor CPTs for the diagnosis of ADHD. Most of the studies were judged to have some concerns of risk of bias due to a lack of detail reported about the methodology used. Five evaluated the QbTest through interviews, surveys or focus groups. Findings were in line with process measures data; clinicians felt it increased confidence in clinical decision making, and both clinicians and families felt it may reduce the time to diagnostic decision. Clinicians and families also felt that the test helped to improve communication. Although, some families felt that the test results were not properly explained to them and did not help them to understand symptoms or how diagnoses were made. Barriers to implementation included staffing, training, and technology requirements. Patients and caregivers highlighted concerns with the length and repetitive content of the test, and staff in one study reported that patients struggled with sensory discomfort and stress during the test. One study of QbCheck reported that participants found it easy to use, however this was from a brief 3-question survey conducted as part of a DTA study. Additionally, two survey studies evaluated EF Sim. Of these, one study, funded by the test manufacturer, reported positive findings concerning acceptability for teachers [redacted] who had implemented the test. The other study also reported positive acceptability from a short survey to children who had used the test in a DTA study.

We did not identify any previous models evaluating cost-effectiveness of diagnostic tests for ADHD, and so we developed a *de novo* model for sensor CPTs for the diagnosis of ADHD in people referred with suspected ADHD (objective 1). We only evaluated the QbTest in addition to clinical assessment vs clinical assessment alone, due to lack of evidence on the inputs needed for our model for other sensor CPTs. We found that QbTest in addition to clinical assessment is likely to be cost-effective, with incremental costs of £238.35 and incremental QALYs of 0.0385 per person evaluated for ADHD. The resulting ICER is £6183 per QALY gained, which is cost-effective at a willingness to pay (WTP) threshold of £20,000 per QALY. The mean incremental net benefit (probability of being cost-effective) is £532.55 (92%) and £918 (84%) at WTP of £20,000 and £30,000 per QALY, respectively. These findings were driven by reduced time waiting for assessment, reduced appointments until diagnosis, and a higher proportion receiving a diagnosis so that more patients with ADHD receive treatment benefits.

Due to data limitations we made several assumptions in our model, which we tested with a wide range of scenario analyses. We found that our overall conclusions were robust to most of our modelling assumptions. However, if the state costs for responders / non-responders on treatment were assumed to be higher, then QbTest in addition to clinical assessment would not be cost-effective, due to the higher proportion who initiate treatment and incur the higher costs. Also, if the proportion of patients with a diagnosis within 6 months for QbTest in addition to clinical assessment is lower (closer to that for clinical assessment alone), then QbTest in addition to clinical assessment becomes cost-saving but also incurs

lower or even less QALYs than clinical assessment alone. In this scenario, the cost savings do not justify the quality of life reductions.

As we did not identify any relevant studies for objective 2, we were unable to properly model the impact of sensor CPTs for the diagnosis of ADHD in people referred with suspected ADHD for whom current assessment cannot reach a diagnosis. We ran some exploratory analyses which demonstrated that if there are no consequences in terms of diagnostic accuracy then using sensor CPTs on the subset of those where a diagnosis is not reached after 1 or 2 appointments would be more cost-effective than using sensor CPTs on all patients, because the test cost is incurred for only some patients.

Six studies provided data for objective 3; all evaluated the QbTest. One DTA study evaluated the accuracy of QbTest as part of dose titration to against the reference standard of "good outcome" at 1-year follow-up. However, the QbTest formed part of the reference standard which is likely to overestimate the accuracy of the test and so it is not possible to draw strong conclusions from this study. One study (the QUOTA trial) provided data on process measures, however it was a small feasibility trial that was not designed and powered to formally evaluate the impact on outcomes. Three RCTs (the AQUA trial and two feasibility RCTs: FACT and QUOTA) and two implementation studies provided interview or survey data on patient/ clinician views of the QbTest for medication management and dose titration. Most of the studies had concerns regarding quality due to lack of information reported on study design. Findings suggested that healthcare staff and families mostly valued the role of the test for dose titration, checking medication utility, and improving medication adherence. However, some studies reported survey data from patients to suggest that the results of the QbTest may not have helped them to understand medication decisions, and some clinicians highlighted that using the QbTest for medication management can present logistical challenges due to having to schedule more appointments.

Due to the limited data on clinical effectiveness for objective 3 and lack of data for objective 4, we did not have sufficient evidence to model the impact of sensor CPTs for dose titration and treatment decisions or long-term treatment monitoring for people with a diagnosis of ADHD.

7.2 Strengths and limitations of the assessment

7.2.1 Systematic review strengths and limitations

Our systematic review followed published guidance on the conduct of systematic reviews of diagnostic test accuracy studies[35] and is reported according to PRISMA-2020 guidance[38] and PRISMA-DTA guidance,[171] making our review processes transparent and robust. The protocol was pre-registered on the PROSPERO database (CRD42023482963). The only changes that we made to the protocol were to clarify that although we had specified that studies need to be conducted in secondary care or remote settings, we would also include studies in which some participants (e.g. control groups) were enrolled in other settings. The

other change was to broaden our inclusion criteria for comparative studies to also include data from studies that compared the accuracy of sensor CPTs (alone or in combination with clinicial diagnosis) with the accuracy of clinical diagnosis alone. We also included one study of the QbMini test despite this not being explicitly mentioned in the protocol as this test is a version of the QbTest but for very young children (aged 5 years). We conducted extensive literature searches designed to maximise retrieval of relevant studies and did not apply any language, date or publication restrictions to these searches or to inclusion in the review. We identified one study reported only as an abstract in Spanish, all other studies were reported in English. We used Google Translate to translate the Spanish abstract, we asked a native Spanish language speaker to verify the accuracy of the translation. We pre-specified clearly defined, objective inclusion criteria. These specified that studies should be conducted in a population with suspected ADHD. We interpreted this broadly such that studies that used a mutli-gate design where patients with known ADHD and a group of controls without ADHD (either with another condition or healthy controls) were also included. We conducted a formal assessment of the risk of bias of included studies using the RoB 2 tool for RCTs,[44] the ROBINS-I study for non-randomised studies,[46] the QUADAS-2 tool for diagnostic test accuracy studies,[45] its extension QUADAS-C[172] for comparative accuracy studies, the CASP checklist for qualitative studies, and the Q-SSP tool for survey studies. Our synthesis included a meta-analysis where more than one study evaluated the same test. We stratified out analyses based on test, test component, and age. There were insufficient data to formally investigate heterogeneity or to look at the impact of other study features such as quality on estimates of accuracy. We did not include a formal assessment of publication bias due to the small number of included studies, and due to the difficulties in assessing publication bias for diagnostic test accuracy studies where there is no clear threshold for "significance". Our synthesis also included formal synthesis of qualitative and survey data to supplement the more formal quantitative evaluations. We used the meta-aggregative approach to qualitative synthesis based on guidance from the Joanna Briggs Institute (JBI) to synthesise data from qualitative studies. Using a mixed methods approach in our review allowed us to add contextual insights from the qualitative data to help understand the findings from the quantitative studies on process measures.

7.2.2 Limitations of the evidence base

The evidence based for this assessment was limited. The most relevant study for our appraisal was the AQUA trial, both in terms of the accuracy data and the information on process measures. However, as highlighted above, this study had methodological limitations both for the main trial and for the diagnostic sub-study. There were no good quality data on the EF Sim or Nesplora tests.

There was very limited RCT data – we only identified 3 RCTs across the four objectives, and two of these were small feasibility studies that were not powered to assess clinical effectiveness. Although we identified a relatively large number of DTA studies, most were at high risk of bias, and only the AQUA trial evaluated the test in the context it would be used in clinical practice. The majority of DTA studies used a multi-gate design which is likely to lead to overoptimistic estimates of accuracy. A challenge in this area is the identification

of an appropriate reference standard, particularly for evaluation of sensor tests in combination with clinical practice. We considered a diagnosis based on DSM-4 or 5 or ICD-10 criteria to be an appropriate reference standard. However, most diagnoses made in clinical practice adhere to these criteria, making it difficult to assess the accuracy of sensor CPT in combination with clinical diagnosis. The AQUA trial used independent assessment by two experienced child psychiatrists based on the DAWBA to make a diagnosis. This combines a range of data including parent interviews, interviews with the young person, a teacher questionnaire and a computer assisted clinical diagnostic rating to generate an ICD-10 or DSM-5 diagnosis. The use of two independent raters to confirm the DAWBA diagnosis is an attempt to separate the reference standard diagnosis from the routine clinical diagnosis, using multiple experienced assessors to make this more robust. This is an appropriate reference standard, however, in the AQUA trial the missing information from one informant for more than half of participants means that it cannot be considered a gold standard diagnosis in this trial. A further limitation with the AQUA trial was that it was restricted to those in whom a diagnosis was made by 6-month follow up. This lead to the exclusion of a large proportion of participants. Very few of the other DTA studies provided any information on whether any of the participants were missing a diagnosis. The multi-gate design will, by the nature of the design, have been restricted to those in whom a diagnosis was made. However, it is possible that other one-gate studies were also restricted to those with a diagnosis, even though this was not explicitly reported.

The QbTest does not specify a threshold to define a positive test result or provide explicit guidance on how results from the different sub-components should be combined to create an overall diagnosis of ADHD. This means that studies had to define their own threshold and define how to combine sub-components to create an overall measure of ADHD. There was therefore some variation in thresholds reported across studies, and as many studies did not pre-specify the threshold used it is possible that data-driven thresholds selected to optimise sensitivity and/or specificity may have been used. This has the potential to introduce bias. Studies also used different methods to derive an overall QbTest results – three studies, all by the same authors, defined a measure based on qualitative analyses of raw scored from the different QbTest sub-categories, others used a mean of the three sub-category scores. Where studies combined the QbTest with clinical information, most did so based on prediction models that combined QbTest sub-category results with specific clinical scales. The AQUA trial allowed clinicians to make their own diagnosis based on the full results of the QbTest and their clinical assessment. This is reflective of how the test is likely to be used in practice, but is difficult to standardise to allow comparison of accuracy across different studies.

The AQUA trial and the before-after implementation studies provided important information on process measures. However, all studies were restricted to children and so it is not clear whether similar results would be obtained in adults. They also included broad, general population and so it is not possible to determine whether similar results would be obtained in specific subpopulations such as those with co-morbidities including other neurodevelopmental conditions such as autism. The largest of the implementation studies, Focus ADHD, was severely impacted by the COVID-19 pandemic which coincided with the period in which the QbTest was implemented, making it very difficult to interpret results on measures such as number of appointments and waiting times. All implementation studies

were judged at high risk of bias, mainly due to lack of adjustment for confounding. The numerical results data reported by the implementation studies was limited in most studies, with few provided formal statistical comparison of results or reporting data such as means and standard deviations that would have allowed us to compare between groups.

Other studies were also limited by poor reporting. We contacted the authors of nine studies with requests for additional data where information was lacking or difficult to understand in the study reports, with five providing further information. However, four did not respond and so we are limited to the data reported in the study reports. Three of these were reported only as abstract and so very limited data were available for these studies,
There was no good quality data on the clinical effectiveness of the use of the QbTest for dose titration; there was one data on the accuracy of QbTest but results form this were difficult to interpret as the QbTest formed part of the reference standard. All other data were qualitative or survey data and that suggested some benefits and challenges of using the QbTest in this role, but high quality quantitative studies are needed to assess the clinical effectiveness of using QbTest for dose titration and treatment decisions.

7.2.3 Economic model strengths and limitations

This is the first economic model developed to evaluate the cost-effectiveness of diagnostic tests in people referred with suspected ADHD. We capture the time waiting for assessment, initial period of assessment, further assessment for a proportion of those without diagnosis following the initial period of assessment, diagnostic accuracy, and initiation of pharmacological treatment in those diagnosed with ADHD. We populated the model using evidence identified in our clinical effectiveness review, our review of cost-effectiveness studies of diagnostic tests for the assessment of ADHD and previous cost-effectiveness models of treatment for ADHD, and using targeted searches for specific inputs required in the economic model. Despite the comprehensive search for model inputs there was a lack of evidence for some of the assumptions and inputs to our model, which we outline below.

The health economic model for the use of sensor CPT in diagnosis of ADHD was only able to include the QbTest CPT and largely relied on data from a single study (the AQUA trial) for the impact of the addition of QbTest to clinical assessment. The AQUA trial recruited children and adolescents from a mix of CAMHS (48%) and community paediatric clinics (52%) in England[18] and so our results are applicable for patients referred through these routes with a similar case-mix. In a scenario where we used the hazard ratio for diagnosis specific to adolescents, there was a reduction in incremental net-benefit and an increase in the ICER, however the addition of QbTest to clinical assessment was still found to be cost-effective. This does rely on all other model inputs being unchanged for adolescents, in particular the proportion who receive a diagnosis within 6 months, which is a big driver of the cost-effectiveness results. We were unable to model the use of sensor CPT in diagnosis of ADHD in adults due to a lack of evidence on use of sensor CPTs in this context. Due to difference in diagnostic assessment between adult and paediatric services, with adult assessment taking place remotely in one extended session, we did not consider that the results from the AQUA trial could be applied in the adult setting. There was insufficient

evidence to conduct subgroup analyses for: sex, ethnicity, people with mental health, behavioural and neurodevelopmental conditions, people with developmental trauma, looked-after children, or people in the Youth Justice System or Adult Criminal Justice System.

We assumed that the sensor CPT would be administered just once during the assessment process, but it is possible that it could be administered again in cases where diagnosis remains unclear after several appointments. In the East Midlands AHSN study[114] one of the sites implemented QbTest in complex cases only, and we heard from our clinical advisors that this is how sensor CPTs may be used in practise. Due to limited data we were only able to explore the cost-effectiveness of sensor CPTs used for complex cases only by making a strong assumption that sensor CPTs would be used for those where a diagnosis was not made in 2 appointments (including the initial appointment) and the benefits seen in the AQUA study were generated by those who had more than 2 appointments, so that the findings would not change if QbTest were only administered after 2 appointments. We found that if this were the case then QbTest in addition to clinical assessment became more cost-effective due to reducing the number of patients for whom it is administered. Whilst this analysis was exploratory and makes assumptions, we hypothesis that using QbTest for those where diagnosis is unclear is likely to be cost-effective.

Waiting times for assessment can be long, and vary across regions, and we had to make assumptions about this. We found that QbTest was cost-effective across the range of mean waiting times we varied (even when we assumed no impact on waiting time), but it was more cost-effective when waiting times were longer, due to the impact of QbTest on reducing waiting times.

As noted above, issues with the reference standard in the AQUA study meant that there was high uncertainty of the diagnostic accuracy of QbTest in addition to clinical assessment compared with clinical assessment alone. We assumed in the model that clinical assessment alone was a gold standard and explored different assumptions on the diagnostic accuracy of QbTest in addition to clinical assessment. We found that results were robust to assumptions on test accuracy, but were driven by the proportion who received a diagnosis within 6 months which was assumed higher for QbTest in addition to clinical assessment based on the findings of the AQUA trial. If there are no differences in the proportion who receive a diagnosis within 6months then QbTest in addition to clinical assessment is not cost-effective compared with clinical assessment alone. We also had to make assumptions about outcomes for those that did not receive a diagnosis within 6 months, including the prevalence of ADHD in this group and the proportion who undergo further assessment and eventually a diagnosis is reached, which represent further uncertainties in the model results.

Patients for whom ADHD is excluded, or not diagnosed may go onto have further assessments for other conditions, or they may appeal the diagnosis and undergo further

assessment for ADHD. Our model does not capture this, although we base the number of appointments after 6 months on audit data from the Focus ADHD study.[31]

We identified three different sources for the post-titration costs incurred by responders and non-responders to treatment, and our results were sensitive to which we used. We preferred the figures used in the NICE guideline CG87 which give an ICER of £6,184/QALY, but if the costs based on Zimovetz 2016[137] are used then the ICER increased to £22,109/QALY, and if the costs based on King HTA[131] were used then the ICER increased to £49,079/QALY which is not cost-effective at normal willingness-to-pay per QALY thresholds. This is a key uncertainty in the model.

To administer the QbTest, a private and quiet room with a computer, desk and chair is needed, but we did not include additional costs for space, but note that appropriate space will need to be available, which may be an issue for implementation. We also did not include costs of time spent completing training for QbTest, as it is a start-up cost that isn't allocated per patient treated, but time will be required for staff to complete the training.

Our model took an NHS PSS perspective, and so did not include the impact of sensor CPTs on education services or educational outcomes. However, reducing school visits to collect evidence was found to be a benefit in the East Midlands AHSN study,[114] which may reduce the burden on schools to provide reports. Appropriate diagnosis and treatment of ADHD is expected to have benefits on educational attainment,[173] forming and maintaining relationships, and self-esteem[8, 9] and wide-ranging long-term outcomes including social function, education, criminality, alcohol use, substance use, and occupational outcomes, [10, 11] which were not captured in our model.

We used a 10-year time horizon, which only captures the period that children are managed within paediatric services. However, benefits of appropriate diagnosis continues into adulthood, and this benefit is not captured in our model. Whilst we acknowledge that it is important to capture life-time costs and benefits, this would have meant extrapolating very short-term data into the long-term. Nearly all previous treatment models for ADHD used a 1-year time horizon, with just a few models using a 10-year time-horizon, and so our model is in line with the longer of these.

7.3 Uncertainties

A key uncertainty, affecting both the clinical and cost-effectiveness reviews, is the accuracy of the QbTest in combination with clinical judgement. Data from the AQUA trial suggest that these are equivalent, but this is based on a single study judged at high risk of bias. The accuracy of the EF Sim, Nesplora Attention and web-versions of the sensor CPT in combination with clinical judgement has not been evaluated and so remains a key uncertainty. There is also insufficient data on the accuracy of any sensor CPT for medication management and so the clinical effectiveness of these tests in this role is unclear. There were also no data for any of the sensor-CPT in subgroups of patient such as sex, ethnicity,

people with mental health, behavioural and neurodevelopmental conditions, people with developmental trauma, looked-after children, or people in the Youth Justice System or Adult Criminal Justice System. Whether the tests perform differently in any of these subgroups remains a key uncertainty.

Another important area of uncertainty is the relative accuracy of sensor and non-sensor CPT for diagnosing ADHD. Limited data included in the review suggest that accuracy may be similar, and as non-sensor CPT are likely to be less costly than sensor CPT, it is possible that it may be more cost-effective to use non-sensor CPT. However, this would depend on whether the non-sensor CPT also have the benefits associated with sensor-CPT such as fewer appointments to reach a diagnosis, reduced consultation time, greater clinician confidence in the diagnostic decision, exclusion of the diagnosis in a greater proportion of children and improved communication. Evaluation of non-sensor CPT was beyond the scope of this appraisal as we only evaluated data on non-sensor CPT when a direct comparison was made with a sensor CPT.

All data on the impact of sensor CPT on process measures was for the QbTest and was in children, it is unclear whether similar results would be seen in adults and for other sensor CPT. Given the differences between the diagnostic pathways between adults and children it is possible that the QbTest would affect process measures in different ways for these different groups. Limited data from the AQUA trial suggested that effects on time to diagnosis may be greatest in younger children (age -7-12) than in adolescents.

Key uncertainties driving the cost-effectiveness results were related to resource costs for patients who do or do not respond to treatment, and the proportion of patients who do not receive a diagnosis following an initial period of assessment (6 months). The AQUA trial found a higher proportion of patients who received a diagnosis for QbTest in addition to clinical assessment compared with clinical assessment alone, but it is unclear what is driving these differences and if they would be seen in practice to the same degree. Those patients without a diagnosis were a mixture of those who were “lost to clinic” and those who were discharged, but it was unknown what proportion of them would return for further assessment at a later date, and the prevalence of ADHD in those that do and do not undergo further assessment. The Focus ADHD study[31] showed that there are a proportion of patients who do undergo further assessment beyond 6 appointments, but unfortunately due to the covid pandemic this study does not provide reliable data on the impact of QbTest on this.

Whilst we did not find evidence on the use of sensor CPTs in those patients where diagnosis is unclear, it is likely that use of QbTest in those where diagnosis is unclear is cost-effective compared with standard clinical assessment. However, we are uncertain how the cost-effectiveness of using QbTest in addition to clinical assessment in all patients would compare with just using it in those where diagnosis is unclear.

7.4 Equality, Diversity and Inclusion

Our research was based on existing literature and so we had no control over the participants enrolled. We were broad in our inclusion criteria such that studies from any country and in any language of publication were eligible. We had intended to investigate how the accuracy of included tests varied across different populations, but there were insufficient data to allow us to do this.

Our team included researchers with a broad range of experience and expertise. The lead authors are junior researchers within Bristol TAG, who were given the opportunity to lead on the writing of this report to help develop their research skills and portfolio. They were supported by the two senior authors, who provided advice and mentorship to the junior researchers leading on the reviews and health economic modelling. The team included those with expertise in systematic reviews, health economics, and medical statistics.

7.5 Patient and Public Involvement

We involved two patient representatives with lived experience of ADHD in this project. One of the co-authors also has recent lived experience of the diagnostic process for ADHD and the Qb-Test as her son has been evaluated with the Qb-Test (6-12).They attended team meetings (one at the beginning of the project and one closer to the end of the project), gave feedback on the plain language summary report, and wrote the section below about the difference sensor CPT may have for patients with ADHD. Involvement of patients had a positive impact on this project, they also contributed to the section on research priorities.

7.6 Impact on Patients

The process of gaining a diagnosis of ADHD, whether for your child or yourself, can be complex, lengthy and difficult to negotiate. Therefore, any improvements to the diagnostic pathway are very welcome. However, it is important to us that any changes to the current process are based on robust evidence of effectiveness as well as being acceptable to patients/ carers, and are valued by the clinical team. We appreciate the careful work the academic team have put into reviewing the evidence, and are disappointed there is not more robust evidence about their effectiveness and acceptability.

Speed of diagnosis is important to us, but accuracy is the most important factor so that people can be supported throughout their lives. Additionally, we feel that cost effectiveness may reduce waiting times for diagnosis (which can be considerable on the NHS – one patient representative waited 4 years), and give more people access to diagnosis. The wait between referral and assessment can be a stressful, uncertain time. Likewise, we feel that support with dose titration could be valuable – we are not aware of any formal clinical process for measuring effectiveness of medication, and people often don't know what to expect or how to really tell whether it's working. We are hopeful that the Qb / other systematic testing tools might contribute to better detection and timely treatment of ADHD

in the future, and whole heartedly support the recommendation of the review team that proper evaluation, including the cost effectiveness to the NHS, is an important next step.

8 Conclusions

8.1 Implications for practice

There was a lack of good quality data on all tests, both for diagnosis and medication management, particularly when evaluated in combination with clinical information. Our results suggest that QbTesting as part of the diagnostic work-up for ADHD in children(age <18 years), when used in combination with clinical assessment, is cost-effective. We found this finding was robust to nearly all assumptions made in the model. It also appears likely that QbTest would be cost-effective if used for the sub-group of patients who are not diagnosed on initial clinical assessment. It is unclear whether it would more cost-effective to perform the test only in this subgroup of patients, compared to using the test in all patients.

There are insufficient data to draw conclusions regarding the clinical or cost effectiveness of any of the other sensor CPTs (QbCheck, EF Sim, EF Sim Web Version, Nesplora Kids and Nesplora adults), including web-based CPT. There are also insufficient data to draw conclusions regarding the use of CPT tests for dose-titration, medication selection, and long-term treatment management.

As highlighted in section 6 the following factors may need to be considered when implementing the test in practice in the NHS these include:

- Potential benefits of sensor CPTs in reducing time consuming appeals
- Higher proportion of patients initiating treatment if sensor CPT are used which could have implications for availability of pharmacological medication.
- Need for private room and training for staff to be able to administer sensor CPTs
- If sensor CPTs were to be used for medication management where appointments are held remotely, administration of the sensor CPT would need to be help in-person Qualitative data suggested concerns with the length and repetitive content of the QbTest, it may be that other tests are more interactive and engaging for patients.

8.2 Suggested research priorities

The section on uncertainties (section 7.3) highlights a number of area where further research is needed. There is a clear need for a robust diagnostic test accuracy study comparing sensor CPT plus clinical assessment and clinical assessment alone with an appropriate reference standard. Such a study could include a direct comparison of the different sensor-CPT (including web-based CPT), and could also comparison with a non-sensor CPT such as the Conners CPT II. It should be powered to compare the accuracy of the test across different sub-groups of patients including age, sex, ethnicity, people with mental health, behavioural and neurodevelopmental conditions, people with developmental trauma, and, if data are available could also consider whether accuracy varies in looked-after children, or people in the Youth Justice System or Adult Criminal Justice System.

There is also a need for further studies to look at the impact of CPT on process measures and patient outcomes. Such studies should use a similar randomised design to the AQUA trial, and should enrol both adults and children and evaluate other sensor CPT and non-sensor CPT, not just the QbTest. They should measure patient outcomes as well as process measures and should also collect quantitative data on outcomes shown to be important to patients and clinicians in the qualitative evaluations, for example confidence in diagnostic decision making, communication between patients, clinicians and schools, patient understanding and acceptance of diagnostic decision, acceptability of the test to patients. It would also be valuable to consider subgroups of patients who are more difficult to diagnose separately from the whole population being evaluated for ADHD. For example, by following up patients who do not receive a diagnosis after an initial period of assessment (beyond 6 months) would be useful to estimate the proportion who subsequently receive further assessment for ADHD, and the proportion of those with further assessment who are diagnosed with ADHD or have ADHD excluded, and whether this differs if a sensor-CPT is used as part of the diagnosis process.

There is currently no good quality quantitative data on the use of sensor CPT for medication management, both for initial dose titration and medication selection and for longer term medication follow-up. Studies are therefore also needed to address this question. A similar design to that test in the QUOTA feasibility study[111] could be employed with participants randomised to treatment arms with and without sensor CPT as part of initial dose-titration and medication selection. Follow-up should be sufficiently long to also consider longer term medication management and provide information on longer term costs to inform the economic model. Important outcomes to consider would be whether patients respond optimally or sub-optimally to treatment, adherence to treatment, control of ADHD symptoms, quality of life, executive function, resource costs for patients depending on response to treatment, as well as process measures including number and length of appointments.

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9.1 Contributions of authors

Penny Whiting provided oversight of the clinical effectiveness sections of report. She drafted the clinical effectiveness sections of the protocol, contributed to the reviews of effectiveness, and drafted sections of the clinical effectiveness report. Eve Tomlinson led the clinical effectiveness reviews as first reviewer, including screening studies, completing data extraction, qualitative synthesis and risk of bias assessment. She also drafted sections of the clinical effectiveness report. Melissa Benevente and Chris Cooper acted as second review for the clinical effectiveness sections. Chris Cooper also designed and undertook the literature searches. He drafted the sections of the report related to searching. Amanda Owen-Smith provided oversight for the qualitative synthesis. She also contributed a patient perspective on the project and drafted the discussion section on Impact on Patients.

Hayley Jones provided statistical supervision. Hanyu Wang undertook the meta-analyses and produced plots for the diagnostic accuracy data. He also carried out the statistical comparison of tests.

Nicky Welton and Josephine Walker provided oversight of the cost-effectiveness analysis, contributing to model conceptualisation, protocol development, review of previous models, identification of inputs to the model, model validation, interpretation and discussion of results of the cost-effectiveness analysis. They drafted the cost effectiveness section of the report. Mary Ward developed and coded the health economic model, produced all model results, reviewed previous models and drafted sections of the report describing previous models, and cost-effectiveness results.

Catalina Lopez Manzano and Sara James provided a patient perspective on the project, edited the plain language summary, and contributed to the discussion section on Impact on Patients.

Dietmar Hank and Richard Lee-Kelland provided clinical advice for the project.

All authors were involved in commenting on the final report. Penny Whiting is the senior author and guarantor.

9.2 Ethics Statement

The research included in this report is secondary research and as such did not require ethical approval.

9.3 Information Governance Statement

There were no personal data involved in the production of this report.

9.4 Data-sharing statement

All data extracted for the systematic review and the results of the risk of bias assessments are provided in full in the appendices to this report. The economic model can be obtained from the corresponding author and will be shared upon reasonable request for academic collaboration.

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Appendix 1

Literature search strategies

a. Clinical effectiveness searches

Resource	N
MEDLINE	100
Embase	143
PsycINFO	362
CINAHL	15
ClinicalTrails.gov	13
ICTRP	30
Total	663
- Duplicates	-155
To screen	508

Database: MEDLINE (MEDALL)

Host: Ovid

Data parameters: 1946 to November 16, 2023

Date of search: 17 Nov 2023

#	Searches	Results
1	(QbTest* or "Qb Test*" or "(Qb) Test*" or "Qb Mini*" or "QbMini*" or (("Quantified Behavior*" or "Quantified Behaviour*") adj5 test*) or QbTech).af.	68
2	(QbCheck* or "Qb Check*" or "(Qb) Check*").af.	1
3	(Nesplora* or "Giunti psychometrics").af.	21
4	(ARVO* or EFSim* or "EF Sim*" or EPELI or "Peili Vision Company").af.	1507
5	Attention Deficit Disorder with Hyperactivity/ or ADHD.af.	44434
6	4 and 5	5
7	((motion* adj5 senso*) and (hyperactivity or ADHD)).ti,ab,kf.	6
8	1 or 2 or 3 or 6 or 7	99
9	NCT03368573.af. or (QUOTA and adhd).ti,kf. [QB test]	3
10	NCT02209116.af. or ((AQUA and ADHD) or AQUA2).ti,kf. [QB test]	5
11	NCT02473185.af. [QB test]	1
12	NCT02477280.af. [QB test]	0
13	NCT05846815.af. [ARVO Test]	0
14	9 or 10 or 11 or 12 or 13	9
15	8 or 14	100

Database: Embase

Host: Ovid

Data parameters: 1974 to 2023 November 16

Date of search: 17 Nov 2023

#	Searches	Results
1	(QbTest* or "Qb Test*" or "(Qb) Test*" or "Qb Mini*" or "QbMini*" or (("Quantified Behavior*" or "Quantified Behaviour*") adj5 test*) or QbTech).af.	89
2	(QbCheck* or "Qb Check*" or "(Qb) Check*").af.	3
3	(Nesplora* or "Giunti psychometrics").af.	24
4	(ARVO* or EFSim* or "EF Sim*" or EPELI or "Peili Vision Company").af.	62360
5	Attention Deficit Disorder with Hyperactivity/ or ADHD.af.	53113
6	4 and 5	21
7	((motion* adj5 senso*) and (hyperactivity or ADHD)).ti,ab,kf.	10
8	1 or 2 or 3 or 6 or 7	143
9	NCT03368573.af. or (QUOTA and adhd).ti,kf. [QB test]	3
10	NCT02209116.af. or ((AQUA and ADHD) or AQUA2).ti,kf. [QB test]	6
11	NCT02473185.af. [QB test]	1
12	NCT02477280.af. [QB test]	0
13	NCT05846815.af. [ARVO Test]	0
14	9 or 10 or 11 or 12 or 13	10
15	8 or 14	143

Database: PsycINFO

Host: Ovid

Data parameters: 1806 to current

Date of search: 17 Nov 2023

#	Searches	Results
1	(QbTest* or "Qb Test*" or "(Qb) Test*" or "Qb Mini*" or "QbMini*" or (("Quantified Behavior*" or "Quantified Behaviour*") adj5 test*) or QbTech).af.	126
2	(QbCheck* or "Qb Check*" or "(Qb) Check*").af.	6
3	(Nesplora* or "Giunti psychometrics").af.	85
4	(ARVO* or EFSim* or "EF Sim*" or EPELI or "Peili Vision Company").af.	5417
5	Attention Deficit Disorder with Hyperactivity/ or ADHD.af.	92604
6	4 and 5	50
7	((motion* adj5 senso*) and (hyperactivity or ADHD)).ti,ab,kf.	100
8	1 or 2 or 3 or 6 or 7	362
9	NCT03368573.af. or (QUOTA and adhd).ti,kf. [QB test]	0
10	NCT02209116.af. or ((AQUA and ADHD) or AQUA2).ti,kf. [QB test]	0
11	NCT02473185.af. [QB test]	0
12	NCT02477280.af. [QB test]	0
13	NCT05846815.af. [ARVO Test]	0
14	9 or 10 or 11 or 12 or 13	0
15	8 or 14	362

Database: CINAHL
Host: EbscoHOST
Data parameters: 1981 to current
Date of search: 17 Nov 2023

#	Searches	Results
1	TI ((QbTest* or "Qb Test*" or "(Qb) Test*" or "Qb Mini*" or "QbMini*" or (("Quantified Behavior*" or "Quantified Behaviour*") N4 test*) or QbTech)) OR AB ((QbTest* or "Qb Test*" or "(Qb) Test*" or "Qb Mini*" or "QbMini*" or (("Quantified Behavior*" or "Quantified Behaviour*") N4 test*) or QbTech))	21
2	TI ((QbCheck* or "Qb Check*" or "(Qb) Check*")) OR AB ((QbCheck* or "Qb Check*" or "(Qb) Check*"))	1
3	TI ((Nesplora* or "Giunti psychometrics")) OR AB ((Nesplora* or "Giunti psychometrics"))	2
4	TI ((ARVO* or EFSim* or "EF Sim*" or EPELI or "Peili Vision Company")) OR AB ((ARVO* or EFSim* or "EF Sim*" or EPELI or "Peili Vision Company"))	16,100
5	TI (("Attention Deficit Disorder" or ADHD)) OR AB (("Attention Deficit Disorder" or ADHD))	92604
6	S4 and S5	1
7	TI (((motion* N4 senso*) and (hyperactivity or ADHD))) OR AB (((motion* N4 senso*) and (hyperactivity or ADHD)))	1
8	S1 OR S2 OR S3 OR S6 OR S7	26
9	S1 OR S2 OR S3 OR S6 OR S7 [remove MEDLINE studies]	15

Database: Clinical Trials.gov
Host: https://www.clinicaltrials.gov/ct2/results/refine?show_xprt=Y
Date of search: 17 Nov 2023

13 Studies found for: (QBTest OR "QB Test" OR QBMini OR "QB Mini" OR QBCheck OR "Qb Check" OR Nesplora OR ARVO OR EFSim OR "EF Sim" OR EPELI)

Database: WHO International Clinical Trials Registry Platform (ICTRP)
Host: https://trialsearch.who.int/Default.aspx
Date of search: 17 Nov 2023

30 Studies found for: (QBTest OR "QB Test" OR QBMini OR "QB Mini" OR QBCheck OR "Qb Check" OR Nesplora OR ARVO OR EFSim OR "EF Sim" OR EPELI)

b. Supplemental cost-effectiveness searches

Resource	N
MEDLINE	491
Embase	319
PsycINFO	284
Econlit	5
Total	1099
- duplicates	-470
Total to screen	629

Database: MEDLINE (MEDALL)
Host: Ovid
Data parameters: 1946 to present
Date of search: 12 Feb 2024

#	Searches	Results
1	*Attention Deficit Disorder with Hyperactivity/	29998
2	((attention and deficit and disorder and hyperact*) or adhd).ti,ab,kf.	41992
3	1 or 2	46558
4	*economics/ or exp *"costs and cost analysis"/	90572
5	((economic$ or cost or costs or costly or costing or budget*) adj3 (effect* or utility or minimisation or consequence or analysis or evaluat* or model or impact*)).ti,ab,kf.	274166
6	("decision tree" or Markov or "semi Markov" or "partitioned adj2 survival" or "discrete event" or "conceptual* adj2 model*" or (decision adj2 model*) or "outcome model*" or "causal model*" or (simulat* adj2 model*) or QALY*).ti,ab,kf.	113692
7	4 or 5 or 6	430699
8	3 and 7	491

Database: Embase
Host: Ovid
Data parameters: 1980 to
Date of search: 12 Feb 2024

#	Searches	Results
1	*attention deficit hyperactivity disorder/	5557
2	((attention and deficit and disorder and hyperact*) or adhd).ti,ab,kf.	59518
3	1 or 2	59716
4	*economic evaluation/ or *health economics/	23367
5	((economic$ or cost or costs or costly or costing or budget*) adj3 (effect* or utility or minimisation or consequence or analysis or evaluat* or model or impact*)).ti,ab,kf.	376011
6	("decision tree" or Markov or "semi Markov" or "partitioned adj2 survival" or "discrete event" or "conceptual* adj2 model*" or (decision adj2 model*) or "outcome model*" or "causal model*" or (simulat* adj2 model*) or QALY*).ti,ab,kf.	147640
7	4 or 5 or 6	497249
8	3 and 7	581
9	Limit 8 to embase	319

Database: PsycINFO

Host: Ovid

Data parameters: 1908 to current

Date of search: 12 Feb 2024

#	Searches	Results
1	*Attention Deficit Disorder with Hyperactivity/	28552
2	((attention and deficit and disorder and hyperact*) or adhd).ti,ab,kf.	39303
3	1 or 2	40289
4	((economic$ or cost or costs or costly or costing or budget*) adj3 (effect* or utility or minimisation or consequence or analysis or evaluat* or model or impact*)).ti,ab,kf.	35826
5	("decision tree" or Markov or "semi Markov" or "partitioned adj2 survival" or "discrete event" or "conceptual* adj2 model*" or (decision adj2 model*) or "outcome model*" or "causal model*" or (simulat* adj2 model*) or QALY*).ti,ab,kf.	21271
6	4 or 5	55090
7	3 and 6	284

Database: Econlit

Host: EbscoHost

Data parameters: 1981-Current

Date of search: 12 Feb 2023

#	Searches	Results
1	TI (("Attention Deficit Disorder with Hyperactivity" or ADHD)) OR AB (("Attention Deficit Disorder with Hyperactivity" or ADHD))	105
2	TI (((economic* or cost or costs or costly or costing or budget*) N2 (effect* or utility or minimisation or consequence or analysis or evaluat* or model or impact*))) OR AB (((economic* or cost or costs or costly or costing or budget*) N2 (effect* or utility or minimisation or consequence or analysis or evaluat* or model or impact*)))	78,438
3	TI (("decision tree" or Markov or "semi Markov" or "partitioned N1 survival" or "discrete event" or "conceptual* N1 model*" or (decision N1 model*) or "outcome model*" or "causal model*" or (simulat* N1 model*) or QALY*)) OR AB (("decision tree" or Markov or "semi Markov" or "partitioned N1 survival" or "discrete event" or "conceptual* N1 model*" or (decision N1 model*) or "outcome model*" or "causal model*" or (simulat* N1 model*) or QALY*))	19,172
S4	S2 or S3	95,519
S5	S1 AND S4	8
S6	S1 and S4 [remove MEDLINE studies]	5

Appendix 2

Tables of included, on-going, or excluded studies

Table 33 Studies included in the review showing primary and secondary reports

Primary reports are the primary publication for the study and are used to refer to that study throughout text and tables.

Study name	Primary Report	Secondary reports	Identified from
NR	Sharma A. SB. Evaluation of the role of Qb testing in attention deficit hyperactivity disorder. *Archives of Disease in Childhood* 2009;**94**A72	None	Checking references of included studies
NR	Hamadache SH, Kathrin Labarga, Sara Zaplana Gunther, Thomas. Is the QbMini a valid instrument for ADHD assessment? [References].DP - Aug 2021. *Journal of Attention Disorders* 2021;**25**(10): 1384-94	Labarga SZH, Kathrin Hamadache, Salsabil Gunther, Thomas. Validation of the QbMini Test to diagnose Attention Deficit and Hyperactivity Disorder (ADHD) in 5-year-old children. Zeitschrift fur Neuropsychologie 2019;30(3): 149-56 Gunther TL, S. V. N. Z. Hoberg, K. First validation of the QbMini to measure symptoms of ADHD in 5-year old children. ADHD Attention Deficit and Hyperactivity Disorders 2017;9(1 Supplement): S15	Main searches
NR	Hult NK, Josefin Kadesjo, Bjorn Gillberg, Christopher Billstedt, Eva. ADHD and the QbTest: Diagnostic Validity of QbTest. Journal of attention disorders. 2018;22(11):1074-80.	None	Main searches
NR	Ulberstad FB, Hans Chavanon, Mira-Lynn Knollmann, Martin Wiley, James Christiansen, Hanna Thorell, Lisa B. Objective measurement of attention deficit hyperactivity disorder symptoms outside the clinic using the QbCheck: Reliability and validity. International journal of methods in psychiatric research. 2020;29(2):e1822.	None	Main searches
NR	Adamou MJ, Sarah L. Marks, Laura Lowe, Deborah. Efficacy of Continuous Performance Testing in Adult ADHD in a Clinical Sample Using QbTest. Journal of attention disorders. 2022;26(11):1483-91.	None	Main searches

Study name	Primary Report	Secondary reports	Identified from
NR	Bijlenga DU, Fredrik Thorell, Lisa B. Christiansen, Hanna Hirsch, Oliver Kooij, J. J. Sandra. Objective assessment of attention-deficit/hyperactivity disorder in older adults compared with controls using the QbTest. International journal of geriatric psychiatry. 2019;34(10):1526-33.	None	Main searches
NR	Brunkhorst-Kanaan NV, Moritz Kittel-Schneider, Sarah Vainieri, Isabella Reif, Andreas Grimm, Oliver. The Quantified Behavioral Test-A Confirmatory Test in the Diagnostic Process of Adult ADHD? Frontiers in psychiatry. 2020;11:216.	None	Main searches
NR	Edebol HH, Lars Holmberg, Ebba Gustafsson, Stig-Arne Norlander, Torsten. In search for objective measures of hyperactivity, impulsivity and inattention in adult attention deficit hyperactivity disorder using the Quantified Behavior Test Plus. Europe's Journal of Psychology. 2011;7(3):443-57.	None	Checking included studies in systematic reviews
NR	Edebol HH, Lars Norlander, Torsten. Measuring adult Attention Deficit Hyperactivity Disorder using the Quantified Behavior Test Plus. Psychology journal 2013;2(1): 48-62	None	Main searches
NR	Edebol HH, Lars Norlander, Torsten. Objective Measures of Behavior Manifestations in Adult ADHD and Differentiation from Participants with Bipolar II Disorder, Borderline Personality Disorder, Participants with Disconfirmed ADHD as Well as Normative Participants. Clinical Practice and Epidemiology in Mental Health 2012;8134-43	None	Main searches
NR	Groom MJY, Zoe Hall, Charlotte L. Gillott, Alinda Hollis, Chris. The incremental validity of a computerised assessment added to clinical rating scales to differentiate adult ADHD from autism spectrum disorder. Psychiatry Research. 2016;243:168-73.	None	Main searches
NR	Johansson VNS, Eva Kuja-Halkola, Ralf Lundstrom, Sebastian Durbeej, Natalie Anckarsater, Henrik Lichtenstein, Paul Hellner, Clara. The Quantified Behavioral Test Failed to Differentiate ADHD in	None	Main searches

Study name	Primary Report	Secondary reports	Identified from
	Adolescents With Neurodevelopmental Problems. Journal of attention disorders. 2021;25(3):312-21.		
AQUA	Hollis CH, Hall Charlotte L., Guo Boliang, James Marilyn, Boadu Janet, Groom Madeleine J., Brown Nikki, Kaylor-Hughes Catherine, Moldavsky Maria, Valentine Althea Z., Walker Gemma M,. Daley David, Sayal Kapil, Morriss Richard. The impact of a computerised test of attention and activity (QbTest) on diagnostic decision-making in children and young people with suspected attention deficit hyperactivity disorder: single-blind randomised controlled trial. Journal of child psychology and psychiatry, and allied disciplines. 2018;59(12):1298-308.	Hall CLV, Althea Z. Walker, Gemma M. Ball, Harriet M. Cogger, Heather Daley, David Groom Madeleine J,. Sayal Kapil, Hollis Chris. Study of user experience of an objective test (QbTest) to aid ADHD assessment and medication management: a multi-methods approach. BMC psychiatry. 2017;17(1):66. Hall CLW, Walker Gemma M,. Valentine Althea Z., Guo Boliang, Kaylor-Hughes Catherine, James Marilyn, Daley David, Sayal Kapil, Hollis Chris. Protocol investigating the clinical utility of an objective measure of activity and attention (QbTest) on diagnostic and treatment decision-making in children and young people with ADHD-'Assessing QbTest Utility in ADHD' (AQUA): a randomised controlled trial. BMJ open. 2014;4(12):e006838. ISRCTN11727351. 2016. Comparing the effects of providing clinicians and patients with the results of an objective measure of activity and attention (QbTest) versus usual care on diagnostic and treatment decision making in children and young people with ADHD. https://www.isrctn.com/ISRCTN11727351 (Accessed November 2023). NCT02209116. 2014. Assessing QbTest Utility in ADHD: A Randomised Controlled Trial. https://clinicaltrials.gov/show/NCT02209116 (Accessed November 2023).	Main searches
NR	Pettersson RS, Staffan Nilsson, Kent W. Diagnosing ADHD in adults: An examination of the discriminative validity of neuropsychological tests	None	Main searches

Study name	Primary Report	Secondary reports	Identified from
	and diagnostic assessment instruments. Journal of Attention Disorders. 2018;22(11):1019-31.		
NR	Soderstrom SP, Richard Nilsson, Kent W. Quantitative and subjective behavioural aspects in the assessment of attention-deficit hyperactivity disorder (ADHD) in adults. Nordic journal of psychiatry. 2014;68(1):30-7.	None	Main searches
NR	Stevanovic DN, Salmir Doric, Ana Wentz, Elisabet Knez, Rajna. The Structure and Diagnostic Accuracy of the QbTest in Pediatric ADHD: A Retrospective Clinical Study. Journal of attention disorders. 2023;27(11):1296-305.	None	Main searches
NR	Tallberg PR, Maria Wenhov, Lena Eliasson, Glen Gustafsson, Peik. Incremental clinical utility of continuous performance tests in childhood ADHD - an evidence-based assessment approach. Scandinavian journal of psychology. 2019;60(1):26-35.	Gustafsson PT, P. Towards evidence-based assessments: Clinical utility of rating scales and cognitive test methods in diagnostic assessment and treatment evaluations in children and adolescents with Attention-Deficit/Hyperactivity Disorder. ADHD Attention Deficit and Hyperactivity Disorders. 2017;9(1 Supplement):S15.	Main searches
NR	Seesjarvi EP, Jasmin Aronen, Eeva T. Lipsanen, Jari Mannerkoski, Minna Hering, Alexandra Zuber, Sascha Kliegel, Matthias Laine, Matti Salmi, Juha. Quantifying ADHD Symptoms in Open-Ended Everyday Life Contexts With a New Virtual Reality Task. Journal of attention disorders. 2022;26(11):1394-411.	None	Main searches
NR	Zulueta AD-O, Unai Crespo-Eguilaz, Nerea Torrano, Fermin. Virtual reality-based assessment and rating scales in ADHD diagnosis. Psicologia Educativa. 2019;25(1):13-22.	None	Main searches
NA	Rufo-Campos, M., Cueto, E., Iriarte, Y., & Rufo-Muñoz, M. (2012). Sensitivity study of a new diagnostic method for ADHD: Aula Nesplora. Rev Neurol; 54 (Suppl3): S67-S93.	None	Nesplora Manufacturer Submission
NR	Emser TSJ, Blair A. Steele, J. Douglas Kooij, Sandra Thorell, Lisa Christiansen, Hanna. Assessing ADHD symptoms in children and adults: Evaluating the role of objective measures. Behavioral and Brain Functions. 2018;14:11.	None	Main searches

Study name	Primary Report	Secondary reports	Identified from
FACT	Chitsabesan PH, C. L. Carter, L. A. Reeves, M. Mohammed, V. Beresford, B. Young, S. Kraam, A. Trowse, S. Wilkinson-Cunningham, L. Lennox, C. Using an objective computer task (QbTest) to aid the identification of attention deficit hyperactivity disorder (ADHD) in the Children and Young People Secure Estate (CYPSE): a feasibility randomised controlled trial. BMJ Open. 2022;12(12):e064951.	ISRCTN17402196. 2019. Feasibility trial to assess Attention Deficit Hyperactivity Disorder (ADHD) in the Criminal Justice System by using QbTest (a computer task). http://isrctn.com/ISRCTN17402196 (Accessed November 2023). Lennox CH, C. L. Carter, L. A. Beresford, B. Young, S. Kraam, A. Brown, N. Wilkinson-Cunningham, L. Reeves, M. Chitsabesan, P. FACT: a randomised controlled trial to assess the feasibility of QbTest in the assessment process of attention deficit hyperactivity disorder (ADHD) for young people in prison -a feasibility trial protocol. BMJ Open. 2020;10(1):035519.	Main searches
QUOTA	Williams LH, Charlotte L. Brown, Susan Guo, Boliang James, Marilyn Franceschini, Matilde Clarke, Julie Selby, Kim Vijayan, Hena Kulkarni, Neeta Brown, Nikki Sayal, Kapil Hollis, Chris Groom, Madeleine J. Optimising medication management in children and young people with ADHD using a computerised test (QbTest): a feasibility randomised controlled trial. Pilot and feasibility studies. 2021;7(1):68.	Hall CLB, Susan James, Marilyn Martin, Jennifer L. Brown, Nikki Selby, Kim Clarke, Julie Williams, Laura Sayal, Kapil Hollis, Chris Groom, Madeleine J. Consensus workshops on the development of an ADHD medication management protocol using QbTest: developing a clinical trial protocol with multidisciplinary stakeholders. BMC medical research methodology. 2019;19(1):126. Hall CLJ, Marilyn Brown, Sue Martin, Jennifer L. Brown, Nikki Selby, Kim Clarke, Julie Vijayan, Hena Guo, Boliang Sayal, Kapil Hollis, Chris Groom, Madeleine J. Protocol investigating the clinical utility of an objective measure of attention, impulsivity and activity (QbTest) for optimising medication management in children and young people with ADHD 'QbTest Utility for Optimising Treatment in ADHD' (QUOTA): a feasibility randomised controlled trial. BMJ open. 2018;8(2):e021104.	Main searches

Study name	Primary Report	Secondary reports	Identified from
		ISRCTN69461593. 2018. QbTest Utility for Optimising Treatment in ADHD (QUOTA). https://www.isrctn.com/ISRCTN69461593 (Accessed November 2023). NCT03368573. 2017. QbTest Utility for Optimising Treatment in ADHD (QUOTA). https://clinicaltrials.gov/show/NCT03368573 (Accessed November 2023).	
NR	Hall Charlotte L, Selby Kim, Guo Boliang, Valentine Althea Z, Walker Gemma M, Hollis Chris,. Innovations in Practice: an objective measure of attention, impulsivity and activity reduces time to confirm attention deficit/hyperactivity disorder diagnosis in children - a completed audit cycle. Child and adolescent mental health. 2016;21(3):175-8.	None	Main searches
NR	Pellegrini SM, Mike Lovett, Ella. The QbTest for ADHD assessment: Impact and implementation in Child and Adolescent Mental Health Services. Children & Youth Services Review 2020;114.n.r.	None	Main searches
NR	Sharma RW, A. Lacey, S. Spiewakowski, D. IMPLEMENTING QB TESTING FOR ADHD: EVALUATING VALUE IN A DGH SETTING. Archives of Disease in Childhood. 2022;107(Supplement 2):A70.	None	Main searches
NR	Vogt CS, A. Assessments for attention-deficit hyperactivity disorder: Use of objective measurements. Psychiatrist. 2011;35(10):380-3.	None	Main searches
NR	Catriona Humphreys, Lucy Sitton-Kent. Transforming ADHD Care Across the East Midlands: An evaluation Report. East Midlands Academic Health Network. 2018. URL: https://healthinnovation-em.org.uk/component/rsfiles/download-file/files?path=our-work%252Four-innovations%252FTransforming-	None	QbTest Manufacturer Submission

Study name	Primary Report	Secondary reports	Identified from
	ADHD-Care%252FFinal_Overall_Evaluation_Report_31May18.pdf&Itemid=1457 (Accessed March 2024).		
NR	Caitlin McKenzie, Benjamin-Rose Ingall, [Dr] Charlotte Hall. Focus ADHD National Programme Evaluation. 2022. URL: https://healthinnovation-em.org.uk/component/rsfiles/download-file/files?path=our-work%252Four-innovations%252FADHD%2BFOCUS%2Bevaluation%2Breport%2B-%2BFINAL%2Bv.1.0%2B18.10.22.pdf&Itemid=1457 (Accessed March 2024).	None	QbTest Manufacturer Submission
NR	Peli Vision Oy. Research behind EFSim and feedback from pilot tests [unpublished report]. n.r.	None	Peili Vision Manufacturer Submission

Table 34 On-going studies that appear to meet inclusion criteria for the review

Author	Identified from	Test	Study details	Estimated completion date
NCT05846815 (Sponsors: Peili Vision).[73]	Our searches	ARVO 2.0	Cross-over RCT in Finland, aiming to assess the performance and safety of web-based ARVO 2.0, for evaluating possible ADHD symptoms, in children aged 8-13 with ADHD and typically developing children of the same age. Comparison of results from ARVO to results from Conners CPT.	June 2024
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Peili Vision	Manufacturer submission	EFSim	Several pilots are being set up for spring 2024 in the UK, using learnings from rolling out EFSim in Finland to implement in the UK as part of an early triage tool.	Not reported
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Table 35 Studies excluded at full-text screening from the identification of studies via databases and registers

Report	Reason for exclusion
2014-001488-11. Effects of expectations, medication and placebo during the Quantified Behavior Test in patients with untreated ADHD and Substance Use Disorder. 2014. URL: https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2014-001488-11 (Accessed October 2023)	Not an evaluation of the test
Areces DD, Julie Garcia, Trinidad Gonzalez-Castro, Paloma Rodriguez, Celestino. Analysis of cognitive and attentional profiles in children with and without ADHD using an innovative virtual reality tool. PLOS ONE 2018;13(8): e0201039	Not an evaluation of the test
Areces DG, Trinidad Cueli, Marisol Rodriguez, Celestino. Is a Virtual Reality Test Able to Predict Current and Retrospective ADHD Symptoms in Adulthood and Adolescence? Brain sciences 2019;9(10): .n.r.	Does not report on one of the outcomes of interest
Areces DR, Celestino Garcia, Trinidad Cueli, Marisol Gonzalez-Castro, Paloma. Efficacy of a Continuous Performance Test Based on Virtual Reality in the Diagnosis of ADHD and Its Clinical Presentations. Journal of attention disorders 2018;22(11): 1081-1091	Does not report on one of the outcomes of interest
Baader AK, B. Brunkhorst-Kanaan, N. Kittel-Schneider, S. Reif, A. Grimm, O. A within-sample comparison of two innovative neuropsychological tests for assessing adhd. Brain Sciences 2021;11(1): 1-21	Does not report on one of the outcomes of interest
Baader AK, B. Brunkhorst-Kanaan, N. Kittel-Schneider, S. Reif, A. Grimm, O. A within-sample comparison of two innovative neuropsychological tests for assessing adhd. Brain Sciences 2021;11(1): 1-21	Duplicate report
Baader AK, B. Brunkhorst-Kanaan, N. Kittel-Schneider, S. Reif, A. Grimm, O. P.632 A within-sample comparison of two innovative neuropsychological tests for diagnosing ADHD. European neuropsychopharmacology 2020;40(Supplement 1): S355-S356	Does not report on one of the outcomes of interest
Bellato AH, Charlotte L. Groom, Madeleine J. Simonoff, Emily Thapar, Anita Hollis, Chris Cortese, Samuele. Practitioner Review: Clinical utility of the QbTest for the assessment and diagnosis of attention-deficit/hyperactivity disorder - a systematic review and meta-analysis. *Journal of child psychology and psychiatry, and allied disciplines* 2023;.n.r.	SR
Berger I, Slobodin O, Cassuto H. Usefulness and validity of continuous performance tests in the diagnosis of attention-deficit hyperactivity disorder children. Archives of Clinical Neuropsychology 2017;32(1): 81-93	Did not report on test of interest
Bhattacharyya NS, S. Banerjee, A. Ghosh, R. Sinha, O. Das, N. Gayen, R. Pal, S. S. Ganguly, S. Dasgupta, T. Mondal, P. Adhikari, A. Sarkar, S. Bhattacharyya, D. Mallick, A. K. Singh, O. P. Pal, S. K. Integration of electroencephalogram (EEG) and motion tracking sensors for objective measure of attention-	Did not report on test of interest

Report	Reason for exclusion
deficit hyperactivity disorder (MAHD) in pre-schoolers. The Review of scientific instruments 2022;93(5): 054101	
Bijlenga DJ, M. Gehlhaar, S. K. Sandra Kooij, J. J. Objective QbTest and subjective evaluation of stimulant treatment in adult attention deficit-hyperactivity disorder. European psychiatry : the journal of the Association of European Psychiatrists 2015;30(1): 179-185	Does not report on one of the outcomes of interest
Brancaccio RK, J. Ayearst, L. E. Using wearables and artificial intelligence to improve diagnostic decisions and treatment in youth with attention-deficit hyperactivity disorder. Innovations in Clinical Neuroscience 2021;18(10-12 SUPPL): S2-S3	Did not report on test of interest
Brocki KCT, Carin M. Bohlin, Gunilla. CPT performance, motor activity, and continuous relations to ADHD symptom domains: A developmental study. European Journal of Developmental Psychology 2010;7(2): 178-197	Not an evaluation of the test
Camacho-Conde JAC, Gema. Attentional profile of adolescents with ADHD in virtual-reality dual execution tasks: A pilot study. Applied Neuropsychology: Child 2022;11(1): 81-90	Not an evaluation of the test
Cedergren K, Östlund S, Åsberg Johnels J, Billstedt E, Johnson M. Monitoring medication response in ADHD: What can continuous performance tests tell us? European Archives of Psychiatry and Clinical Neuroscience 2022;272(2): 291-299	Duplicate report
Cedergren K, Östlund S, Åsberg Johnels J, Billstedt E, Johnson M. Monitoring medication response in ADHD: What can continuous performance tests tell us? European Archives of Psychiatry and Clinical Neuroscience 2022;272(2): 291-299	Not an evaluation of the test
Climent GR, Celestino Garcia, Trinidad Areces, Debora Mejias, Miguel Aierbe, Amaia Moreno, Marta Cueto, Eduardo Castella, Judit Feli Gonzalez, Mari. New virtual reality tool (Nesplora Aquarium) for assessing attention and working memory in adults: A normative study. Applied neuropsychology Adult 2021;28(4): 403-415	Does not report on one of the outcomes of interest
Climent GR, Celestino Garcia, Trinidad Areces, Debora Mejias, Miguel Aierbe, Amaia Moreno, Marta Cueto, Eduardo Castella, Judit Feli Gonzalez, Mari. New virtual reality tool (Nesplora Aquarium) for assessing attention and working memory in adults: A normative study. Applied neuropsychology Adult 2021;28(4): 403-415	Duplicate report
Cole E. Qb test improves diagnosis of attention deficit disorder. Nursing children and young people 2015;27(2): 10-11	Not a primary study or SR
Diaz-Orueta U. Advances in neuropsychological assessment of attention: From initial computerized continuous performance tests to AULA. The role of technology in clinical neuropsychology 2017;103.n.r.	Not a primary study or SR
Diaz-Orueta UF-F, M. A. Morillo-Rojas, M. D. Climent, G. [Efficacy of lisdexamphetamine to improve the behavioural and cognitive symptoms of attention deficit hyperactivity disorder: treatment monitored by means of the AULA Nesplora virtual reality test]. Eficacia de la lisdexanfetamina en la mejora sintomatica conductual y cognitiva del trastorno por deficit de	Not an evaluation of the test

Report	Reason for exclusion
atencion/ hiperactividad: tratamiento monitorizado mediante el test AULA Nesplora de realidad virtual 2016;63(1): 19-27	
Diaz-Orueta UG-L, Cristina Crespo-Eguilaz, Nerea Sanchez-Carpintero, Rocio Climent, Gema Narbona, Juan. AULA virtual reality test as an attention measure: convergent validity with Conners' Continuous Performance Test. Child neuropsychology : a journal on normal and abnormal development in childhood and adolescence 2014;20(3): 328-342	Does not report on one of the outcomes of interest
DRKS00030766. Identification of objective markers for the evaluation and prediction of the treatment of children and adolescents with ADHD. 2022. URL: http://drks.de/search/en/trial/DRKS00030766 (Accessed October 2024).	Not an evaluation of the test
Faraone SV, Banaschewski T, Coghill D, Zheng Y, Biederman J, Bellgrove MA, et al. The World Federation of ADHD International Consensus Statement: 208 Evidence-based conclusions about the disorder. Neuroscience and Biobehavioral Reviews 2021;128789-818	Background
Fernandez-Martin PL, J. J. Rodriguez-Herrera, R. Canovas, R. Martinez De Salazar, A. Cobos-Sanchez, L. Sanchez-Santed, F. Flores, P. Dimensional analysis of adolescent attention-deficit/ hyperactivity disorder. European Psychiatry 2020;63(Supplement 1): S677	Not an evaluation of the test
Fernandez-Martin PR-H, Rocio Canovas, Rosa Diaz-Orueta, Unai Martinez de Salazar, Alma Flores, Pilar. Data-driven profiles of attention-deficit/hyperactivity disorder using objective and ecological measures of attention, distractibility, and hyperactivity. European child & adolescent psychiatry 2023[Epub ahead of print]	Does not report on one of the outcomes of interest
Fischer SK, M. Lehfeld, H. Niklewski, G. Brandl, C. Influence of depressive symptoms on Qb test performance in adult ADHD patients. ADHD Attention Deficit and Hyperactivity Disorders 2015;7(SUPPL. 1): S77	Does not report on one of the outcomes of interest
Garcia Murillo LC, S. Anderson, D. Di Martino, A. Castellanos, F. Meta-analysis of locomotor activity measures in attention-deficit/hyperactivity disorder. European Child and Adolescent Psychiatry 2015;24(1 SUPPL. 1): S154	Did not report on test of interest
Hager LAO, Geir Danielsen, Maria Billstedt, Eva Gillberg, Christopher Johnels, Jakob Asberg. Indexing executive functions with test scores, parent ratings and ERPs: How do the measures relate in children versus adolescents with ADHD? [References].DP - Feb 17, 2020. Neuropsychiatric Disease and Treatment 2020;16465-477	Not an evaluation of the test
Hall CLB, A. Kirk, J. D. Hollis, C. The clinical utility of QbTest in supporting the assessment and monitoring of attention-deficit/hyperactivity disorder (ADHD): what do paediatricians need to know? Paediatrics and Child Health (United Kingdom) 2023;33(9): 259-264	Background
Hall CLV, Althea Z. Groom, Madeleine J. Walker, Gemma M. Sayal, Kapil Daley, David Hollis, Chris. The clinical utility of the	SR

Report	Reason for exclusion
continuous performance test and objective measures of activity for diagnosing and monitoring ADHD in children: A systematic review. European child & adolescent psychiatry 2016;25(7): 677-699	
Hall CLW, G. M. Valentine, A. Z. Correction. Protocol investigating the clinical utility of an objective measure of activity and attention (QbTest) on diagnostic and treatment decision-making in children and young people with ADHD - 'Assessing QbTest Utility in ADHD' (AQUA): a randomised controlled trial. BMJ open 2015;5(5): e006838corr006831	Erratum
Hall CLW, G. M. Valentine, A. Z. Erratum: Protocol investigating the clinical utility of an objective measure of activity and attention (QbTest) on diagnostic and treatment decision-making in children and young people with ADHD - 'Assessing QbTest Utility in ADHD' (AQUA): A randomised controlled trial (BMJ Open (2014) 4 (e006838)). BMJ Open 2015;5(5): 006838corr006831	Erratum
Hall CLW, G. M. Valentine, A. Z. Erratum: Protocol investigating the clinical utility of an objective measure of activity and attention (QbTest) on diagnostic and treatment decision-making in children and young people with ADHD-'Assessing QbTest Utility in ADHD'(AQUA): A randomised controlled trial (BMJ Open (2014) 4 (e006838)). BMJ Open 2016;6(1): e006838	Erratum
Hamadache SH, Kathrin Labarga, Sara Zaplana Gunther, Thomas. Is the QbMini a valid instrument for ADHD assessment? [References].DP - Aug 2021. Journal of attention disorders 2021;25(10): 1384-1394	Duplicate report
Hirsch OC, Hanna. Factorial Structure and Validity of the Quantified Behavior Test Plus (Qb+©). Assessment 2017;24(8): 1037-1049	Does not report on one of the outcomes of interest
Iriarte YD-O, Unai Cueto, Eduardo Irazustabarrena, Paula Banterla, Flavio Climent, Gema. AULA-Advanced virtual reality tool for the assessment of attention: Normative study in Spain. Journal of attention disorders 2016;20(6): 542-568	Does not report on one of the outcomes of interest
Jansson LL, Monica Ostlund, Mona Domingo, Blanca. Effects of one single-dose methylphenidate compared to one single-dose placebo on QbTest performance in adults with untreated ADHD: a randomized controlled trial. BMC Psychiatry 2023;23(1): 762	Not an evaluation of the test
Jylkka JR, Liisa Merzon, Liya Kangas, Suvi Kliegel, Matthias Zuber, Sascha Hering, Alexandra Laine, Matti Salmi, Juha. Assessment of goal-directed behavior and prospective memory in adult ADHD with an online 3D videogame simulating everyday tasks. Scientific reports 2023;13(1): 9299	Did not report on test of interest
Knez RS, Dejan Nasic, Salmir Doric, Ana Wentz, Elisabet. The Impact of Methylphenidate on QbTest Performance of Children with ADHD: A Retrospective Clinical Study. Neuropsychiatric disease and treatment 2021;1719-32	Not an evaluation of the test

Report	Reason for exclusion
Kooij JJS, Bijlenga D, Salerno L, Jaeschke R, Bitter I, Balázs J, et al. Updated European Consensus Statement on diagnosis and treatment of adult ADHD. European Psychiatry 2019;5614-34	Background
Kuhle H. J., Lefering R. Video-assisted behavior observation as a tool for methylphenidate dose finding in ADHD: Longer term outcome. Neuropediatrics 2013;44(2): PS20-1146	Did not report on test of interest
Kvitland LRJ, K. Achkhan, H. Berg, T. Dahlen, N. R. Kirkholt, G. M. Koren, K. N. Naess, M. F. The CPT-3 versus the QB-test: A task-oriented computerized assessment of attention-related problems in out-patient children: Will diagnosis predict the atypical attention scores? ADHD Attention Deficit and Hyperactivity Disorders 2019;11(1 Supplement): S18-S19	Does not report on one of the outcomes of interest
Lindhiem OG, Mayank Shaaban, Sam Mak, Kristie J. Chikersal, Prerna Feldman, Jamie Harris, Jordan L. Objective Measurement of Hyperactivity Using Mobile Sensing and Machine Learning: Pilot Study. JMIR formative research 2022;6(4): e35803	Did not report on test of interest
Lohman MD, Blanca Ostlund, Mona Jansson, Lennart. Contrasting expectancy effects with objective measures in adults with untreated ADHD during QbTest. Scandinavian journal of psychology 2023;64(4): 461-469	Not an evaluation of the test
Luderer MS, Johanna Gerhardt, Sarah Hoffmann, Sabine Vollstadt-Klein, Sabine Reif, Andreas Sobanski, Esther. Drinking alcohol to cope with hyperactive ADHD? Self-reports vs. continuous performance test in patients with ADHD and/or alcohol use disorder. Frontiers in psychiatry 2023;141112843	Does not report on one of the outcomes of interest
Manning D, Olety S. Qb technology - evaluating its use in adhd diagnosis within a child and adolescent mental health service. European Psychiatry 2021;64(Supplement 1): S225	Does not report on one of the outcomes of interest
Marshall P, Hoelzle J, Nikolas M. Diagnosing attention-deficit/hyperactivity disorder (ADHD) in young adults: A qualitative review of the utility of assessment measures and recommendations for improving the diagnostic process. The Clinical Neuropsychologist 2021;35(1): 165-198	SR
Martin-Key NA, Stevenson A, Roy P. Investigating the Clinical Utility of the Combined Use of Objective and Subjective Measures of ADHD During Treatment Optimization. Journal of clinical psychopharmacology 2022;42(2): 146-153	Does not report on one of the outcomes of interest
NCT02473185. Effects of Expectation, Medication and Placebo on Objective and Self-rated Performance During the QbTest. 2015. URL: https://clinicaltrials.gov/show/NCT02473185 (Accessed October 2023).	Not an evaluation of the test
NCT02477280. Effects of Expectation, Medication and Placebo on Objective and Self-rated Performance. 2015. URL: https://clinicaltrials.gov/show/NCT02477280 (Accessed October 2023).	Not an evaluation of the test
Nylander Elin, Sparding Timea, Floros Orestis, Ryden Eleonore, Landen Mikael, Hansen Stefan. The quantified behavioural test plus (qbtest+) in adult adhd. *Nordic Psychology* 2022;75(1):20-34.	Does not report on one of the outcomes of interest

Report	Reason for exclusion
Peñuelas-Calvo I, Jiang-Lin LK, Girela-Serrano B, Delgado-Gomez D, Navarro-Jimenez R, Baca-Garcia E, et al. Video games for the assessment and treatment of attention-deficit/hyperactivity disorder: a systematic review. European Child and Adolescent Psychiatry 2022;31(1): 5-20	SR
Prasad V, Rezel-Potts E, White P, Downs J, Boddy N, Sayal K, et al. Use of healthcare services before diagnosis of attention-deficit/hyperactivity disorder: a population-based matched case-control study. Archives of disease in childhood 2023;109(1): 46-51	Background
Puzzo IS, Ottilie Kelly, Rachel Greer, Ben Kumari, Veena Gujonsson, Gisli Young, Susan. Attention problems predict risk of violence and rehabilitative engagement in mentally disordered offenders. Frontiers in Psychiatry 2019;10279	Not an evaluation of the test
Ramtvedt B E, Sundet K. Relationships between computer-based testing and behavioral ratings in the assessment of attention and activity in a pediatric ADHD stimulant crossover trial. The Clinical Neuropsychologist 2014;28(7): 1146-1161	Does not report on one of the outcomes of interest
Reh VS, Martin Lam, Le Schimmelmann, Benno G. Hebebrand, Johannes Rief, Winfried Christiansen, Hanna. Behavioral Assessment of Core ADHD Symptoms Using the QbTest. Journal of attention disorders 2015;19(12): 1034-1045	Does not report on one of the outcomes of interest
Rodriguez CA, Debora Garcia, Trinidad Cueli, Marisol Gonzalez-Castro, Paloma. Comparison between two continuous performance tests for identifying ADHD: Traditional vs. virtual reality. International journal of clinical and health psychology 2018;18(3): 254-263	Does not report on one of the outcomes of interest
Santosh P, Cortese S, Hollis C, Bölte S, Daley D, Coghill D, et al. Remote assessment of adhd in children and adolescents: Recommendations from the european adhd guidelines group following the clinical experience during the covid-19 pandemic. European child & adolescent psychiatry 2023;32(6): 921-935	Background
Sanwo O, Huzair H. What's new in attention-deficit/hyperactivity disorder: updates on assessment and management. Paediatrics and Child Health (United Kingdom) 2022;32(8): 282-289	Background
Schworer M, Jascenoka J, Nitkowski D, Petermann F, Vasileva M, Petermann U. Deficits in executive functions of children with ADHD: Clinical validity of a diagnostic instrument for ADHD in children and adolescents (ADHS-KJ). Kindheit und Entwicklung: Zeitschrift fur Klinische Kinderpsychologie 2019;28(2): 96-105	Did not report on test of interest
Selaskowski BA, Laura Marie Wiebe, Annika Kannen, Kyra Aslan, Behrem Gerding, Thiago Morano Sanchez, Dario Ettinger, Ulrich Kolle, Markus Lux, Silke Philipsen, Alexandra Braun, Niclas. Gaze-based attention refocusing training in virtual reality for adult attention-deficit/hyperactivity disorder. BMC Psychiatry 2023;2374	Did not report on test of interest

Report	Reason for exclusion
Slobodin O, Davidovitch M. Gender differences in objective and subjective measures of ADHD among clinic-referred children. Frontiers in Human Neuroscience 2019;13441	Did not report on test of interest
Stevanovic DW, Elisabet Nasic, Salmir Knez, Rajna. ASD with ADHD vs. ASD and ADHD alone: a study of the QbTest performance and single-dose methylphenidate responding in children and adolescents. BMC Psychiatry 2022;22(1): 282	Does not report on one of the outcomes of interest
Stuart E, Torres S, Gutierrez B. B - 04 Evaluating the Efficacy of a Virtual Reality Neuropsychological Assessment in Detecting ADHD Subtypes. Archives of clinical neuropsychology : the official journal of the National Academy of Neuropsychologists 2023;38(7): 1368	Does not report on one of the outcomes of interest
Valentine AZ, Brown BJ, Groom MJ, Young E, Hollis C, Hall CL. A systematic review evaluating the implementation of technologies to assess, monitor and treat neurodevelopmental disorders: A map of the current evidence. Clinical Psychology Review 2020;80101870	SR
Vogt C. Clinical Conundrums When Integrating the QbTest into a Standard ADHD Assessment of Children and Young People. Neuropediatrics 2021;52(3): 155-162	Background
Wang XQ, Albitos PJ, Hao YF, Zhang H, Yuan LX, Zang YF. A review of objective assessments for hyperactivity in attention deficit hyperactivity disorder. Journal of neuroscience methods 2022;370109479	Not a primary study or SR
Wehmeier P, Bender M. ADHD core symptom assessment in adults with ADHD, depression, addiction or borderline personality disorder using the Qb test. ADHD Attention Deficit and Hyperactivity Disorders 2017;9(1 Supplement): S13	Does not report on one of the outcomes of interest
Wehmeier P, Wolff J, Cabanas N, Bender M. ADHD core symptom assessment in adults with ADHD compared to adults with ADHD and comorbid borderline personality disorder using a computer-based continuous performance test (cb-CPT) combined with an infra-red motion-tracking device. ADHD Attention Deficit and Hyperactivity Disorders 2019;11(1 Supplement): S22	Does not report on one of the outcomes of interest
Wehmeier PM, Dittmann RW, Banaschewski T, Schacht A. Does stimulant pretreatment modify atomoxetine effects on core symptoms of ADHD in children assessed by quantitative measurement technology? Journal of attention disorders 2014;18(2): 105-116	Not an evaluation of the test
Wehmeier PM, Schacht A, Ulberstad F, Lehmann M, Schneider-Fresenius C, Lehmkuhl G, et al. Does atomoxetine improve executive function, inhibitory control, and hyperactivity? Results from a placebo-controlled trial using quantitative measurement technology. Journal of Clinical Psychopharmacology 2012;32(5): 653-660	Not an evaluation of the test
Wehmeier PMK, Laura Banaschewski, Tobias Dittmann, Ralf W. Schacht, Alexander. Does comorbid disruptive behavior modify the effects of atomoxetine on ADHD symptoms as measured by a continuous performance test and a motion tracking device?	Not an evaluation of the test

Report	Reason for exclusion
[References].DP - Jul 2015. Journal of attention disorders 2015;19(7): 591-602	
Wehrmann T, Jorg M. An objective measure of hyperactivity aspects with compressed webcam video. Child and adolescent psychiatry and mental health 2015;945	Did not report on test of interest
Williams LH, Charlotte L. Brown, Susan Guo, Boliang James, Marilyn Franceschini, Matilde Clarke, Julie Selby, Kim Vijayan, Hena Kulkarni, Neeta Brown, Nikki Sayal, Kapil Hollis, Chris Groom, Madeleine J. Correction to: Optimising medication management in children and young people with ADHD using a computerised test (QbTest): a feasibility randomised controlled trial. Pilot and feasibility studies 2021;7(1): 94	Erratum
Young SA, Nicoletta Asgeirsdottir, Bryndis Bjork Branney, Polly Beckett, Michelle Colley, William Cubbin, Sally Deeley, Quinton Farrag, Emad Gudjonsson, Gisli Hill, Peter Hollingdale, Jack Kilic, Ozge Lloyd, Tony Mason, Peter Paliokosta, Eleni Perecherla, Sri Sedgwick, Jane Skirrow, Caroline Tierney, Kevin van Rensburg, Kobus Woodhouse, Emma. Females with ADHD: An expert consensus statement taking a lifespan approach providing guidance for the identification and treatment of attention-deficit/ hyperactivity disorder in girls and women. BMC Psychiatry 2020;20404	Background
Young SA, Philip Lloyd, Tony Absoud, Michael Arif, Muhammad Colley, William Andrew Cortese, Samuele Cubbin, Sally Doyle, Nancy Morua, Susan Dunn Ferreira-Lay, Philip Gudjonsson, Gisli Ivens, Valerie Jarvis, Christine Lewis, Alexandra Mason, Peter Newlove-Delgado, Tamsin Pitts, Mark Read, Helen van Rensburg, Kobus Zoritch, Bozhena Skirrow, Caroline. Failure of Healthcare Provision for Attention-Deficit/Hyperactivity Disorder in the United Kingdom: A Consensus Statement. Frontiers in psychiatry 2021;12649399	Background

Table 36 Studies excluded at full text screening from checking manufacturer websites

Study details	Manufacturer's website	Reason for exclusion
Lis S, Baer N, Stein-en-Nosse C, Gallhofer B, Sammer G, Kirsch P. Objective measurement of motor activity during cognitive performance in adults with attention-deficit/hyperactivity disorder. Acta Psychiatrica Scandinavica. 2010 Oct;122(4):285-94.	QbTech	Does not report on one of the outcomes of interest
Merzon L. Real-world goal-directed behavior reveals aberrant functional connectivity in children with ADHD.	Peili Vision	Does not report on one of the outcomes of interest
Salmi J, Merzon L, Eräste T, Seesjärvi E, Huhdanpää H, Aronen ET, Mannerkoski M, MacInnes WJ, Laine M. Fluctuations of Attention During Self-paced Naturalistic Goal-Directed Behavior in Attention-Deficit/Hyperactivity Disorder. JAACAP Open. 2023 Dec 21.	Peili Vision	Does not report on one of the outcomes of interest
Merzon L, Pettersson K, Aronen ET, Huhdanpää H, Seesjärvi E, Henriksson L, MacInnes WJ, Mannerkoski M, Macaluso E, Salmi J. Eye movement behavior in a real-world virtual reality task reveals ADHD in children. Scientific reports. 2022 Nov 24;12(1):20308.	Peili Vision	Does not report on one of the outcomes of interest
Seesjärvi E, Puhakka J, Aronen ET, Hering A, Zuber S, Merzon L, Kliegel M, Laine M, Salmi J. EPELI: A novel virtual reality task for the assessment of goal-directed behavior in real-life contexts. Psychological Research. 2023 Sep;87(6):1899-916.	Peili Vision	Did not include population with suspected or confirmed ADHD
Rebon F, Altuna I, Lobo A, Salillas E, Climent G. Validity Performance in the AULA Nesplora Test.	Nesplora	Does not report on one of the outcomes of interest
Teruel MA, Sanchis J, Ruiz-Robledillo N, Albaladejo-Blázquez N, Ferrer-Cascales R, Trujillo J. Measuring attention of ADHD patients by means of a computer game featuring biometrical data gathering. Heliyon. 2024 Feb 23.	Nesplora	Did not report on test of interest
Zakani Z, Moradi H, Ghasemzadeh S, Riazi M, Mortazavi F. The Validity of a Machine Learning-Based Video Game in the Objective Screening of Attention Deficit Hyperactivity Disorder in Children Aged 5 to 12 Years. arXiv preprint arXiv:2312.11832. 2023 Dec 19.	Nesplora	Did not report on test of interest
https://nesplora.com/investigaci%C3%B3n/head-mounted-display-versus-computer-monitor-for-visual-attention-screening-a-comparative-study/	Nesplora	Did not report on test of interest

Table 37 Studies excluded at full text screening from checking the studies included in systematic reviews

Study details	Reason for exclusion
Delgado-Gomez D, Peñuelas-Calvo I, Masó-Besga AE, VallejoOñate S, Tello IB, Duarte EA et al (2017) Microsoft kinect-based continuous performance test: an objective attention defcit hyperactivity disorder assessment. J Med Internet Res 19(3):e79	Did not report on test of interest
Faraone SV, Newcorn JH, Antshel KM, Adler L, Roots K, Heller M (2016) The groundskeeper gaming platform as a diagnostic tool for attention-defcit/hyperactivity disorder: sensitivity, specifcity, and relation to other measures. J Child Adolesc Psychopharmacol 26(8):672–685	
Heller MD, Roots K, Srivastava S, Schumann J, Srivastava J, Hale TS (2013) A machine learning-based analysis of game data for attention defcit hyperactivity disorder assessment. Games Health J 2(5):291–298	
Pollak Y, Weiss PL, Rizzo AA, Weizer M, Shriki L, Shalev RS et al (2009) The utility of a continuous performance test embedded in virtual reality in measuring ADHD-related defcits. J Dev Behav Pediatr 30(1):2–6	
Shaw R, Grayson A, Lewis V (2005) Inhibition, ADHD, and computer games: the inhibitory performance of children with ADHD on computerized tasks and games. J Atten Disord 8(4):160–168	
Eom, H., Kim, K. K., Lee, S., Hong, Y. J., Heo, J., Kim, J. J., & Kim, E. (2019). Development of Virtual Reality Continuous Performance Test Utilizing Social Cues for Children and Adolescents with Attention-Deficit/Hyperactivity Disorder. Cyberpsychology, Behavior and Social Networking, 22(3), 198-204. doi: https://doi.org/1089/cyber.2018.0377	
Shema-Shiratzky, S., Brozgol, M., Cornejo-Thumm, P., Geva-Dayan, K., Rotstein, M., Leitner, Y., Hausdorff, J. M., & Mirelman, A. (2018). Virtual reality training to enhance behavior and cognitive function among children with attention-deficit/hyperactivity disorder: brief report. Developmental neurorehabilitation, 22(6), 431-436. https://doi.org/ 10.1080/17518423.2018.1476602	
Wehmeier PM, Schacht A, Wolff C, Otto WR, Dittmann RW, Banaschewski T. Neuropsychological outcomes across the day in children with attention-deficit/hyperactivity disorder treated with atomoxetine: results from a placebo-controlled study using a computer-based continuous performance test combined with an infra-red motion-tracking device. Journal of child and adolescent psychopharmacology. 2011 Oct 1;21(5):433-44.	Not an evaluation of the test
Reh V, Schmidt M, Lam L, Schimmelmann BG, Hebebrand J, Rief W, Christiansen H (2013) Behavioral assessment of core ADHD symptoms using the QbTest. J Atten Disord. doi:10.1177/1087054712472981	Does not report on one of the outcomes of interest

Table 38 Studies excluded at full text screening from checking the QbTech Manufacturer Submission

The Tables below report studies included in manufacturer submissions. We report the citation, as provided by the manufacturer, and record how the study has been processed in this review.

Study Details	Reason for exclusion
Ulberstadt et al, the 6th World Congress on ADHD, April 20 - April 23, 2017, Vancouver, Canada	Does not report on one of the outcomes of interest
Wehmeier PM, Schacht A, Wolff C, Otto WR, Dittmann RW, Banaschewski T. Neuropsychological outcomes across the day in children with attention-deficit/hyperactivity disorder treated with atomoxetine: results from a placebo-controlled study using a computer-based continuous performance test combined with an infra-red motion-tracking device. J Child Adolesc Psychopharmacol 2011;21:433–44. https://doi.org/10.1089/cap.2010.0142	Not an evaluation of the test
Roughan LA, Stafford J. Demand and capacity in an ADHD team: reducing the wait times for an ADHD assessment to 12 weeks. BMJ Open Qual. 2019 Oct 30;8(4):e000653. doi: 10.1136/bmjoq-2019-000653. PMID: 31750403; PMCID: PMC6830462	Did not report on test of interest
Gustafsson U, Hansen M. QbTest in the clinical assessment of attention deficit hyperactivity disorder: A review of the evidence. Mental Health Science. 2023.	Systematic review (we screened the studies)
Gustafsson U, Hansen M. QbTest for Monitoring Medication Treatment Response in ADHD: A Systematic Review. Clinical Practice & Epidemiology in Mental Health. 2023.	Systematic review (we screened the studies)

Table 39 Studies excluded at full text screening from checking the Peili Vision Manufacturer Submission

The Tables below report studies included in manufacturer submissions. We report the citation, as provided by the manufacturer, and record how the study has been processed in this review.

Study Details	Reason for exclusion
Seesjärvi, E., Puhakka, J., Aronen, E. T., Hering, A., Zuber, S., Kliegel, M., Laine., M. & Salmi, J.(lähetty arvioitavaksi). EPELI: a novel virtual reality task for the assessment of goal-directed behavior in real-life contexts. https://psyarxiv.com/aqbwt/	Does not report on one of the outcomes of interest
Toplak, M. E., West, R. F., & Stanovich, K. E. (2013). Practitioner review: Do performance-based measures and ratings of executive function assess the same construct? Journal of Child	Not a primary study or SR
Seesjärvi E, Laine M, Kasteenpohja K, Salmi J. Assessing goal-directed behavior in virtual reality with the neuropsychological task EPELI: Children prefer head-mounted display but flat screen provides a viable performance measure for remote testing. Frontiers in Virtual Reality. 2023 May 26;4:1138240.	Does not report on one of the outcomes of interest

Table 40 Studies excluded at full text screening from checking the Nesplora Manufacturer Submission

The Tables below report studies included in manufacturer submissions. We report the citation, as provided by the manufacturer, and record how the study has been processed in this review.

Study details	Reason
Fernandez M, Morillo Rojas MD. *[Test-retest validation of AULANESPLORA. (Virtual reality continuous performance test) for ADHD]*. 2012. URL: https://giuntipsy-my.sharepoint.com/personal/crodriguez_nesplora_com/_layouts/15/onedrive.aspx?id=%2Fpersonal%2Fcrodriguez%5Fnesplora%5Fcom%2FDocuments%2FDatos%20adjuntos%2FTest%2Dretest%20validation%20of%20AULANESPLORA%20%28virtual%20reality%20continuous%20performance%20test%29%20for%20adhd%2Epdf&parent=%2Fpersonal%2Fcrodriguez%5Fnesplora%5Fcom%2FDocuments%2FDatos%20adjuntos&ga=1 (Accessed March 2024).	Does not report on one of the outcomes of interest
Daniel Ursu, Z., & Ahmed, R. (n.d.). Assessing the Learning Effect of the Aquarium Test on ADHD: A Test-Retest Study with adults. In Press. https://doi.org/In press	Does not report on one of the outcomes of interest
Climent, G., Moreno Oyarzabal, M., González, M., Mejías, M., & Redondo, M. (2019). Nesplora Aquarium: Utilidad de la herramienta para la identificación y evaluación del TDAH en adultos.	Not a primary study or SR
Voinescu, A., Petrini, K., Stanton Fraser, D. et al. The effectiveness of a virtual reality attention task to predict depression and anxiety in comparison with current clinical measures. Virtual Reality (2021). https://doi.org/10.1007/s10055-021-00520-7	Does not include population with suspected or confirmed ADHD
J.L. González. Aplicación de realidad virtual (Nesplora Aquarium) en la valoración cognitiva y control de incapacidad temporal por contingencia común en pacientes con trastorno psiquiátrico menor. Rev Asoc Esp Espec Med Trab 2020; 29(3): 223-235	Does not include population with suspected or confirmed ADHD
Díaz-Orueta, U., Climent-Martínez, G., otros autores (in press). Los Tests de Rendimiento Continuo en Neurofeedback. Utilidad y Aplicaciones. En: I. Moreno (Ed.). Neurofeedback aplicado al TDAH/Use of Neurofeedback at ADHD	Not a primary study or SR
Koch, M., Becker, N., Spinath, F., & Greiff, S. (2021). Assessing intelligence without intelligence tests. Future perspectives. Intelligence, 101596. https://doi.org/10.1016/j.intell.2021.101596	Not a primary study or SR
Koch, M., Becker, N., Spinath, F., & Greiff, S. (2021). Assessing intelligence without intelligence tests. Future perspectives. Intelligence, 101596. https://doi.org/10.1016/j.intell.2021.101596	Not a primary study or SR
Gettman, J. (2022). Best Practices in School Neuropsychology: Guidelines for Effective Practice, Assessment, and Evidence-Based Intervention (D. Miller, D. Maricle, & C. Bedford, Eds.; 1st ed.). Wiley.	Not a primary study or SR
Parsons, T., Duffield, T., Mcmahan, T., & Diaz-Orueta, U. (2019). Virtual School Environments for Neuropsychological Assessment and Training: Learning in the Age of Emerging Technologies (pp. 123–157).	Not a primary study or SR
Mejías, M., Redondo, M., Fernández, M., Díaz-Orueta, U. (2016). Eficacia del metilfenidato de liberación prolongada en la mejora sintomática cognitiva y conductual del TDAH monitorizado a través del Test AULA Nesplora. XXIV Congreso de la Academia Iberoamericana de Neurología Pediátrica (AINP). Madrid, España, 8-10 de septiembre 2016	Does not report on one of the outcomes of interest

Study details	Reason
Zulueta, A., Iriarte, Y., Díaz-Orueta, U., & Climent, G. (2013). AULA NESPLORA: AVANCE EN LA EVALUACIÓN DE LOS PROCESOS ATENCIONALES. ESTUDIO DE LA VALIDEZ CONVERGENTE CON EL TEST DE PERCEPCIÓN DE DIFERENCIAS "CARAS" (VERSIÓN AMPLIADA). 04, 8.	Does not report on one of the outcomes of interest
Díaz-Orueta, U., Alonso-Sánchez, B., & Climent-Martínez, G. (2014). AULA versus d2 Test of Attention: Convergent validity and applicability of virtual reality in the study of reading disorders. 42nd Annual Meeting of the International Neuropsychological Society. Seattle, Washington, USA, 12th-15th February, 2014	Does not include population with suspected or confirmed ADHD
Díaz-Orueta, U., García-Cueto, E., Alonso-Sánchez, B., Crespo-Eguílaz, N., Fernández-Fernández, M.A., Otaduy, C., PérezLozano, C., & Zulueta, A. (2014). AULA Virtual Reality based attention test: factorial validity and convergent validity with EDAH scale and DSM criteria. 9th Conference of the International Test Commission, San Sebastián, Spain, 2nd-5th July, 2014	Does not include population with suspected or confirmed ADHD
Moreno-García, I., Espinosa-Oneto, N., Camacho-Vara, C., Díaz-Orueta, U. (2015). Evaluación del trastorno por dé cit de atención e hiperactividad mediante realidad virtual. Comparación con escalas conductuales. Comunicación y Pedagogía, 287-288: 33-37	Does not report on one of the outcomes of interest
Díaz-Orueta, U., Iriarte, Y., Climent-Martínez, G. & Banterla, F. (2012). An ecological virtual reality test with distractors for attention in children and adolescents. Journal of Virtual Reality, 5, 1-20	Does not report on one of the outcomes of interest
Redondo, M., González, N., Mejias, M., González, MF., Aierbe, A., Moreno, M., Pérez, C. (2018). Validez convergente entre las herramientas Nesplora Aula y el CPT de Conners 3. [Convergent validity between the tools Nesplora Aula and the CPT of Conners 3]. Oral communication presented at the II Ibero-American Congress Of Neuropsychology, Almería, 3-5 May 2018.	Does not include population with suspected or confirmed ADHD
Rebon Ortiz, F., Altuna, I., Lobo, A., & Climent, G. (2022). Validity Performance in the AULA Nesplora Test.	Does not include population with suspected or confirmed ADHD
Climent-Martínez, G., Banterla, F. (2011). AULA. Theoretical Manual. San Sebastian: Nesplora.	Not a primary study or SR
Mujika, J., Climent, G., Banterla F. (2011). Classroom a virtual reality task for attention assessment and ADD diagnosis support. Rev Neurol; 53 (10): 619-635.	Not an evaluation of the test
Herman, H., Díaz-Orueta, U. (2013). Rehabilitation Gaming. In S. Arnab, I. Dunwell, K. Debattista, (Eds.). Serious Games for Healthcare: Applications and Implication, (pp. 50-75), United States of America: Medical Information Science Reference.	Not a primary study or SR
Díaz-Orueta, U. (2015). Processes and programmes to develop attention and improve attention deficit and hyperactivity. Processes and programmes in educational neuropsychology. General Technical Secretariat. Publications Centre. Ministry of Education, Culture and Sport, pp. 154-168.	Not a primary study or SR
Moreno, I., Díaz-Orueta, U., others (in press). Assessment of ADHD based on virtual reality. Monographic review on ADHD and virtual reality.	Not a primary study or SR
Iriarte, Y., Climent, G., Banterla, F. (2011). AULA, the latest innovation in the neuropsychological measurement of ADHD. Oral communication at the Colegio de Psicólogos de Madrid y de Asturias. November 2011.	Not an evaluation of the test
Sánchez-Carpintero, R., Crespo-Eguílaz, N., Banterla, F., Climent-Martínez, G. (2013). Cognitive profiles of executive dysfunction in attention deficit disorder according to performance in the AULA virtual reality test. XV International Refresher Course in Neuropediatrics and Child Neuropsychology. Valencia, Spain, 28 February-1 March 2013.	Not an evaluation of the test

Study details	Reason
Zulueta, A., Díaz-Orueta, U., Crespo-Eguilaz, N. and Ruiz de Eguino, S. (2014). AULA virtual reality test and EDAH scale: complementary resources in the identification of ADHD. Communication presented at the VII National Congress of Neuropsychology: Neuropsychology 3.0. Bilbao, Spain, 15-17 October 2014	Not an evaluation of the test
Díaz-Orueta, U., Fernández-Fernández, M.A., & Climent-Martínez, G. (2015). Objectivity in Clinical Diagnosis of ADHD by means of AULA virtual reality based neuropsychological test: Initial findings. 5th World Conference on ADHD. Glasgow, Scotland, UK. 28-31 May 2015. 0.1007/s12402-015-0169-y/89	Does not report on one of the outcomes of interest
U. Diaz-Orueta*, A. Zulueta, N. Crespo-Eguılaz.(2015) AULA virtual reality test and EDAH observation scale: Complementary resources in the identification of ADHD. 5th World Conference on ADHD. Glasgow, Scotland, United Kingdom. 28-31 May 2015. 0.1007/s12402-015-0169-y/89	Does not report on one of the outcomes of interest
Zulueta, A., Redondo, M., Mejías, M., González, E. (2016). Reaction time in GO/NO GO task of AULA in children aged 6 to 16 years with and without ADHD. 60th Congress of Child and Adolescent Psychiatry (AEPNYA). San Sebastian, Spain, 1-4 June 2016.	Not an evaluation of the test
González, M.F., Zulueta, A., Redondo, M., Mejías, M., Otaduy, C. and González-Fraile, E. (2016) Differential pattern of responses of children with ADHD to visual and auditory stimuli. IX International and XIV National Congress of Clinical Psychology. Santander, Spain, 17-20 November 2016.	Not an evaluation of the test
Redondo, M., Mejías, M., González, M.F., Zulueta, A. & Lizarazu, B. (2016). Effects of impulsivity (commissions) on reaction times in children with ADHD. II International Congress of Clinical and Health Psychology on Children and Adolescents. Barcelona, Spain, 17-19 November 2016.	Not an evaluation of the test
Redondo, M., González, M.F., Mejías, M., Lizarazu, B., Rebón, F. (2016). Ceiling and floor effect in a test (NESPLORA Attention AULA) for the assessment of attentional processes. II International Congress of Clinical and Health Psychology on Children and Adolescents. Barcelona, Spain, 17-19 November 2016.	Does not include population with suspected or confirmed ADHD
González, M.F., Mejías, M., Redondo, M., Otaduy, C., Crespo, N. and Pérez, C. (2017). Per les of impulsivity and inattention in children with ADHD according to age. XIX International Conference on Neurodevelopmental Disorders. Valencia, Spain, 3-4 March 2017	Not an evaluation of the test
Mejias, M., Delgado-Mejía, I.D., González, M.F., Redondo, C., Abadi, A. and Lalor, S. (2017). Comparison between processing speed of WISC-IV and response time of the CPT NESPLORA AULA in children with ADHD. Poster presented at 6th World Conference on ADHD, Vancouver, Canada, 20-23 April 2017.	Not an evaluation of the test
Fernández, Fernández, M., Redondo, Zaballos, M., Mejías, M., González, Pérez, M.F. and Díaz-Orueta, U. (2017). Differential effect of methylphenidate and lisdexamfetamine on the performance of the AULA Nesplora neuropsychological test in children under treatment for ADHD. Poster presented at the XI SENEP Annual Meeting, Madrid, Spain, 25-27 May 2017.	Not an evaluation of the test
Moreno, M., Aierbe, A., González, M.F. and Mejías, M. (2018). Convergent validity between computerized and virtual reality continuous performance tasks. Poster presented at the XX Congreso Internacional de Actualización en Trastornos del Neurodesarrollo, Valencia, Spain, 9-10 March 2018.	Not an evaluation of the test

Study details	Reason
Mejías, M., Redondo, M., Moreno, M., Aierbe, A. and González, M (2018). Nesplora Aula School: development of a neuropsychological tool for the educational eld. Oral presentation held at the I Congreso de Psicología, Innovación Tecnológica y Emprendimiento, Almería, Spain, 19-21 April 2018.	Not an evaluation of the test
Mejías, M., Climent, G., González, M., Moreno, M., Aierbe, A. (2018). VRMIND: Development of neuropsychological assessment tools in Virtual Reality. Oral presentation held at the I Congreso de Psicología, Innovación Tecnológica y Emprendimiento, Almería, Spain, 19-21 April 2018.	Not an evaluation of the test
Moreno, M., Rebón, F., Aierbe, A., Mejías, M., González, M., Climent, G. (2018). Attentional development in childhood: Stability in the results of cognitive exploration. XIX International Congress of Psychology and Education, 20-23 June, Logroño, Spain.	Did not report on test of interest
Ruiz-Ruano García, A.M., López Puga, J., Lizarazu Rodrigo, B., Moreno Oyarzabal, M., Aierbe Pombo, A., Mejías Pérez, M. and Climent Martínez, G. (2018). Comparing attentional performance with Calibrated Bayes Factors in virtual reality-based continuous performance test. Oral Communication presented at ICERI2018 - International Conference Of Education, Research and Innovation. Seville, Spain, 12-14 November 2018.	Not an evaluation of the test
Moreno, M. (2018). Nesplora Aula School: a neuropsychological test for the educational environment. Oral communication at the IX Encuentro Nacional de Orientadores, Zaragoza, 18-20 May 2018.	Not an evaluation of the test
Ruiz-Ruano García, A., López Puga, J., Rodrigo, B., Moreno Oyarzabal, M., Pombo, A., Mejías, M., & Climent, G. (2018). COMPARING ATTENTIONAL PERFORMANCE WITH CALIBRATED BAYES FACTORS IN A VIRTUAL REALITY-BASED CONTINUOUS PERFORMANCE TEST. https://doi.org/10.21125/iceri.2018.0557	Not an evaluation of the test
García, A. I. (2021). EVALUACIÓN PSICOMÉTRICA DEL TEST DE AULA NESPLORA: APLICACIÓN[PhD Thesis].	Does not report on one of the outcomes of interest
Areces, D., Rodríguez, C., García, T., & Cueli, M. (2020). Is an ADHD Observation-Scale Based on DSM Criteria Able to Predict Performance in a Virtual Reality Continuous Performance Test? Applied Sciences, 10(7), 2409. https://doi.org/10.3390/app10072409	Not an evaluation of the test
Areces, D., Rodríguez, C., Garcia, T., Cueli, M., & Gonzalez-Castro, P. (2021). The Influence of State and Trait Anxiety on the Achievement of a Virtual Reality Continuous Performance Test in Children and Adolescents with ADHD Symptoms. Journal of Clinical Medicine, 10. https://doi.org/10.3390/jcm10122534	Not an evaluation of the test
Corrigan, N., Păsărelu, C.-R., & Voinescu, A. (2023). Immersive virtual reality for improving cognitive deficits in children with ADHD: A systematic review and meta-analysis. Virtual Reality, 1–20. https://doi.org/10.1007/s10055-023-00768-1	Did not report on test of interest
Doulou, A., & Skianis, C. (2023). VR & electronic games based Assessment for ADHD. Dialogues in Clinical Neuroscience & Mental Health, 6(4), Article 4. https://doi.org/10.26386/obrela.v6i4.276	Not a primary study or SR
Parsons, T. D., Kane, R., & Duffield, T. C. (2022). Virtual-Reality-Based Neuropsychological Assessments of Everyday Functioning. 37.	Not an evaluation of the test
Wiguna, T., Bahana, R., Dirgantoro, B., Minayati, K., Teh, S. D., Ismail, R., Kaligis, F., & Wigantara, N. (2022). Developing attention deficits/hyperactivity disorder-virtual reality diagnostic tool with machine learning for children and adolescents. Frontiers in Psychiatry, 13, 984481.	Did not report on test of interest

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K., Pramme, L., Blumenthal, N., Li, M., Asché, L., Jonas, S., Bey, K., Schulze, M., Steffens, M., Pensel, M., Guth, M., Rohlfsen, F., Ekhlas, M., Lügering, H., Fileccia, H., & Braun, N. (2022). Virtual reality in the diagnostic and therapy for mental disorders: A systematic review. Clinical Psychology Review, 98, 102213. https://doi.org/10.1016/j.cpr.2022.102213	Systematic review (we screened the studies)
Yongmei. (2022). Application of Virtual Reality Technology in Pediatric Clinical Practice.	Not a primary study or SR
A Review on Machine Learning Approaches in Diagnosis of ADHD Based on Big Data. (n.d.). Nesplora. Retrieved December 12, 2023, from	Not a primary study or SR
Adabla, S., Nabors, L., & Hamblin, K. (2021). A Scoping Review of Virtual Reality Interventions for Youth with Attention-Deficit/Hyperactivity Disorder. Advances in Neurodevelopmental Disorders, 5. https://doi.org/10.1007/s41252-021-00207-9	Not a primary study or SR
Alam, S., Raja, P., & Gulzar, Y. (2022). Investigation of Machine Learning Methods for Early Prediction of Neurodevelopmental Disorders in Children. Wireless Communications and Mobile Computing, 2022, 1–12. https://doi.org/10.1155/2022/5766386	Not a primary study or SR
Alava Sordo, S. (2018). Relación entre diagnóstico de TDAH y los procesos intelectuales y atencionales en muestra clínica comparación entre TDAH y Trastorno de Aprendizaje.pdf[PhD Thesis].	Did not report on test of interest
Alberca. (2014). TDAH, Diagnóstico, prácticas y estrategias de tratamiento_2014.pdf[PhD Thesis].	Did not report on test of interest
Alcañiz, M., Parra, E., & Giglioli, I. A. C. (2018). Virtual Reality as an Emerging Methodology for Leadership Assessment and Training. Front. Psychol. https://doi.org/10.3389/fpsyg.2018.01658	Not a primary study or SR
Alqithami, S. (2021). A serious-gamification blueprint towards a normalized attention. Brain Informatics, 8(1), 6. https://doi.org/10.1186/s40708-021-00127-3	Not a primary study or SR
Alqithami, S., Alzahrani, M., Alzahrani, A., & Mustafa, A. (2019). AR-Therapist: Design and Simulation of an AR-Game Environment as a CBT for Patients with ADHD. Healthcare, 7, 146. https://doi.org/10.3390/healthcare7040146	Not a primary study or SR
Araiza-Alba, P., Keane, T., Beaudry, J., & Kaufman, J. (2020). Immersive Virtual Reality Implementations in Developmental Psychology. International Journal of Virtual Reality, 20. https://doi.org/10.20870/IJVR.2020.20.2.3094	Not a primary study or SR
Arboleda Gil, S. V. (2020). Desempeño ejecutivo y procesos de monitoreo y control metacognitivo en niños. Tempus Psicológico, 3(2). https://doi.org/10.30554/tempuspsi.3.2.3405.2020	Not an evaluation of the test
Baggio, S., Hasler, R., Giacomini, V., El-Masri, H., Weibel, S., Perroud, N., & Deiber, M.-P. (2020). Does the Continuous Performance Test Predict ADHD Symptoms Severity and ADHD Presentation in Adults? Journal of Attention Disorders, 24(6), 840–848. https://doi.org/10.1177/1087054718822060	Did not report on test of interest
Bahana, R., Abdurachman, E., Lumban Gaol, F., Wiguna, T., Hutagalung, F., Dirgantoro, B., & Nugroho, E. (2023). A therapy game for elementary students with ADHD. AIP Conference Proceedings, 2508. https://doi.org/10.1063/5.0114939	Did not report on test of interest
Bassano, C., Chessa, M., & Solari, F. (2022). Visualization and interaction technologies in serious and exergames for cognitive assessment and training: A survey on available solutions and their validation. IEEE Access, PP, 1–1. https://doi.org/10.1109/ACCESS.2022.3210562	Not a primary study or SR
Batlle. (2020). Test_d_Atencio_Selectiva_i_Sostinguda_TA.pdf [PhD Thesis].	Did not report on test of interest

Study details	Reason
Bejarano, A., Correa, J., & Figueroa, P. (2020). Escape Room Virtual Reality: A Tool for Diagnosis and Treatment of Attention Deficit Disorder. 338. https://doi.org/10.1109/SVR51698.2020.00056	Did not report on test of interest
Bernardelli, G., Flori, V., Greci, L., Scaglione, A., & Zangiacomi, A. (2021). A Virtual Reality Based Application for Children with ADHD: Design and Usability Evaluation. In L. T. De Paolis, P. Arpaia, & P. Bourdot (Eds.), Augmented Reality, Virtual Reality, and Computer Graphics (Vol. 12980, pp. 363–375). Springer International Publishing. https://doi.org/10.1007/978-3-030-87595-4_27	Did not report on test of interest
Binz, T., Williner, E., Strajhar, P., Dolder, P., Liechti, M., Baumgartner, M., Kraemer, T., & Steuer, A. (2017). Chiral Analysis of Amphetamines in Hair by Liquid Chromatography-Tandem Mass Spectrometry: Compliance-Monitoring of attention deficit hyperactivity disorder (ADHD) patients under Elvanse® therapy and identification after controlled low dose application: Compliance-monitoring of amphetamine in hair. Drug Testing and Analysis, 10. https://doi.org/10.1002/dta.2208	Did not report on test of interest
Biomedical Engineering Research Group, Stellenbosch University, Swarts, R., Fourie, P. R., Biomedical Engineering Research Group, Stellenbosch University, van den Heever, D., & Biomedical Engineering Research Group, Stellenbosch University. (2019). ADHD Screening Tool: Investigating the effectiveness of a tablet-based game with machine learning. GLOBAL HEALTH INNOVATION, 2(2). https://doi.org/10.15641/ghi.v2i2.809	Did not report on test of interest
Björling, E. A., Sonney, J., Rodriguez, S., Carr, N., Zade, H., & Moon, S. H. (2022). Exploring the Effect of a Nature-based Virtual Reality Environment on Stress in Adolescents. Frontiers in Virtual Reality, 3. https://www.frontiersin.org/article/10.3389/frvir.2022.831026	Did not report on test of interest
Boechi, L. C., Encina Benítez, F. L., Rodas Jara, R. L., Rodas Jara, L. R., Villagra, M. D. R., Báez, D., Navarro, R., Almirón-Santacruz, J., Barrios, I., Castaldelli-Maia, J. M., Ventriglio, A., & Torales, J. (2023). Tecnologías para la Evaluación, Diagnóstico y Tratamiento del Trastorno por Déficit de Atención e Hiperactividad: Una Revisión Preliminar e Integradora. Revista Científica Ciencias de La Salud, 5, 01–07. https://doi.org/10.53732/rccsalud/2023.e5301	Not a primary study or SR
Borgnis, F., Baglio, F., Pedroli, E., Rossetto, F., Meloni, M., Riva, G., & Cipresso, P. (2021). EXIT 360°—EXecutive-Functions Innovative Tool 360°—A Simple and Effective Way to Study Executive Functions in Parkinson's Disease by Using 360° Videos. Applied Sciences, 11(15), 6791. https://doi.org/10.3390/app11156791	Did not report on test of interest
Bozkir, E. (2021). Towards Everyday Virtual Reality through Eye Tracking. 192.	Did not report on test of interest
Cabas-Hoyos, K., Figueroa, P., & Bracamonte, Y. (2022). Programas de intervención basados en tecnologías para niños y adolescentes diagnosticados con TDAH: Una revisión sistemática.	Systematic review (we screened the studies)
calzón, lopez. (2012). ANÁLISIS Y VALORACIÓN DE ALGUNOS PATRONES DIAGNÓSTICOS DIFERENCIALES EN LOS SUBTIPOS DEL TDAH[PhD Thesis].	Did not report on test of interest
Candela, G. (2018). Candela_Attentional variables and BCI_InPACT_2018.pdf.	Not an evaluation of the test
Castellaano. (2015). INTERVENCIÓN EN EL AULA PARA LA MEJORA DE LA ATENCIÓN Y EL RENDIMIENTO EN EL ALUMNADO DE SEGUNDO NIVEL DE EDUCACIÓN PRIMARIA: EFICACIA DE LAS AUTOINSTRUCCIONES Y DE LA AUTOOBSERVACIÓN.pdf[PhD Thesis].	Not an evaluation of the test

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Castilla, N., Higuera-Trujillo, J. L., & Llinares, C. (2023). The effects of illuminance on students' memory. A neuroarchitecture study. Building and Environment, 228, 109833. https://doi.org/10.1016/j.buildenv.2022.109833	Did not report on test of interest
Chen, I.-C., Chen, C.-L., Chang, C.-H., Fan, Z.-C., Chang, Y., Lin, C.-H., & Ko, L.-W. (2022). Task-Rate-Related Neural Dynamics Using Wireless EEG to Assist Diagnosis and Intervention Planning for Preschoolers with ADHD Exhibiting Heterogeneous Cognitive Proficiency. Journal of Personalized Medicine, 12, 731. https://doi.org/10.3390/jpm12050731	Did not report on test of interest
Cho, Y., Yum, J., Kim, K., Shin, B., Eom, H., Hong, Y., Heo, J., Kim, J.-J., Lee, H., & Kim, E. (2022). Evaluating attention deficit hyperactivity disorder symptoms in children and adolescents through tracked head movements in a virtual reality classroom: The effect of social cues with different sensory modalities. Frontiers in Human Neuroscience, 16. https://doi.org/10.3389/fnhum.2022.943478	Did not report on test of interest
Cibrian, F., Hayes, G., & Lakes, K. (2020). Research Advances in ADHD and Technology. Synthesis Lectures on Assistive, Rehabilitative, and Health-Preserving Technologies, 9, i–156. https://doi.org/10.2200/S01061ED1V01Y202011ARH015	Not a primary study or SR
Company, R. (2022). Estatus socioeconnómico y desarrollo cognitivo en la infancia y adolesecnecia[PhD Thesis].	Not an evaluation of the test
Crepaldi, M., Colombo, V., Mottura, S., Baldassini, D., Sacco, M., Cancer, A., & Antonietti, A. (2020). The Use of a Serious Game to Assess Inhibition Mechanisms in Children. Frontiers in Computer Science, 2. https://doi.org/10.3389/fcomp.2020.00034	Did not report on test of interest
De La Fuente, J. (2018). LIBRO RESUMENES CIPI 2018.pdf.	Did not report on test of interest
de la Fuente, J., González-Torres, M. C., Aznárez-Sanado, M., Martínez-Vicente, J. M., Peralta-Sánchez, F. J., & Vera, M. M. (2019). Implications of Unconnected Micro, Molecular, and Molar Level Research in Psychology: The Case of Executive Functions, Self-Regulation, and External Regulation. Frontiers in Psychology, 10, 1919. https://doi.org/10.3389/fpsyg.2019.01919	Not a primary study or SR
delgado, G. (2012). Anuario de Psicología Clínica y de la Salud Annuary of Clinical and Health Psychology_Monografico sobre Realidad Virtual.pdf.	Not a primary study or SR
Delgado Reyes, A., & Lopez, J. (2021). Escenarios Virtuales para la evaluación Neuropsicológica: Una Revisión de Tema.2–196. https://doi.org/10.7714/CNPS/15.2.216	Did not report on test of interest
Delgado-Reyes, A. C. (2021). REALIDAD VIRTUAL: EVALUACIÓN E INTERVENCIÓN EN EL TRASTORNO POR DÉFICIT DE ATENCIÓN/HIPERACTIVIDAD (TDAH). 28.	Did not report on test of interest
Diaz-Orueta, U., Facal, D., Nap, H. H., & Ranga, M.-M. (2012). What Is the Key for Older People to Show Interest in Playing Digital Learning Games? Initial Qualitative Findings from the LEAGE Project on a Multicultural European Sample. Games for Health Journal, 1(2), 115–123. https://doi.org/10.1089/g4h.2011.0024	Does not include population with suspected or confirmed ADHD
Dittmann, R., Cardo, E., Nagy, P., Anderson, C., Adeyi, B., Caballero, B., Hodgkins, P., Civil, R., & Coghill, D. (2014). Treatment Response and Remission in a Double-Blind, Randomized, Head-to-Head Study of Lisdexamfetamine Dimesylate and Atomoxetine in Children and Adolescents with Attention-Deficit Hyperactivity Disorder. CNS Drugs, 28. https://doi.org/10.1007/s40263-014-0188-9	Did not report on test of interest
DÖNMEZ, A., & TÜRK, A. (2023). Çocukluk Dönemi Korkuları ve Bir Müdahale Aracı Olarak Sanal Gerçeklik Uygulamasının Kullanımı. Hemşirelik Bilimi Dergisi. https://doi.org/10.54189/hbd.1088650	Not an evaluation of the test

Study details	Reason
Doulou, A., & Drigas, A. (2022). Virtual Reality & Electronic Games for Assessment in ADHD. International Journal of Recent Contributions from Engineering, Science & IT (iJES), 10(02), 4–15. https://doi.org/10.3991/ijes.v10i02.29735	Did not report on test of interest
Drane, D., Pedersen, N., Sabsevitz, D., Block, C., Dickey, A., Alwaki, A., & Kheder, A. (2021). Cognitive and Emotional Mapping With SEEG. Frontiers in Neurology, 12, 627981. https://doi.org/10.3389/fneur.2021.627981	Did not report on test of interest
Drigas, A., Mitsea, E., & Skianis, C. (2022). Virtual Reality and Metacognition Training Techniques for Learning Disabilities. Sustainability, 14, 1–19. https://doi.org/10.3390/su141610170	Did not report on test of interest
Duffield, T. C., Parsons, T. D., Landry, A., Karam, S., Otero, T., Mastel, S., & Hall, T. A. (2018). Virtual environments as an assessment modality with pediatric ASD populations: A brief report. Child Neuropsychology, 24(8), 1129–1136. https://doi.org/10.1080/09297049.2017.1375473	Did not report on test of interest
Edwards, J., & Parsons, T. D. (2017). Virtual Reality Applications for Neuropsychological Assessment in the Military. In The Role of Technology in Clinical Neuropsychology. Oxford University Press. https://doi.org/10.1093/oso/9780190234737.003.0014	Did not report on test of interest
Emmelkamp, P., & Meyerbröker, K. (2021). Virtual Reality Therapy in Mental Health. Annual Review of Clinical Psychology, 17. https://doi.org/10.1146/annurev-clinpsy-081219-115923	Not a primary study or SR
Fang, Y., Han, D., & Luo, H. (2019). A virtual reality application for assessment for attention deficit hyperactivity disorder in school-aged children. Neuropsychiatric Disease and Treatment, Volume 15, 1517–1523. https://doi.org/10.2147/NDT.S206742	Did not report on test of interest
Faria, A. L., & Pinho, M. S. (2016). DO PAPEL-E-LÁPIS À REALIDADE VIRTUAL: UMA NOVA ABORDAGEM PARA REABILITAÇÃO COGNITIVA PERSONALIZADA. 9.	Did not report on test of interest
Fei, C., Sun, B., Li, Y., & Zhang, Q. (2022). A Study of Virtual Reality Systems for Attention Stabilization. In H. Liu, Z. Yin, L. Liu, L. Jiang, G. Gu, X. Wu, & W. Ren (Eds.), Intelligent Robotics and Applications (pp. 105–113). Springer International Publishing. https://doi.org/10.1007/978-3-031-13844-7_11	Did not report on test of interest
Fernandez. (2012). Fenández_Valoración_Aula_TDAH_Rev_Neurol_2012.pdf. Rev Neurol 2012; 54 (Supl 3): S67-S93. https://doi.org/10.33588/rn.54S03.2012203	Does not report on one of the outcomes of interest
Ferreira-Brito, F., Fialho, M., Virgolino, A., Neves, I., Miranda, A., Sousa-Santos, N., Caneiras, C., Carriço, L., Verdelho, A., & Santos, O. (2019). Game-based interventions for neuropsychological assessment, training and rehabilitation: Which game-elements to use? A systematic review. Journal of Biomedical Informatics, 98, 103287. https://doi.org/10.1016/j.jbi.2019.103287	Does not include population with suspected or confirmed ADHD
Feu, A. M. (2017). REALIDAD VIRTUAL APLICADA A LA EVALUACIÓN DEL TDAH EN EL DEPARTAMENTO DE ORIENTACIÓN. AULA NESPLORA [PhD Thesis].	Does not report on one of the outcomes of interest
Flores, P. (n.d.). NEUROPSYCHOLOGICAL PROFILES OF ATTENTION AND INHIBITORY CONTROL IN NEURODEVELOPMENTAL DISORDERS THROUGH A VIRTUAL REALITY TEST. Retrieved May 2, 2023, from https://www.unioviedo.es/psicobiologia/wp-content/uploads/2017/12/Abstract-book-%C3%81vila-2017.pdf	Did not report on test of interest
fuentes. (2019). TDaHpp: App para Android para detección temprana en TDAH.pdf[PhD Thesis].	Not an evaluation of the test
Gabay, M., & Schonberg, T. (2022). Passive identification of subjective preferences towards individual items using eye-tracking in a virtual	Did not report on test of interest

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Gao, H. (n.d.). Assessment of Human Behavior in Virtual Reality by Eye Tracking. Retrieved May 2, 2023, from	Did not report on test of interest
Gao, H., Bozkir, E., Hasenbein, L., Hahn, J.-U., Göllner, R., & Kasneci, E. (2021). Digital Transformations of Classrooms in Virtual Reality.	Did not report on test of interest
García. (2013). García_Executive functions in kids_Int Journal Psychology, 2013.pdf.	Did not report on test of interest
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García, A. I. (2021). EVALUACIÓN PSICOMÉTRICA DEL TEST DE AULA NESPLORA: APLICACIÓN[PhD Thesis].	Does not report on one of the outcomes of interest
García Fernández, T., Rodríguez Pérez, C., González Castro, M. P., & González-Pienda García, J. A. (2014). The assessment of executive functioning in childhood and adolescence: Current situation and future lines of research. Executive Functioning: Role in Early Learning Processes, Impairments in Neurological Disorders and Impact of Cognitive Behavior Therapy	Not a primary study or SR
García Matilla, E. (2022). Caso Clínico: Trastorno por déficit de atención e hiperactividad con síntomas de ansiedad infantil[PhD Thesis].	Not an evaluation of the test
George, A. (2022). The Connections between Attention-Deficit/Hyperactivity Disorder and Levels of Criminal Behavior among Adults. Open Journal of Social Sciences, 10, 1–45. https://doi.org/10.4236/jss.2022.102001	Did not report on test of interest
Gettman, J. (2022). Best Practices in School Neuropsychology: Guidelines for Effective Practice, Assessment, and Evidence-Based Intervention (D. Miller, D. Maricle, & C. Bedford, Eds.; 1st ed.). Wiley. https://doi.org/10.1002/9781119790563	Not a primary study or SR
Gizatdinova, Y., Remizova, V., Sand, A., Sharma, S., Rantanen, K., Helminen, T., & Kylliäinen, A. (2022). PigScape: An embodied video game for cognitive peer-training of impulse and behavior control in children with ADHD. Proceedings of the 24th International ACM SIGACCESS Conference on Computers and Accessibility, 1–4. https://doi.org/10.1145/3517428.3550401	Did not report on test of interest
Goharinejad, S., Goharinejad, S., Hajesmaeel Gohari, S., & Bahaadinbeigy, K. (2022). The usefulness of virtual, augmented, and mixed reality technologies in the diagnosis and treatment of attention deficit hyperactivity disorder in children: An overview of relevant studies. BMC Psychiatry, 22, 1–13. https://doi.org/10.1186/s12888-021-03632-1	Did not report on test of interest
gonzalez lajas, J. (2016). Trastorno por Déficit de Atención con Hiperactividad (TDAH)_algoritmos y GPCI_aepap. Aepap.	Not an evaluation of the test
Gualtieri, L. (2021). METHODOLOGIES AND GUIDELINES FOR THE DESIGN OF SAFE AND ERGONOMIC COLLABORATIVE ROBOTIC ASSEMBLY SYSTEMS IN INDUSTRIAL SETTINGS [PhD Thesis].	Did not report on test of interest
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Gutiérrez-Maldonado, J. (2022). The Use of Virtual Reality Technology in the Treatment of Psychopathological Disorders. Journal of Clinical Medicine, 11, 5358. https://doi.org/10.3390/jcm11185358	Did not report on test of interest
Halder, S., & Halder, S. (2022). Application of Virtual Reality in Cognitive Rehabilitation: A Road Ahead. In Https://services.igi-	Not a primary study or SR

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Harstad, E., Weaver, A., Katusic, S., Colligan, R., Kumar, S., Chan, E., Voigt, R., & Barbaresi, W. (2014). ADHD, Stimulant Treatment, and Growth: A Longitudinal Study. Pediatrics, 134. https://doi.org/10.1542/peds.2014-0428	Did not report on test of interest
Hayden, A., Hooley, J. M., Dougherty, D. D., Camprodon, J. A., & Chou, T. (2023). Neuroticism modulates the qualitative effects of inferior parietal tDCS on negatively-valenced memories. Journal of Psychiatric Research, 161, 467–475. https://doi.org/10.1016/j.jpsychires.2023.04.005	Did not report on test of interest
Herrán Paz, M. E., Ortiz Monasterio, R., Herrán Ramírez, M. A., Rodríguez-Díaz, A., & García Villalpando, A. K. (2014). Narrative review of scales assessing attention-deficit/hyperactivity disorder in children and adolescents. Medwave, 14(01), e5887–e5887.	Did not report on test of interest
Higuera-Trujillo, J. L., Millán, C. L., Aviñó, A. M. i, Cueco, J. T., & Omarrementeria, C. S. (2021, January 21). The cognitive effect of university classroom geometry. A virtual reality study focused on memory and attention. INNODOCT 2020. INNODOCT 2020.	Did not report on test of interest
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Jung, E., Eun, S., Cho, S., Kim, H., & Park, D. (2019). Virtual Reality in Psychiatry. SPG BioMed. https://doi.org/10.32392/biomed.55.1	Not a primary study or SR
JUNIOR, F. (2019). Transtorno de déficit de atenção e hiperatividade (TDAH): Informações gerais e os jogos como uma das principais técnicas para o ensino de crianças com esse transtorno. https://doi.org/10.29327/710987	Did not report on test of interest
Kakoulidou, M. (2022). Understanding the Role of Motivation in the Reading of Children With ADHD-related Characteristics [PhD Thesis].	Does not report on one of the outcomes of interest
Kakoulidou, M., Knight, F., Filippi, R., & Hurry, J. (2021). The Effects of Choice on the Reading Comprehension and Enjoyment of Children with Severe Inattention and no Attentional Difficulties. Journal of Abnormal Child Psychology, 49. https://doi.org/10.1007/s10802-021-00835-8	Not an evaluation of the test
Kállai J. (2019). A komputer által létrehozott virtuális valóság pszichológiai mechanizmusai: Téri reprezentációs sajátosságok. Magyar Pszichológiai Szemle, 74(2), 181–200. https://doi.org/10.1556/0016.2019.74.2.4	Did not report on test of interest
Kim, E., Han, J., Choi, H., Prie, Y., Vigier, T., Bluteau, S., & Kwon, G. H. (2021). Examining the Academic Trends of Neuropsychological Tests for Executive Functions Using Virtual Reality: Systematic Literature Review (Preprint). JMIR Serious Games, 9. https://doi.org/10.2196/30249	Did not report on test of interest
Knight, F. L. C., & Dimitriou, D. (2019). Poor Sleep Has Negative Implications for Children With and Without ADHD, but in Different Ways. Behavioral Sleep Medicine, 17(4), 423–436. https://doi.org/10.1080/15402002.2017.1395335	Did not report on test of interest
Krieger, V., & Amador-Campos, J. (2021). Clinical presentations of attention-deficit/hyperactivity disorder (ADHD) in children and adolescents: Comparison of neurocognitive performance. Child Neuropsychology : A Journal on Normal and Abnormal Development in Childhood and Adolescence, 27, 1–30. https://doi.org/10.1080/09297049.2021.1917530	Did not report on test of interest
Kwan, H., Lin, L., Fahy, C., Shell, J., Pang, S., & Xing, Y. (2022). Designing VR training systems for children with attention deficit hyperactivity disorder (ADHD) (p. 89). https://doi.org/10.1109/VRW55335.2022.00030	Did not report on test of interest

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León, J. M. R. S. D. (2016). Manual de neuropsicología pediátrica. José María Ruiz Sánchez de León. https://doi.org/10.13140/RG.2.1.3492.6968	Not a primary study or SR
Liberatore, M., & Wagner, W. (2021). Virtual, mixed, and augmented reality: A systematic review for immersive systems research. Virtual Reality, 25, 1–27. https://doi.org/10.1007/s10055-020-00492-0	Does not include population with suspected or confirmed ADHD
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Liu, T.-C., Lin, Y.-C., Wang, T.-N., Yeh, S.-C., & Kalyuga, S. (2021). Studying the effect of redundancy in a virtual reality classroom. Educational Technology Research and Development, 69. https://doi.org/10.1007/s11423-021-09991-6	Did not report on test of interest
Lopez, J. V. S. (2021). Andrés Camilo Delgado-Reyesa. 15, 21.	Not a primary study or SR
Loyer Carbonneau, M., Demers, M., Bigras, M., & Guay, M.-C. (2020). Meta-Analysis of Sex Differences in ADHD Symptoms and Associated Cognitive Deficits. Journal of Attention Disorders, 1087054720923736. https://doi.org/10.1177/1087054720923736	Did not report on test of interest
Lozano-Álvarez, M., Rodríguez-Cano, S., Delgado-Benito, V., & Mercado Val, E. (2023). A Systematic Review of Literature on Emerging Technologies and Specific Learning Difficulties. Education Sciences, 13, 298. https://doi.org/10.3390/educsci13030298	Did not report on test of interest
Lv, Z., Wang, J.-Y., Kumar, N., & Lloret, J. (2021). Special Issue on "Augmented Reality, Virtual Reality & Semantic 3D Reconstruction." Applied Sciences, 11, 8590. https://doi.org/10.3390/app11188590	Not an evaluation of the test
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Madalena, I., Paskakulis, M., Torres, C., Queiroz, A., & Paula-Silva, F. (2021). Use of midazolam for behavioral management in dental care of a child with attention deficit hyperactivity disorder: A case report. RSBO, 18, 368–374. https://doi.org/10.21726/rsbo.v18i2.1617	Did not report on test of interest
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Management Association, I. R. (Ed.). (2018). Virtual and Augmented Reality: Concepts, Methodologies, Tools, and Applications. IGI Global. https://doi.org/10.4018/978-1-5225-5469-1	Not a primary study or SR
Martínez-Álvarez, I. (2018). Neuropsychology Applied to Education: Theoretical Framework and Intervention Areas for the Reading Competence and Attention Difficulties. 14.	Did not report on test of interest
Mash, L. E., Klein, R. M., & Townsend, J. (2018). Brief Report: A Gaming Approach to the Assessment of Attention Networks in Autism Spectrum Disorder and Typical Development. Journal of Autism and Developmental Disorders. https://doi.org/10.1007/s10803-018-3635-5	Did not report on test of interest
McKay, E., Kirk, H., Coxon, J., Courtney, D., Bellgrove, M., Arnatkeviciute, A., & Cornish, K. (2022). Training inhibitory control in adolescents with elevated attention deficit hyperactivity disorder traits: A randomised controlled trial of the Alfi Virtual Reality programme. BMJ Open, 12, e061626. https://doi.org/10.1136/bmjopen-2022-061626	Did not report on test of interest

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MUÑOZ, A. (2018). REVISION CPTS PARA EVALAUCION DE LA ATENCION_TFM_MUÑOZ CASTILLEJO, ANGELA.pdf [PhD Thesis].	Does not report on one of the outcomes of interest
Musalek, M., Kovar, I., & Sysala, T. (2019). Use of Virtual Reality for the Therapy of Children with Attention Deficit Hyperactivity Disorder. MATEC Web of Conferences, 292, 01042. https://doi.org/10.1051/matecconf/201929201042	Did not report on test of interest
Nasiri, E., Khalilzad, M., Hakimzadeh, Z., Isari, A., Faryabi-Yousefabad, S., Sadigh-Eteghad, S., & Naseri, A. (2023). A comprehensive review of attention tests: Can we assess what we exactly do not understand? The Egyptian Journal of Neurology, Psychiatry and Neurosurgery, 59. https://doi.org/10.1186/s41983-023-00628-4	Did not report on test of interest
Neguț, A., Jurma, A. M., & David, D. (2017). Virtual-reality-based attention assessment of ADHD: ClinicaVR: Classroom-CPT versus a traditional continuous performance test. Child Neuropsychology, 23(6), 692–712. https://doi.org/10.1080/09297049.2016.1186617	Did not report on test of interest
Neguț, A., Matu, S.-A., Sava, F. A., & David, D. (2016). Virtual reality measures in neuropsychological assessment: A meta-analytic review. The Clinical Neuropsychologist, 30(2), 165–184. https://doi.org/10.1080/13854046.2016.1144793	Did not report on test of interest
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Nolé, M. L., Soler, D., Higuera-Trujillo, J. L., & Llinares, C. (2022). Optimization of the Cognitive Processes in a Virtual Classroom: A Multi-objective Integer Linear Programming Approach. Mathematics, 10(7), 1184. https://doi.org/10.3390/math10071184	Did not report on test of interest
Obrist, V. U., & Martínez, E. A. (2016). Application of Virtual Reality in a Learning Experience. 6(2), 5.	Did not report on test of interest
Ortiz de Gortari, A., & Panagiotidi, M. (2022). The interplay between executive function deficits, psychopathological traits and dysfunctional gaming habits in the context of Game Transfer Phenomena. Computers in Human Behavior, 138, 107469. https://doi.org/10.1016/j.chb.2022.107469	Did not report on test of interest
Ortiz Pérez, A. (2017). Evaluación de la sintomatología, comorbilidad e impacto del trastorno por déficit de atención con hiperactividad a partir de evaluación electroencefalográfica, tests de rendimiento continuo y escalas de valoración.https://idus.us.es/handle/11441/69053	Did not report on test of interest
Pardos, A. P. (2014). Análisis descriptivo de la batería Test of everyday attention for children (TEA-Ch) en niños españoles de educación primaria[PhD Thesis].	Not an evaluation of the test
Parsons, T. D., & Carlew, A. R. (2016). Bimodal Virtual Reality Stroop for Assessing Distractor Inhibition in Autism Spectrum Disorders. Journal of Autism and Developmental Disorders, 46(4), 1255–1267. https://doi.org/10.1007/s10803-015-2663-7	Did not report on test of interest
Parsons, T. D., Carlew, A. R., Magtoto, J., & Stonecipher, K. (2017). The potential of function-led virtual environments for ecologically valid measures of executive function in experimental and clinical neuropsychology. Neuropsychological Rehabilitation, 27(5), 777–807. https://doi.org/10.1080/09602011.2015.1109524	Did not report on test of interest

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Parsons, T. D., & Phillips, A. S. (2016). Virtual reality for psychological assessment in clinical practice. Practice Innovations, 1(3), 197–217. https://doi.org/10.1037/pri0000028	Did not report on test of interest
Parsons, T. D., Riva, G., Parsons, S., Mantovani, F., Newbutt, N., Lin, L., Venturini, E., & Hall, T. (2017). Virtual Reality in Pediatric Psychology. Pediatrics, 140(Supplement_2), S86–S91. https://doi.org/10.1542/peds.2016-1758I	Not a primary study or SR
Parsons, T., & Duffield, T. (2020). Paradigm Shift Toward Digital Neuropsychology and High-Dimensional Neuropsychological Assessments: Review. Journal of Medical Internet Research, 22(12), e23777. https://doi.org/10.2196/23777	Not a primary study or SR
Parsons, T., & Kane, R. (2017). The Role of Technology in Clinical Neuropsychology. https://academic.oup.com/book/40883?login=true#login-purchase#login-purchase	Not a primary study or SR
Perra, A. (n.d.). Virtual Reality Frontiers in Bipolar Disorders: A Recovery Oriented Cognitive Rehabilitation tool.	Did not report on test of interest
Perra, A., Riccardo, C. L., De Lorenzo, V., De Marco, E., Di Natale, L., Kurotschka, P. K., Preti, A., & Carta, M. G. (2023). Fully Immersive Virtual Reality-Based Cognitive Remediation for Adults with Psychosocial Disabilities: A Systematic Scoping Review of Methods Intervention Gaps and Meta-Analysis of Published Effectiveness Studies. International Journal of Environmental Research and Public Health, 20(2), 1527. https://doi.org/10.3390/ijerph20021527	Did not report on test of interest
Pflueger, M., Mager, R., Graf, M., & Stieglitz, R.-D. (2023). Encoding of everyday objects in older adults: Episodic memory assessment in virtual reality. Frontiers in Aging Neuroscience, 15, 1100057. https://doi.org/10.3389/fnagi.2023.1100057	Did not report on test of interest
Pinnow, D., Hubbard, H., & Meulenbroek, P. (2021). Assessment of Attention and Memory Utilizing Ecologically Valid Distractions: A Scoping Review. Frontiers in Virtual Reality, 2, 685921. https://doi.org/10.3389/frvir.2021.685921	Not a primary study or SR
Polanczyk, G., Salum, G., Sugaya, L., Caye, A., & Rohde, L. (2015). Annual Research Review: A meta-analysis of the worldwide prevalence of mental disorders in children and adolescents. Journal of Child Psychology and Psychiatry, and Allied Disciplines, 56. https://doi.org/10.1111/jcpp.12381	Did not report on test of interest
Rasoulian Kasrineh, M., & Tabatabaei, S. M. (2021). Virtual reality among children with mental disorders: A mini-review. Advances in Health and Behavior, 4, 177–181. https://doi.org/10.25082/AHB.2021.01.004	Not a primary study or SR
Rodríguez, C., Areces, D., Garcia, T., Cueli, M., & Gonzalez-Castro, P. (2021). Neurodevelopmental disorders: An innovative perspective via the response to intervention model. World Journal of Psychiatry, 11, 1017–1026. https://doi.org/10.5498/wjp.v11.i11.1017	Not a primary study or SR
Rodríguez, C., Garcia, T., & Areces, D. (2017). New and Future Challenges Concerning the Use of Virtual Reality Tools for Assessing ADHD. Current Developmental Disorders Reports, 4. https://doi.org/10.1007/s40474-017-0103-4	Not a primary study or SR
Rodrıguez-Barranco, M., Gil, F., Herna, A. F., Alguacil, J., Lorca, A., Molina-Villalba, I., Gonza, B., Aguilar-Garduno, C., Rohlman, D. S., &	Not an evaluation of the test

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Lacasana, M. (2016). Postnatal arsenic exposure and attention impairment in school children. 13.	
Romero-Ayuso, D. (2021). Assessment of cognitive instrumental activities of daily living: A systematic review. https://www.tandfonline.com/doi/full/10.1080/09638288.2019.1665720	Not an evaluation of the test
Romero-Ayuso, D., Alcantara-Vázquez, P., Almenara, A., Núñez-Camarero, I., Triviño, J., Ariza-Vega, P., Molina Masso, J. P., & González, P. (2020). Self-Regulation in Children with Neurodevelopmental Disorders "SR-MRehab: Un Colegio Emocionante": A Protocol Study. International Journal of Environmental Research and Public Health, 17. https://doi.org/10.3390/ijerph17124198	Did not report on test of interest
Romero-Ayuso, D., Toledano-González, A., Rodríguez-Martínez, M., Arroyo Castillo, P., Triviño, J., González, P., Ariza-Vega, P., González, A., & Segura-Fragoso, A. (2021). Effectiveness of Virtual Reality-Based Interventions for Chil- dren and Adolescents with ADHD: A Systematic Review and Meta-Analysis. Children, 18, 70. https://doi.org/10.3390/children8020070	Not an evaluation of the test
Ruiz-Ruano-García, A. M., Sánchez-Kuhn, A., Flores, P., & López-Puga, J. (2023). Social Expectancy Increases Skin Conductance Response in Mobile Instant Messaging Users. Psicothema, 35.4, 414–422. https://doi.org/10.7334/psicothema2022.362	Did not report on test of interest
Salas-Bravo, S., Gonzalez-Arias, M., Araya-Piñones, A., Valencia-Jimenez, M., & Oyarce-Cortes C., S. (2017). Uso del Testde Rendimiento Continuo de Conners para diferenciar niños normales y con TDAH en Chile. Terapia psicológica, 35(3), 283–291. https://doi.org/10.4067/S0718-48082017000300283	Did not report on test of interest
Sánchez-Kuhn, A., León, J. J., Gôngora, K., Pérez-Fernández, C., Sánchez-Santed, F., Moreno, M., Taba, R. G. P., Manuel, V., Madrigal, M., Salgado, J. M., & Rodríguez, M. Á. V. (2015). Does the Go/No-Go task measure Impulsivity or Compulsivity? 82.	Did not report on test of interest
Satu, P., Minna, L., & Satu, S. (2023). Immersive VR Assessment and Intervention Research of Individuals with Neurodevelopmental Disorders Is Dominated by ASD and ADHD: A Scoping Review. Review Journal of Autism and Developmental Disorders, 1–19. https://doi.org/10.1007/s40489-023-00377-3	Not a primary study or SR
Schöne, B., Kisker, J., Sylvester, R. S., Radtke, E. L., & Gruber, T. (2021). Library for universal virtual reality experiments (luVRe): A standardized immersive 3D/360° picture and video database for VR based research. Current Psychology. https://doi.org/10.1007/s12144-021-01841-1	Did not report on test of interest
Schweitzer & Rizzo. (2022). Virtual Reality and ADHD: Clinical Assessment and Treatment in the Metaverse \textbar The ADHD Report. https://guilfordjournals.com/doi/abs/10.1521/adhd.2022.30.3.1	Not a primary study or SR
Seesjärvi, E., Laine, M., Kasteenpohja, K., & Salmi, J. (2023). Assessing goal-directed behavior in virtual reality with the neuropsychological task EPELI: Children prefer head-mounted display but flat screen provides a viable performance measure for remote testing. Frontiers in Virtual Reality, 4.	Did not report on test of interest
Seivane, M. S., & Brenlla, M. E. (2022). Aplicaciones de la realidad virtual en el campo de la evaluación psicológica: Una revisión sistemática. Aloma: Revista de Psicologia, Ciències de l'Educació i de l'Esport, 40(2), Article 2. https://doi.org/10.51698/aloma.2022.40.2.21-31	Not an evaluation of the test

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Sempere-Tortosa, M., Fernández-Carrasco, F., Mora-Lizán, F., & Rizo-Maestre, C. (2020). Objective Analysis of Movement in Subjects with ADHD. Multidisciplinary Control Tool for Students in the Classroom. International Journal of Environmental Research and Public Health, 17(15), 5620. https://doi.org/10.3390/ijerph17155620	Did not report on test of interest
Seo, S., Kim, E., Mundy, P., Heo, J., & Kim, K. K. (2019). Joint Attention Virtual Classroom: A Preliminary Study. Psychiatry Investigation, 16(4), 292–299. https://doi.org/10.30773/pi.2019.02.08	Did not report on test of interest
Serrano-Barroso, A., Siugzdaite, R., Guerrero-Cubero, J., Molina-Cantero, A. J., Gomez-Gonzalez, I. M., Lopez, J. C., & Vargas, J. P. (2021). Detecting Attention Levels in ADHD Children with a Video Game and the Measurement of Brain Activity with a Single-Channel BCI Headset. Sensors, 21(9), 3221. https://doi.org/10.3390/s21093221	Did not report on test of interest
Simões, E. N., Carvalho, A. L. N., & Schmidt, S. L. (2021). The Role of Visual and Auditory Stimuli in Continuous Performance Tests: Differential Effects on Children With ADHD. Journal of Attention Disorders, 25(1), 53–62. https://doi.org/10.1177/1087054718769149	Did not report on test of interest
Sinha, S. (2018). A Step Towards the Design of a Collaborative Virtual Reality-based Story-telling Environment [PhD Thesis]. https://doi.org/10.13140/RG.2.2.35115.92965	Did not report on test of interest
Skalski, S. (2020). Impact of placebo-related instruction on HEG biofeedback outcomes in children with ADHD. Applied Neuropsychology Child. https://doi.org/10.1080/21622965.2020.1861546	Did not report on test of interest
Skalski, S., Konaszewski, K., Pochwatko, G., Balas, R., & Surzykiewicz, J. (2021). Effects of hemoencephalographic biofeedback with virtual reality on selected aspects of attention in children with ADHD. International Journal of Psychophysiology, 170, 59–66. https://doi.org/10.1016/j.ijpsycho.2021.10.001	Did not report on test of interest
Son, H., Lee, D., Joung, Y.-S., Lee, J., Seok, E., Chung, T.-M., & Oh, S. (2021). A novel approach to diagnose ADHD using virtual reality. International Journal of Web Information Systems, ahead-of-print. https://doi.org/10.1108/IJWIS-03-2021-0021	Did not report on test of interest
Sordo, S., Garrido-Hernansaiz, H., Cantero-García, M., Sánchez-Iglesias, I., González-Moreno, J., & Santacreu, J. (2021). Validez de las pruebas de atención para el diagnóstico diferencial de TDAH infantil y Trastornos del Aprendizaje /// Validity of attention tests for differential diagnosis of childhood ADHD and Learning Disabilities. Electronic Journal of Research in Educational Psychology, 19, 437–464.	Not an evaluation of the test
Soroa Martínez, G., Revert Sánchez, L., & Aritzeta Galán, A. (2020). Familia eta hiperaktibitatea elkarrekin biziz: Atxikimendua eta heziketa-estiloak. Uztaro: giza eta gizarte-zientzien aldizkaria, 114, 81–106.	Did not report on test of interest
Sowell, M. M. (2014). Diagnosis and Assessment of Adult Attention Deficit Hyperactivity Disorder: Symptom Severity and Performance on Cognitive and Achievement Testing [Thesis]. https://oaktrust.library.tamu.edu/handle/1969.1/153987	Did not report on test of interest
Spesialpedagogikk, M. I., & Healy, C. (n.d.). There is something “extra” with my child.	Not an evaluation of the test
Stokes, J. D., Rizzo, A., Geng, J. J., & Schweitzer, J. B. (2022). Measuring Attentional Distraction in Children With ADHD Using Virtual Reality Technology With Eye-Tracking. Frontiers in Virtual Reality, 3. https://www.frontiersin.org/articles/10.3389/frvir.2022.855895	Did not report on test of interest
Sujar, A., Bayona, S., Delgado-Gómez, D., Miguélez-Fernández, C., Ardoy-Cuadros, J., Peñuelas-Calvo, I., Baca-García, E., & Blasco-Fontecilla, H. (2022). Attention Deficit Hyperactivity Disorder Assessment Based on Patient Behavior Exhibited in a Car Video Game: A	Did not report on test of interest

Study details	Reason
Pilot Study. Brain Sciences, 12(7), Article 7. https://doi.org/10.3390/brainsci12070877	
Sung, D., Park, B., Kim, B., Kim, H., Jung, K.-I., Lee, S.-Y., Kim, B., Park, S., & Park, M.-H. (2021). Gray Matter Volume in the Developing Frontal Lobe and Its Relationship With Executive Function in Late Childhood and Adolescence: A Community-Based Study. Frontiers in Psychiatry, 12, 686174. https://doi.org/10.3389/fpsyt.2021.686174	Did not report on test of interest
Tärning, B., Ternblad, E.-M., Haake, M., Gulz, A., & Nirme, J. (2021). Lessons Learned from a Study on Distractions in Virtual Learning Environments: Reliability, Ecological Validity and an Elusive Social Component. PRESENCE: Virtual and Augmented Reality, 28, 1–51. https://doi.org/10.1162/pres_a_00342	Did not report on test of interest
Ticknor, B. (2019). Virtual Reality and Correctional Rehabilitation: A Game Changer. Criminal Justice and Behavior, 46, 009385481984258. https://doi.org/10.1177/0093854819842588	Did not report on test of interest
Trigueiro, M. (2023). The effect of a virtual reality based intervention on processing speed and working memory in individuals with ADHD—A pilot-study. Frontiers in Virtual Reality, 4. https://doi.org/10.3389/frvir.2023.1108060	Did not report on test of interest
Valladares-Rodriguez, S., Fernández-Iglesias, M. J., Anido-Rifón, L., Facal, D., & Pérez-Rodríguez, R. (2018). Episodix: A serious game to detect cognitive impairment in senior adults. A psychometric study. PeerJ, 6, e5478. https://doi.org/10.7717/peerj.5478	Not an evaluation of the test
Vaz de Carvalho, C., González González, C., Popescu, E., & Rugelj, J. (2021). Serious Games. https://doi.org/10.3389/978-2-88966-944-8	Not a primary study or SR
Vicente, raquel. (n.d.). Trabajo teórico de revisión, actualización y análisis de un tema Raquel Vicente García.	Not an evaluation of the test
Villani, D. (Ed.). (2016). Integrating technology in positive psychology practice. Information Science Reference, an imprint of IGI Global.	Not a primary study or SR
Voinescu, A., & David, D. (2019). The Effect of Learning in a Virtual Environment on Explicit and Implicit Memory by Applying a Process Dissociation Procedure. International Journal of Human–Computer Interaction, 35(1), 27–37. https://doi.org/10.1080/10447318.2018.1424102	Did not report on test of interest
Volkov, A., Obukhov, A., Nazarova, A., & Patutin, K. (2023). Structural model of the microservice architecture of the control system for training complexes. AIP Conference Proceedings, 2910(1), 020164. https://doi.org/10.1063/5.0166558	Did not report on test of interest
Wallisch, A., Little, L. M., Dean, E., & Dunn, W. (2018). Executive Function Measures for Children: A Scoping Review of Ecological Validity. OTJR: Occupation, Participation and Health, 38(1), 6–14. https://doi.org/10.1177/1539449217727118	Did not report on test of interest
Wang, Z., Xu, H., & Yuan, H. (2020). Research on Design and Experience of Immersive Virtual Reality Psychological Relaxation Game Based on Image. IOP Conference Series: Materials Science and Engineering, 740(1), 012118. https://doi.org/10.1088/1757-899X/740/1/012118	Did not report on test of interest
Wiederhold, B. K., & Riva, G., G. (2018). The Virtual Reality Working-MemoryTraining Program (VR WORK M): Description of an Individualized, Integrated Program. https://www.arctt.info/volume-16-summer-2018	Did not report on test of interest
Wiguna, T., Wigantara, N., Ismail, R., Kaligis, F., Minayati, K., Bahana, R., & Dirgantoro, B. (2020). A Four-Step Method for the Development of an ADHD-VR Digital Game Diagnostic Tool Prototype for Children Using a DL Model. Frontiers in Psychiatry, 11, 829. https://doi.org/10.3389/fpsyt.2020.00829	Not an evaluation of the test

Study details	Reason
Yeh, S.-C., Lin, S.-Y., Wu, E., Zhang, K.-F., Xu, X., Rizzo, A., & Chung, C.-R. (2020). A Virtual-Reality System Integrated With Neuro-Behavior Sensing for Attention-Deficit/Hyperactivity Disorder Intelligent Assessment. IEEE Transactions on Neural Systems and Rehabilitation Engineering, PP, 1–1. https://doi.org/10.1109/TNSRE.2020.3004545	Not an evaluation of the test
Yez Tellez, Ma. G. (2016). Neuropsicologia de los trastornos del neurodesarrollo: Diagnostico, evaluacion e intervencion.	Did not report on test of interest
YILMAZ, N., Duran, F., & Fidan, U. (2021). Psikiyatrik Rahatsızlıklarda Sanal Gerçeklik ve Artırılmış Gerçeklik. Gazi Üniversitesi Fen Bilimleri Dergisi Part C: Tasarım ve Teknoloji, 9. https://doi.org/10.29109/gujsc.961331	Not an evaluation of the test
Żyła, K. (2019). Attention Deficit Hyperactivity Disorder Detection – from Psychological Checklists to Mobile Solutions. Studies in Logic, Grammar and Rhetoric, 60(1), 85–100. https://doi.org/10.2478/slgr-2019-0047	Not an evaluation of the test
Aierbe, A., & Climent, G. (2018). Factorial structure of Nesplora Aquarium_INS 2018.pdf. International Neuropsychological Society 2018 Mid-Year Meeting, Praga, República Checa.	Does not report on one of the outcomes of interest
Aierbe Pombo, A., Moreno Oyarzabal, M., Redondo, M., Mejías, M., & González, M. (2018). Comparison of the execution in the Nesplora Aquarium test between monolingual and bilingual people. X Congreso Nacional de Neuropsicología FANPSE.	Does not report on one of the outcomes of interest
Climent, G. (2018). Manual Nesplora Aquarium.	Not a primary study or SR
González, M., Redondo, M., Mejías, M., Aierbe Pombo, A., & Moreno Oyarzabal, M. (2017). Evolución de los procesos atencionales en función de la edad, medidos a través de una herramienta en realidad virtual. Congreso Nacional de Psicología, Oviedo, 3-7 de julio de 2017.	Did not report on test of interest
Mejias, M., Aierbe Pombo, A., Gonzalez, M. a F., & Moreno Oyarzabal, M. (2018). Development of a Virtual Reality-based Continuous Performance Test for the assessment of attention in adults. Nesplora Aquarium. I Congreso de Psicología, Innovación Tecnológica y Emprendimiento, Almería, España.	Did not report on test of interest
Mejías, M., González, M., Redondo, M., Aierbe Pombo, A., Moreno Oyarzabal, M., & Guinea, J. (2017). Attention assessment in adults through virtual reality. 6th Scientific Meeting of the Federation of the European Societies of Neuropsychology, Maastricht, 13-15 de septiembre de 2017.	Did not report on test of interest
Alshehri, A., Shehata, S., Almosa, K., & Awadalla, N. (2020). Schoolteachers' Knowledge of Attention-Deficit/Hyperactivity Disorder—Current Status and Effectiveness of Knowledge Improvement Program: A Randomized Controlled Trial. International Journal of Environmental Research and Public Health, 17, 5605. https://doi.org/10.3390/ijerph17155605	Did not report on test of interest
Duan, D., Wu, Z., Zhou, Y., Wan, X., & Wen, D. (2023). Working memory training and evaluation based on brain-computer interface and virtual reality: Our opinion. Frontiers in Human Neuroscience, 17. https://www.frontiersin.org/articles/10.3389/fnhum.2023.1291983	Not a primary study or SR
Fernández, M., Morillo, M., Gilibert, N., Carvalho, C., & Bello, S. (2020). The technological tools of the diagnosis and treatment of attention deficit disorder and hyperactivity. Medicina, 80 Suppl 2, 67–71.	Not primary study or SR
Geraets, C., Wallinius, M., & Sygel, K. (2022). Use of Virtual Reality in Psychiatric Diagnostic Assessments: A Systematic Review. Frontiers in Psychiatry, 13. https://doi.org/10.3389/fpsyt.2022.828410	Does not include population with suspected or confirmed ADHD
González Torrecillas, J. L., Marín, B., & Alonso, B. (2020). Aplicación de realidad virtual (Nesplora Aquarium) en la valoración cognitiva y control	Does not include population with suspected or confirmed ADHD

Study details	Reason
de incapacidad temporal por contingencia común en pacientes con trastorno psiquiátrico menor. Revista de La Asociación Española de Especialistas En Medicina Del Trabajo, 29(3), 223–235.	
Neguț, A., Matu, S.-A., Sava, F. A., & David, D. (2016). Virtual reality measures in neuropsychological assessment: A meta-analytic review. The Clinical Neuropsychologist, 30(2), 165-184. https://doi.org/10.1080/13854046.2016.1144793	Not an evaluation of the test
Voinescu, A., Fodor, L. A., Fraser, D. S., & David, D. (2020). Exploring attention in vr: Effects of visual and auditory modalities. International Conference on Applied Human Factors and Ergonomics, 677–683.	Does not report on one of the outcomes of interest
Voinescu, A., Fodor, L.-A., Fraser, D. S., Mejías, M., & David, D. (2019). Exploring the Usability of Nesplora Aquarium, a Virtual Reality System for Neuropsychological Assessment of Attention and Executive Functioning. 2019 IEEE Conference on Virtual Reality and 3D User Interfaces (VR), 1207–1208. https://doi.org/10.1109/VR.2019.8798191	Does not include population with suspected or confirmed ADHD
Akram, U., Barclay, N., Milkins, B., Stevenson, J., & Gardani, M. (2023). Sleep-Related Attentional and Interpretive-Bias in Insomnia: A Systematic Review and Meta-Analysis. Sleep Medicine Reviews, 67. https://doi.org/10.1016/j.smrv.2022.101713	Does not include population with suspected or confirmed ADHD
Alam, F., & Matava, C. (2022). A New Virtual World? The Future of Immersive Environments in Anesthesiology. Anesthesia and Analgesia, 135(2), 230–238. https://doi.org/10.1213/ANE.0000000000006118	Not a primary study or SR
Areces, D. (2014). Velocidad nombramiento dificultades lectoras y atencionales_2014.pdf [PhD Thesis].	Did not report on test of interest
Baertsch, T., Huang, Y.-Y., & Menozzi, M. (2023). Head-mounted display versus computer monitor for visual attention screening: A comparative study. Heliyon, 0(0). https://doi.org/10.1016/j.heliyon.2023.e16610	Did not report on test of interest
beristain, garcia. (2019). 7th World Congress on ADHD: From Child to Adult Disorder: 25th–28th April, Lisbon Portugal. ADHD Attention Deficit and Hyperactivity Disorders, 11(S1), 1–89. https://doi.org/10.1007/s12402-019-00295-7	Does not report on one of the outcomes of interest
Borgnis, F., Baglio, F., Pedroli, E., Rossetto, F., Meloni, M., Riva, G., & Cipresso, P. (2022). A Psychometric Tool for Evaluating Executive Functions in Parkinson's Disease. Journal of Clinical Medicine, 11. https://doi.org/10.3390/jcm11051153	Did not report on test of interest
Borgnis, F., Baglio, F., Pedroli, E., Rossetto, F., Uccellatore, L., Oliveira, J., Riva, G., & Cipresso, P. (2022). Available Virtual Reality-Based Tools for Executive Functions: A Systematic Review. Frontiers in Psychology, 13. https://doi.org/10.3389/fpsyg.2022.833136	Does not include population with suspected or confirmed ADHD
CIMA aeroespacial. (n.d.). Centro de Instrucción de Medicina Aeroespacial—Investigación—Investigaciones anteriores. Retrieved August 15, 2022, from https://ejercitodelaire.defensa.gob.es/EA/cima/investigacion/invAnteriores/#	Did not report on test of interest
Contreras-González, N., Téllez-Alanís, B., Haro, R., Jiménez-Correa, U., & Poblano, A. (2015). Executive dysfunction in patients with chronic primary insomnia treated with clonazepam. Neurological Research, 37(12), 1047–1053. https://doi.org/10.1080/01616412.2015.1114740	Did not report on test of interest
di, T. di D., Borgnis, F., & Matricola, N. (n.d.). EXecutive-functions Innovative Tool—EXIT 360: Development and Validation of a new 360-video instrument for executive functions.	Did not report on test of interest
Expósito, M. Á. F. (2019). TDaHpp: App para Android para detección temprana en TDAH [PhD Thesis].	Not an evaluation of the test
Fernández, M. A., Morillo, M. D., Gilibert, N., Carvalho, C., & Bello, S. (2020). Herramientas tecnológicas del diagnóstico y tratamiento del	Not a primary study or SR

Study details	Reason
trastorno por déficit de atención e hiperactividad. Medicina (Buenos Aires), 80, 67–71.	
Floris, M. (n.d.). La realtà virtuale nei disturbi affettivi: Uno studio pilota sulla prestazione cognitiva e i correlati elettroencefalografici della depressione.	Not an evaluation of the test
Friedenberg, J. (2020). The Future of the Self: An Interdisciplinary Approach to Personhood and Identity in the Digital Age (First edition). University of California Press.	Not an evaluation of the test
Hurtado-Pomares, M., Carmen Terol-Cantero, M., Sánchez-Pérez, A., Peral-Gómez, P., Valera-Gran, D., & Navarrete-Muñoz, E. M. (2018). The frontal assessment battery in clinical practice: A systematic review. International Journal of Geriatric Psychiatry, 33(2), 237–251. https://doi.org/10.1002/gps.4751	Did not report on test of interest
Jensen, T. D., Korbutt, W. K., Nedelev, G. P., & Bemman, B. (2022). Towards Diagnostic Support of Hyperactivity in Adults with ADHD Using a Virtual Reality Based Continuous Performance Test and Motion Sensor Data. International Conference on Pervasive Computing Technologies for Healthcare, 505–521.	Did not report on test of interest
kolk. (2022). Power of combined modern technology: Multitouch-multiuser tabletops and virtual reality platforms (PowerVR) in social communication skills training for children with neurological disorders: A pilot study: Applied Neuropsychology: Child: Vol 0, No 0. https://www.tandfonline.com/doi/abs/10.1080/21622965.2022.2066532	Not an evaluation of the test
Mazancová, F. (n.d.). Cognitive screening tests and their potential to detect cognitive impairment in neurodegenerative diseases.pdf [PhD Thesis]. Retrieved May 23, 2022, from https://dspace.cuni.cz/bitstream/handle/20.500.11956/152560/140095799.pdf?sequence=1	Not an evaluation of the test
Montoya-Arenas, D. A., Arbeláez-Vargas, J. F., & Díaz-Soto, C. M. (2018). Rendimiento frontal y ejecutivo en niños en proceso de restablecimiento de derechos en Antioquia, Colombia. Cuadernos Hispanoamericanos de Psicología, 18(2), 1–16. https://doi.org/10.18270/chps..v18i2.3051	Did not report on test of interest
Oliveira, J., Gamito, P., Alghazzawi, D. M., Fardoun, H. M., Rosa, P. J., Sousa, T., Picareli, L. F., Morais, D., & Lopes, P. (2018). Performance on naturalistic virtual reality tasks depends on global cognitive functioning as assessed via traditional neurocognitive tests. Applied Neuropsychology: Adult, 25(6), 555–561. https://doi.org/10.1080/23279095.2017.1349661	Did not report on test of interest
Panerai, S., Catania, V., Rundo, F., & Ferri, R. (2018). Remote Home-Based Virtual Training of Functional Living Skills for Adolescents and Young Adults With Intellectual Disability: Feasibility and Preliminary Results. Frontiers in Psychology, 9, 1730. https://doi.org/10.3389/fpsyg.2018.01730	Did not report on test of interest
Parsons, T. D. (2019). Technologically Enhanced Neuropsychological Assessments. 35.	Not a primary study or SR
Parsons, T. D., Lin, L., & Cockerham, D. (2018). Mind, Brain and Technology: Learning in the Age of Emerging Technologies. Springer. https://link.springer.com/book/10.1007/978-3-030-02631-8	Not a primary study or SR
Rodríguez, C., Garcia, T., Areces, D., Rodríguez-Díaz, F., Arteaga, G., & Ramos-Quiroga, A. (2021). Retrospective symptoms and learning difficulties predicting ADHD in adults: Differences between prison inmates and the clinical population. Scandinavian Journal of Psychology. https://doi.org/10.1007/s10.1111/sjop.12716	Did not report on test of interest

Study details	Reason
Sahu, A., & Bajaj, J. (2022). Evidence-Based Immersive Technology Use in Cognitive Assessments and Cognition-Based Interventions. In Emerging Advancements for Virtual and Augmented Reality in Healthcare (pp. 193–215). IGI Global	Not primary study or SR
Shams, S., & Farhadi, H. (2021). Effectiveness of The Virtual Reality Package on Social panic and social lectures.	Did not report on test of interest
Simons, A., Wohlgenannt, I., Zelt, S., Weinmann, M., Schneider, J., & Brocke, J. vom. (2023). Intelligence at play: Game-based assessment using a virtual-reality application. Virtual Reality, 1–17. https://doi.org/10.1007/s10055-023-00752-9	Did not report on test of interest
Voinescu, A., Petrini, K., & Stanton Fraser, D. (2023). Presence and simulator sickness predict the usability of a virtual reality attention task. Virtual Reality. https://doi.org/10.1007/s10055-023-00782-3	Does not include population with suspected or confirmed ADHD
Parsons, T.D. Bowerly, T. Buckwalter, J.G. Rizzo, A.A. (2007) A controlled clinical comparison of attention performance in children with adhd in a virtual reality classroom compared to standard neuropsychological methods. Child neuropsychology: A journal on normal and abnormal development in childhood and adolescence, 13(4):363_381, Jul 2007.	Did not report on test of interest
Adams, R. Finn, P. Moes, E. Flannery, K. Rizzo, A.A. (2009) Distractibility in attention/deicit/ hyperactivity disorder (adhd): he virtual reality classroom. Child Neuropsychol. 15: 120-135. 120. hurstone, L.L. Yela, M. (2001) CARAS: Test de percepción de diferencias (9a Edición). Madrid: TEA Ediciones.	Did not report on test of interest

Appendix 3

Data extraction tables and risk of bias tables

Table 41 Baseline Details for DTA studies included for objective 1

Study Details	Setting and Population	Index test	Reference standard
Adamou (2022)[83] **Design** One-gate **Country** United Kingdom **Funding** Unfunded	**Setting:** Secondary care **Population:** Adults **Inclusion criteria:** Adults (18+ years) referred to Specialist Adult ADHD and Autism service; good comprehension of the English language; IQ >70. **Exclusion criteria:** Age <18 years; intellectual disability **Number enrolled (number analysed):** 71 (69)	**Sensor CPT** QbTest (12-60)	**Reference standard** DSM-5 **Details** All patients underwent routine clinical evaluation which involved a "thorough psychiatric assessment by a doctor with expertise in ADHD and General Psychiatry.. Including full psychiatric history, mental state examination, observations during assessments, and informant history". This included the Diagnostic Interview for ADHD in Adults 2.0. Assessment led to 38 ADHD diagnoses and 31 non-ADHD.
Bijlenga (2019)[80] **Design** Two-gate **Country** The Netherlands; Germany; Sweden **Funding**	**Setting:** Secondary care **Population:** Older adults **Inclusion criteria:** ADHD Group (n=97): 55+ years and meet DSM-4 ADHD diagnostic criteria. Control group: healthy controls (n=112): 55+ years and no ADHD diagnosis. **Exclusion criteria:** Both groups: concurrent diagnosis that may affect test performance; mini mental state examination score =<23; other	**Sensor CPT** QbTest (12-60)	**Reference standard** ADHD group (n=97): DSM-5 ADHD diagnosis. Controls (n=112): Healthy controls, with score below cutoff on symptom severity measures. **Details** No further details

Study Details	Setting and Population	Index test	Reference standard
Not reported - 2nd author employed by QbTech	conditions that could affect test performance (e.g. migraine/ physical disability); concurrent medications that could affect test performance significantly. Control group: past or current ADHD diagnosis; scored below cutoff on self-report measure for ADHD symptom severity. **Number enrolled (number analysed):** 234 (209)	**Sensor CPT** QbTest (12-60) + Clinical judgment **Clinical component** Symptom severity self-report scales	**Reference standard** ADHD group (n=97): DSM-4-TR ADHD diagnosis, based on Diagnostic Interview for ADHD in Adults (DIVA 2.0) and rating scales. Controls (n=112): Healthy controls, with score below cutoff on symptom severity measures **Details** No further details
Brunkhorst-Kanaan (2020)[70] **Design** One-gate **Country** Germany **Funding** Non industry + industry	**Setting:** Secondary care **Population:** Adults **Inclusion criteria:** Patients referred for diagnostic assessment for adult ADHD between Jul 2018-Jul 2018 at the Department of Psychiatry, Psychosomatic Medicine and Psychotherapy. Following ADHD assessment, patients were separated into ADHD group (n=94): confirmed ADHD diagnosis, and control group (n=20): ADHD disconfirmed during diagnostic process. **Exclusion criteria:** None reported **Number enrolled (number analysed):** 114 (114)	**Sensor CPT** QbTest (12-60)	**Reference standard** DSM-5 (DIVA interview) **Details** Clinical ADHD diagnosis: DIVA interview undertaken, in which if certain criteria are met then a diagnosis of ADHD is plausible using DSM-5 criteria. Assessment led to 94 ADHD diagnoses and 20 non-ADHD.

Study Details	Setting and Population	Index test	Reference standard
Edebol(2011)[86] **Design** One-gate **Country** Sweden **Funding** Not reported	**Setting:** Secondary care **Population:** Adults **Inclusion criteria:** Clinic-referred adult patients awaiting clinical assessment of ADHD at the "NU-health care" hospital group. **Exclusion criteria:** None reported **Number enrolled (number analysed):** 19 (19)	**Sensor CPT** QbTest (12-60)	**Reference standard** DSM-4 **Details** "Clinical assessments were made by trained clinicians in the NU-health care and typically included observations, childhood anamnesis, self-report symptom scales, information from relatives, psychological or occupational-therapeutic tests and sometimes additional batteries of well-chosen psychological tests performed by specialists in neuropsychiatry. The psychiatric center asserted the DSM-4 for diagnostic considerations." This led to 12 ADHD diagnoses and 7 non-ADHD.
Edebol (2012)[78] **Design** Four-gate **Country** Sweden **Funding** Industry & non-industry	**Setting:** Secondary care **Population:** Adults **Inclusion criteria:** 306 participants were included belonging to four groups: ADHD (n=53): confirmed ADHD, as per DSM criteria, following assessment at outpatient clinic. Borderline/ Bipolar (n=45): confirmed borderline personality disorder or bipolar disorder. Disconfirmed (n=29): assessed for ADHD but disconfirmed diagnosis. Healthy controls (n=179): people aged 18-65 who had no known psychiatric diagnoses and were willing to sign consent and complete study. **Exclusion criteria:** None reported **Number enrolled (number analysed):** 306 (306)	**Sensor CPT** QbTest (12-60)	**Reference standard** ADHD group: DSM diagnosis (version not specified) (n=53) B/B group: diagnosed with borderline/ bipolar (n=45) Disconfirmed ADHD (n=29)[retained for analysis] Healthy controls (n=179) **Details** No further details

Study Details	Setting and Population	Index test	Reference standard
Edebol (2013)[81] **Design** Two-gate **Country** Sweden; Germany **Funding** Industry & non-industry	**Setting:** Secondary care **Population:** Adults **Inclusion criteria:** ADHD (n=55): Aged 18-65 years; DSM-4 ADHD diagnosis; chronic ADHD symptamology from childhood-adulthood with some symptoms present before 7 years old; accepted withdrawal from central stimulant treatment 24hr to QbTest. Non-ADHD controls (n=202): 18-65 years; sign informed consent and complete procedures; no known psychiatric diagnoses. **Exclusion criteria:** ADHD: clinically unstable psychiatric condition including acute mood disorder, acute bipolar disorder, acute OCD, or not meeting DSM-4 ADHD diagnosis. Non-ADHD controls: known psychiatric diagnosis. **Number enrolled (number analysed):** 261 (257)	**Sensor CPT** QbTest (12-60)	**Reference standard** ADHD group (n=55): Diagnosed with ADHD following clinical assessment adhering to DSM-4 Non-ADHD control group (n=202): Healthy controls with no known psychiatric diagnoses. **Details** No further details
Emser (2018)[85] **Design** Two-gate **Country** Germany **Funding** "Not applicable"	**Setting:** Secondary care **Population:** Adults and children **Inclusion criteria:** Children ADHD: Meet DSM-4 criteria for ADHD; IQ =>80 on short version of Wechsler Intelligence Scale for Children IV; stop taking medication 2 days before sensor CPTs. Adult ADHD: Same as for children, except IQ not assessed (but all estimated to have =>80IQ due to completing middle school). **Exclusion criteria:** ADHD: symptoms of inattention, hyperactivity or impulsivity due to other medical conditions; any genetic/ medical disorder associated with externalising behaviour. Controls: Established or suspected ADHD diagnosis or family history of ADHD. **Number enrolled (number analysed):** 136 (NR)	**Sensor CPT** QbTest (12-60) + Clinical judgment **Clinical component** TAP **Sensor CPT** QbTest (6-12) + clinical judgement **Clinical component** KiTap	**Reference standard** ADHD (n=68): DSM-4-oriented clinical interview by experienced clinician including KSADS and rating scales. Controls (n=68): No established or suspected ADHD diagnosis or family history of ADHD, unclear how assessed. Age/gender matched at group level. **Details** No further details

Study Details	Setting and Population	Index test	Reference standard
Groom (2016)[82] **Design** Two-gate **Country** United Kingdom **Funding** Industry & non-industry	**Setting:** Secondary care **Population:** Adults **Inclusion criteria:** ADHD group (n=32): DSM-5 diagnosis of ADHD. Autism (ASD) group (n=25): IC10 diagnosis of Asperger's syndrome **Exclusion criteria:** ADHD group: Disconfirmed ADHD diagnosis; non-completion of the test; continuation of ADHD medication medication during trial; dual diagnosis of ADHD and ASD; unavailable AQ10 scores. Autism group: ADHD group: Disconfirmed Autism diagnosis; non-completion of the test; continuation of psychostimulant medication medication during trial; dual diagnosis of ADHD and ASD **Number enrolled (number analysed):** 84 (57)	**Sensor CPT** QbTest (12-60) + Clinical judgment **Clinical component** Conners Adult Rating Scale and Autism Quotient-10	**Reference standard** ADHD group (n=32): DSM-5 diagnosis using DIVA interview, in addition to clinical rating scales CAARS & AQ10 Autism (ASD) group (n=25): ICD10 diagnosis of Asperger's syndrome **Details** No further details
Hamadache (2021)[29] **Design** Three-gate **Country** Germany **Funding** Unfunded	**Setting:** Secondary care **Population:** Children (age 5) **Inclusion criteria:** Healthy controls: tested at pre-scools within early research efforts and found to be normally developing. Cases and controls with specific language impairment: 63 children recruited from hospital social-paediatric centre. **Exclusion criteria:** None reported **Number enrolled (number analysed):** NR (119)	**Sensor CPT** QbMini	**Reference standard** ADHD based on DSM-4 (n=37) Specific language impairment (n=27) Healthy controls: tested at pre-schools and found to be normally developing (n=55) **Details** ADHD assessment was done using Fremdbeurteilungsbogen für Vorschüler mit Aufmerksamkeits- und Hyperaktivitätsstörungen (FBB-ADHS-V). A questionnaire which consists of four parts, of which the second part checks diagnostic criteria per DSM-4.

Study Details	Setting and Population	Index test	Reference standard
Hollis (2018)[18] **Design** One-gate **Country** England **Funding** Non-industry	**Setting:** Secondary care; Community **Population:** Children & Adolescents (age 6-16 years) **Inclusion criteria:** Children aged 6-17 years referred for their first ADHD assessment **Exclusion criteria:** Previous or current ADHD diagnosis; non-fluent in English; suspected moderate/ severe intellectual disability **Number enrolled (number analysed):** 267 (250)	**Sensor CPT** QbTest (6-12) or QbTest (12-60) + clinical judgement **Clinical component** Clinical judgement	**Reference standard** Consensus diagnosis using DAWBA[91] DSM-5 & ICD-10. **Details** Independent consensus research diagnosis made blind to group allocation using the Development and Wellbeing Assessment (DAWBA). Two experienced child psychiatrists reached clinical consensus diagnoses using DSM-5 and ICD-10 They had access, where available, to the Children's Global Assessment Scale (CGAS) and SNAP-IV but not clinic records or structured pro formas. Assessment led to 69 ADHD diagnoses and 25 non-ADHD.
Hult (2018)[69] **Design** One-gate **Country** Sweden **Funding** Unfunded	**Setting:** Secondary care **Population:** Children (age 6-12 years) **Inclusion criteria:** Children (age 6-12 years) with suspected ADHD, autism, or another neurodevelopmental disorder. Diagnosis based on DSM-4; assessed by multi-professional team. Following ADHD assessment, patients separated into ADHD group (n=124; ADHD diagnosis confirmed) and non-ADHD group (n=58; ADHD diagnosis disconfirmed). **Exclusion criteria:** Medication with central stimulants at time of assessment; not valid QbTest; Weschler scale assessment for IQ below 70; syndromal medical disorder diagnosis. **Number enrolled (number analysed):** 182 (182)	**Sensor CPT** QbTest (6-12)	**Reference standard** DSM-4 **Details** All participants were assessed by multi-professional team using LEAD procedure, with clinical diagnosis of ADHD based on behavioural criteria according to DSM-4. This led to 124 ADHD diagnoses and 58 non-ADHD.

Study Details	Setting and Population	Index test	Reference standard
Johansson (2018)[72] **Design** One-gate **Country** Sweden **Funding** Non-industry	**Setting:** Community **Population:** Adolescents (age 15 years) **Inclusion criteria:** Individual twins recruited from the DOGSS study if they had suspected neurodevelopmental disorder(s) and had been clinically assessed, including completion of the QbTest. Following ADHD assessment, participants were grouped into ADHD confirmed and ADHD disconfirmed. **Exclusion criteria:** Incomplete diagnostic information; taken ADHD medication prior to testing procedure. **Number enrolled (number analysed):** 356 (340)	**Sensor CPT** QbTest (12-60)	**Reference standard** K-SADS-PL interview **Details** Psychologists used the diagnostic interview Schedule for Affective Disorders and Schizophrenia in School-Age Children (K-SADS-PL). This led to 89 ADHD diagnoses and 248 non-ADHD.
Pettersson (2018)[84] **Design** One-gate **Country** Sweden **Funding** Non-industry	**Setting:** Secondary care **Population:** Adults **Inclusion criteria:** Referral for ADHD assessment; age 18+ years; informant who knew patient as child willing to participate in clinical interview. Following ADHD assessment, patients separated into ADHD group (n=60; ADHD diagnosis confirmed) and non-ADHD group (n=48; ADHD diagnosis disconfirmed). **Exclusion criteria:** Treatment with medications targeting ADHD; IQ =<70 on WAIS-IV; substance-related disorder. **Number enrolled (number analysed):** 108 (108)	**Sensor CPT** QbTestPlus **Comparator CPT** CPT-II: Conners' Continuous Performance Test II	**Reference standard** DSM-4 **Details** The reference standard was expert clinical consensus. Clinical assessment was undertaken by team of psychologists/ occupational therapist/ MD specialising in neuropsychology (including interview using DIVA 2.0 (based on DSM-4 criteria), SCID-I, SCID-II). This led to 60 ADHD diagnoses and 48 non-ADHD.

Study Details	Setting and Population	Index test	Reference standard
Rufo-Campos(2012)[65] **Design** Two-gate **Country** Not reported **Funding** Not reported	**Setting:** Not reported **Population:** Children (age not reported) **Inclusion criteria:** ADHD group (n=62): children diagnosed with ADHD. Non-ADHD group (n=62): children without diagnosis. **Exclusion criteria:** not reported. **Number enrolled (number analysed):** 124 (124)	**Sensor CPT** Nesplora AULA	**Reference standard** Not reported
Seesjarvi (2022)[77] **Design** Two-gate **Country** Finland **Funding** Non-industry (but authors developed test)	**Setting:** Secondary care **Population:** Children (age 9-12 years) **Inclusion criteria:** ADHD group (n=38): ADHD diagnosis by licensed physician using ICD-10 (with mainly hyperactive/impulsive subtype or combined inattention and hyperactive/ impulsive subtype); age 9-12 years when recruited; native language Finnish. Non-ADHD group (n=38): No mental or behavioural disorder. **Exclusion criteria:** ADHD group: Any nervous system disease (ICD-10, G00–G99); any mental/ behavioral disorders (F00–F99) except a secondary diagnosis of emotional disorder with childhood onset and unspecified behavioral and emotional disorder. Non-ADHD group: same as ADHD group except any mental or behavioural disorder excluded. **Number enrolled (number analysed):** 115 (76)	**Sensor CPT** EPELI **Comparator CPT** Continuous Performance Task	**Reference standard** ADHD group (n=38): ADHD diagnosis by licensed physician using ICD-10 Non-ADHD group (n=38): No mental or behavioural disorder; matched to cases; identified from questionnaires to the parents of the child where they were asked to list any diagnoses the child had. **Details** No further details

Study Details	Setting and Population	Index test	Reference standard
Sharma (2009)[64] **Design** Unclear **Country** UK **Funding** Not reported	**Setting:** Secondary care **Population:** Children and adolescents (aged 5-15 years) **Inclusion criteria:** Children and adolescents (aged 5-15 years) selected from QbTest database, which were evaluated for ADHD as per local protocol or as diagnosed by child/ family guidance. **Exclusion criteria:** Age <5 years or >15 years **Number enrolled (number analysed):** 50 (50)	**Sensor CPT** QbTest (6-12) or QbTest (12-60)	**Reference standard** Assessment of disruptive behaviour pathway used locally as standard **Details** No further information; no. with/ without ADHD not reported.
Soderstrom (2014)[76] **Design** One-gate **Country** Sweden **Funding** Non-industry	**Setting:** Secondary care **Population:** Adults **Inclusion criteria:** Referred to Neuropsychological Clinic in Vasteras Sweden for ADHD assessment between 1 Sep 2009 and 1 March 2011. Following ADHD assessment, patients separated into ADHD group (ADHD confirmed; n=41) and non-ADHD group (ADHD disconfirmed, n=20) **Exclusion criteria –** none reported **Number enrolled (number analysed):** 61 (61)	**Sensor CPT** QbTest (12-60)	**Reference standard** DSM-4 **Details** Clinical assessment for ADHD including self-rating scales, clinical interview, intelligence testing, and general psychiatric assessment. These relate to DSM-4 criteria, and led to 41 ADHD diagnoses and 20 non-ADHD.

Study Details	Setting and Population	Index test	Reference standard
Stevanovic (2023)[41] **Design** One-gate **Country** Sweden **Funding** Non-industry	**Setting:** Secondary care **Population:** Children and adolescents (mean age 13.5 years) **Inclusion criteria:** age 6-18 years; undergone QbTest or QbTest Plus at department of child and adolescent psychiatry in one of a few general hospitals in Sweden; availability of reliable QbTest scores. Following ADHD assessment, participants separated into ADHD group (n=708) **Exclusion criteria:** severe mental and/or neurodevelopmental disorders meaning could not understand or perform test accurately; inability to understand/ perform test accurately **Number enrolled (number analysed):** 1274 (928)	**Sensor CPT** QbTest (12-60) QbTest (6-12)	**Reference standard** Diagnostic process according to clinic's standard diagnostic procedure - no further information. Process led to ADHD confirmed (n=708); no-ADHD (n=220)
Tallberg (2019)[68] **Design** One-gate **Country** Sweden **Funding** Non-industry	**Setting:** Secondary care **Population:** Children (age 9-14 years) **Inclusion criteria:** Diagnostic study: children who screened positive for ADHD and were referred for further assessments in Child and Adolescent Psychiatry (CAP) clinic in southern Sweden between 1 Nov 2009-31 Dec 2010 (n=118, of which, following assessment, 80 were diagnosed with ADHD and 38 had disconfirmed diagnosis). **Exclusion criteria:** None reported **Number enrolled (number analysed):** 118 (118)	**Sensor CPT** QbTest (6-12) **Comparator CPT** Conners CPT II confidence index	**Reference standard** DSM-4. Process led to ADHD confirmed (n=80); no-ADHD (n=38).

Study Details	Setting and Population	Index test	Reference standard
Ulberstad (2020)[79] **Design** Two-gate **Country** Germany, Sweden, USA **Funding** Industry - authors employed by QbTech	**Setting:** Secondary care **Population:** Adolescents and adults (12-59 years) **Inclusion criteria** Cases (n=69): Meet ADHD diagnostic criteria according to DSM-5. Controls (n=73): Healthy controls (convenience sample). **Exclusion criteria** Control group: High levels of inattention or hyperactivity/ impulsivity according to DSM-5. **Numbers** 142 (142)	**Sensor CPT** QbCheck	**Reference standard** ADHD (n=69): DSM-5 diagnostic criteria Controls (n=73): Healthy controls; those with high levels of inattention/hyperactivity/ impulsivity according to DSM-5 excluded **Details** No further details
Zulueta (2019)[75] **Design** Two-gate **Country** Spain **Funding** Not reported	**Setting:** Secondary care **Population:** Children (age 6-16 years) **Inclusion criteria:** ADHD group recruited from outpatient services (n=213): Age 6-16 years; ADHD positive from ADHD diagnostic assessment at outpatient service (neuropsychology clinic or paediatric neurology clinic); IQ within the normal limits (IQ > 80); consent to participate; off stimulants medication for 48hr prior to testing. Typically developing controls recruited from schools (n=194): Age 6-16 years; IQ within the normal limits (IQ > 80); consent to participate; ADHD negative (/minimal ADHD symptoms) from ADHD diagnostic assessment at outpatient service and no other behavioural disorder. **Exclusion criteria** – None reported **Number enrolled (number analysed):** 407 (407)	**Sensor CPT** Nesplora Kids (AULA)	**Reference standard** ADHD (n=213): DSM-5 criteria, measured using ADHD Rating Scale-IV Healthy control group (n=194): from schools and neurology clinics minimal ADHD symptoms and no other behavioural disorder **Details** No further details

Table 42 Progress Plus information reported in DTA studies and RCTs included for objective 1

Study Details	Progress Plus Item	Details
Adamou (2022)[83]	Age - Mean (SD; range)	33 (9.9; not reported)
	Sex (% male)	65.2%
	Neurodevelopmental/learning disorders	No intellectual disability
Bijlenga (2019)[80]	Age - Mean (SD; range)	**ADHD:** 63.2 (4.8); **Control:** 64.4 (5.4). **Total sample range:** 55-79.
	Sex (% male)	**ADHD:** 46.4%; **Control:** 45.5%
	Education (% highest education)	**ADHD:** Primary school/ none 10.6%; Lower level professional education 25.5%; Higher level professional education 17%; College/ university 46.8%. **Control**: Primary school/ none 20.2%; Lower level 13.1%; Higher level 9.5%; College/ university 57.1%.
	Mental health disorders	**ADHD:** depression 26.8%; anxiety 12.4%; bipolar depression 4.1%; substance use or addiction 4.1%; other 13.4%; use of psychiatric medication 30.9%. **Control:** not reported.
	Neurodevelopmental/learning disorders	**ADHD:** ADHD combined subtype 79.4%; inattentive subtype 20.6%; symptom severity mean 56.7 (SD 16). **Control:** ADHD subtypes not reported; symptom severity mean 22.1 (SD 10.8).
Brunkhorst-Kanaan (2020)[70]	Age - Mean (SD; range)	**ADHD:** 34.7 (11.05; not reported); **Control:** 35.8 (10.6; not reported)
	Sex (% male)	**ADHD:** 57.4%; **Control:** 40%
	Mental health disorders	**ADHD:** depression 27.7%; substance use disorder 18.1%; bipolar 2.1%; other (e.g. PTSD, OCD, somatization disorders) 8.5%. Overall, 47.9% had a comorbidity with =>1 other psychiatric disorder, 4.4% had >2 other psychiatric disorders. Patients with affective comorbidities all suffered moderate-severe depressive episodes at time of examination. **Control:** depression 45%; substance use disorder 10%; bipolar 5%; other 15%. 12/20 patients had a psychiatric disorder.
Chitsabesan (2022)[74] **(RCT)**	Age - Percentages in each age category	**QbTest (n=30)**: age 16: 20%; a17: 26.7%; age 18: 50%; missing: 3.3%. **Usual care (n=30)**: age 16: 10%; age 17: 36.7%; age 18: 53.3%; missing: 0%.
	Sex (% male)	100%
	Ethnicity	**QbTest (n=30)**: White 76.7%; Other 20%; Missing 3.3%. **Usual care (n=30)**: White 80%; Other 20%; Missing 0%.
	Education	**QbTest (n=30):** Mainstream 20%; Pupil referral unit 10%; None 66.7%; Other 0%; Missing 3.3%. **Usual care (n=30)**: Mainstream 20%; Pupil referral unit 16.7%; None 56.7%; Other 6.7%; Missing 0%.
	Time-Dependent Relationships	All participants in youth justice system
Edebol (2011)[86]	Age - Mean (SD; range)	31.7 (9.3; 20-54)
	Sex (% male)	47%
	Occupation	Majority were unemployed, on sick leave or carried sickness pension (n=14) and the remaining had full or part time work (n=1), arranged daytime activities (n=1), studied (n=1), were on parents leave (n=1) or retired (n=1).
	Education	1 person had not begun high school but a majority had completed it (n=6) or made part of it (n=9) and some (n=3) had studied at post graduate levels.

Study Details	Progress Plus Item	Details
	Mental health disorders	Mean age for initial psychiatric contact was 20.2 (SD 10.9, n=12) and 10 people had undertaken psychiatric hospitalisation one or more times starting at the mean age of 27.1 (SD9.9, range 14-48). The sample indicated both serious symptoms and dysfunctions with Global Assessment of Functioning symptom severity at mean 49.9 (SD6.9, range 40=60) and level of adaptive functioning at M48.2 (SD8.8, range 35-60). Prior to ADHD assessment, all but two participants had at least one psychiatric diagnosis and some (n=8) had two. In total, relapsing episodes of depression or dysthymia (7); anxiety disorders or mixed anxiety/ depression (5); bipolar disorder (3); substance use disorder (3); personality disorder (2); adaptive disorder (1); acute stress reaction (1).
	Neurodevelopmental/learning disorders	Majority (n=14) had no family or relative with ADHD, and none had undergone ADHD assessment before.
	Relationship Features	Nine were single, six either married or sharing household with a partner, three had a relationship and one person was divorced.
Edebol (2012)[78]	Age - Mean (SD; range)	**ADHD (n=53)**: 35.89 (12.25; 18-64). **Bipolar/Borderline personality (B/B; n=45)**: 42.33 (11.63, 22-60). **Disconfirmed Group (n=29):** 35.21 (10.31, 20-54). **Normative Group (n=179):** 31.45 (10.33, 18-53).
	Sex (% male)	**ADHD:** 45%; **B/B:** 29%; **Disconfirmed:** 45%; **Normative**: 55%.
	Occupation (% employed)	**ADHD:** 58%; **B/B**: 27%; **Disconfirmed:** 38%; **Normative:** not reported.
	Education (% highest education)	**ADHD:** high school 23%; senior high school 57%; graduate school 19%; **B/B:** high school 27%; senior high school 62%; graduate school 9%; **Disconfirmed:** high school 21%; senior high school 69%; graduate school 10%; **Normative:** not reported.
	Mental health disorders	**ADHD:** Nine participants had one (n=7) or two (n=2) psychiatric disorders including dyslexia (3); social phobia (3); generalised anxiety disorder (1); depression (2); stress reaction (1), emotionally instable personality disorder (1). **B/B:** Bipolar disorder (27); borderline personality disorder (18). 13 participants had one or several additional diagnoses including psychological and behavioural disturbances because of substance use (4); generalised anxiety disorder (3); social phobia (2); panic disorders (1); anxiety and depression (2); adaption disorder (1); relapsing depression (1); two with borderline personality disorder also had bipolar disorders. **Disconfirmed:** no psychiatric diagnoses (8); two psychiatric diagnoses (12). Of the people with diagnoses, these included Aspergers syndrome (6); dyslexia (4); personality disorders (4); borderline personality disorder (1); bipolar unspecified (2); OCD (1): PTSD (1); memory disorder unspecified (1); as well as secondary diagnoses of depression (3); dyscalulia (2); attention disorders unspecified (2); developmental coordination disorder (1); tics (1); social phobia (1); dysmorphobia (1); mixed substance use disorder (1). **Normative:** exclusion criteria was any known psychiatric diagnoses.
	Relationship Features (marital status)	**ADHD:** 51% single; 38% married/ spouse; 9% divorced/ separated. **Disconfirmed:** 62% single; 34% married/ spouse; 3% divorced/ separated. **B/B:** 38% single; 51% married/ spouse; 9% divorced/ separated. **Normative:** Not reported.
	Place of residence	**ADHD:** live alone 60%; live with spouse 38%; group home 0%. **B/B:** live alone 33%; live with spouse 60%; group home 4%. **Disconfirmed:** live alone 55%; live with spouse 45%; group home 0%. **Normative:** Not reported.

Study Details	Progress Plus Item	Details
Edebol (2013)[81]	Age - Mean (SD; range)	**ADHD:** 33.35 (8.84; not reported); **Non-ADHD:** 31.06 (10.27; 18-53)
	Sex (% male)	**ADHD:** 45.5%. **Non-ADHD**: 56%.
	Occupation (% employment type)	**ADHD:** Sick leave 32.7%; full/part time employment 23.6%; rehabilitation/ practice 12.7%; unemployed 10.9%; studying 9.1%; retired 7.3%; parental leave 3.6%. **Non-ADHD**: not reported.
	Education (% highest education)	**ADHD:** Junior high school 21.8%; Partial high school 27.3%; complete high school 34.6%; partial graduate school 9.1%; complete graduate school 7.3%. **Non-ADHD**: not reported.
	Socioeconomic status (% income type)	**ADHD:** Income by public maintenance 68.7%; employment 20.4%; student loans 7.4%; other income 3.7%. **Non-ADHD**: not reported.
	Mental health disorders	**ADHD:** substance abuse 18.4%; relapsing/ moderate depression 18.4%; anxiety disorders 21.1%; mixed anxiety/ depression 5.3%; bipolar disorders 15.8%; personality disorders 10.5%; adjustment disorders 5.3%; 43.6% had no current psychiatric comorbidity, 43.6% had one and 12.7% had two. **Non-ADHD:** not reported, but an exclusion criterion is presence of "unstable psychiatric condition".
	Neurodevelopmental/learning disorders	**ADHD:** Autism 2.6%; dyslexia 2.6%; adjustment disorders (5.3%); personality disorders (10.5%); bipolar disorders (15.8%); mixed anxiety/depression (5.3%); anxiety disorders (21.1%); relapsing/moderate depression (18.4%); substance abuse (18.4%). **Non-ADHD:** not reported.
	Relationship Features (marital status; household set-up)	**Total sample:** 38.2% married/ common law; 41.9% single; 20% partner. **Total sample:** 43.6% single household; 56.4% shared household.
Emser (2018)[85]	Age - Mean (SD; range)	**ADHD (adults):** 35.1 (11.7; 19-63); **Control (adults):** 32.2 (9.6; 21-56). **ADHD (children):** 8.9 (1.4; 7-11). **Control (children):** 8.7 (1.2; 6.9-10.8)
	Sex (% male)	**ADHD (adults):** 65.8%; **Control (adults):** 65.8%. **ADHD (children):** 70%; **Control (children):** 63.3%.
	Education	All adults included had completed middle school.
	Neurodevelopmental/learning disorders	**ADHD (adults):** not reported; **Control (adults):** not reported; **ADHD (children):** Mean IQ 113.1 (SD 11.6). **Control (children):** Mean IQ 125.8 (SD 10.8).
	Place of residence	Small university town: "The high mean IQ of our ADHD and control groups is most likely due to the high percentage of children from academic families in a small university town (80.000 inhabitants of which 27.000 are students and ~ 10.000 academics working at the university with a further ~ 10.000 working in related academic institutions)."
Groom (2016)[82]	Age - Mean (SD; range)	**ADHD:** 31.64 (10.17; not reported); **ASD:** 33.22 (11.74; not reported)
	Sex (% male)	**ADHD:** 63%; **ASD:** 76%
	Socioeconomic status (index of multiple deprivation categories; decile ranks; low ranks indicate high level of deprivation, high ranks indicate low deprivation)	**ADHD:** low 50%, middle 18%, high 32%. **ASD:** low 64%, middle 12%, high 24%.

Study Details	Progress Plus Item	Details
	Mental health disorders	**ADHD:** depression (2); anxiety disorder (2); emotionally unstable personality disorder (i.e, borderline personality) (2). **ASD:** anxiety (4); depression (2); anxiety and depression (1); bipolar (1); substance misuse (1).
Hamadache (2021)[29]	Age - Mean (SD; range)	**ADHD:** 5.53 (not reported) **Controls:** 5.45 (not reported). All aged 5.
	Sex (% male)	**ADHD:** 81% boys; **Control** 56% boys; **Specific language impairment (SLI)**: 67%
	Neurodevelopmental/learning disorders	**ADHD:** Motor disorder 8.3%; epilepsy 2.8%; Language disorder 27.8%; Tic disorder 5.5%; IQ 100.69. **SLI:** Motor disorder 4%; epilepsy 0%; Language disorder 100%; Tic disorder 0%; IQ 97.27.
	Developmental Trauma (% premature birth)	**ADHD:** 11%; **SLI**: 4%
Hollis (2018)[18] **(RCT with DTA sub-study)**	Age - Mean (SD; range)	**QbOpen:** 9.5 (2.8; 6.0-17.4); **QbBlind:** 9.4 (2.8; 5.9-16.2)
	Sex (% male)	**QbOpen:** 77%; **QbBlind:** 80%.
	Ethnicity (% white, mixed, other)	**QbOpen** (data from 83/123 participants): White 88%; Mixed and other 12%. **QbBlind** (89/127 participants): White 90%; Mixed and other 10%.
	Neurodevelopmental/learning disorders	Diagnoses (n=241; allows more than one diagnosis per patient): 71% ADHD; 35% oppositional defiant disorder/ conduct disorder; 20% any anxiety disorder; 17% chronic tic disorder/ Tourette syndrome; 9% autism spectrum disorder; 3% depressive disorder; 11% learning difficulties; 0.4% attachment disorder; 19% no psychiatric diagnoses.
Hult (2018)[69]	Age - Mean (SD; range)	**ADHD:** 10.3 (1.7; not reported); **non-ADHD:** 10.8 (1.8; not reported)
	Sex (% male)	**ADHD:** 97%; **non-ADHD:**: 53%
	Mental health disorders	**ADHD:** depression/ anxiety 5%; **non-ADHD:** depression/ anxiety 7%.
	Neurodevelopmental/learning disorders	**ADHD:** autism spectrum disorders 28%; tic disorders 4%; developmental coordination disorder (DCD) 32%; borderleine intellectual functioning 10%; dyslexia 31%; language disorder 9%; mean full scale IQ (SD): 89.5 (13.2). **non-ADHD:**: autism spectrum disorders 81%; tic disorders 12%; developmental coordination disorder (DCD) 7%; borderleine intellectual functioning 16%; dyslexia 10%; language disorder 10%; mean full scale IQ (SD) 92.2 (14.6).
Johansson (2018)[72]	Age - Mean (SD; range)	15 (not reported; 14-16)
	Sex (% male)	**ADHD:** 70.79%; **Non-ADHD:** 49.8%
	Education (Parental education of mother and father)	**Mother - ADHD:** elementary school 8.99%; secondary school 59.55%; high school 29.21%; unknown 2.25%. **Mother - Non-ADHD:** elementary school 8.76%; secondary school 49.41%; high school 37.06%; unknown 4.71%. **Father - ADHD**: elementary school 11.24%; secondary school 42.7%; high school 23.6%; unknown 22.47%. **Father - Non-ADHD:** elementary school 15.14%; secondary school 37.45%; high school 28.69%; unknown 18.73%.
	Features of relationships	**ADHD:** Major school problems (failing to receive grades or repeating school year): 40.45%; Antisocial behaviour (criminal or violent behaviour): 14.61% **Non-ADHD:** Major school problems: 11.95%; Antisocial behaviour 17.13%.

Study Details	Progress Plus Item	Details
	Mental health disorders	**ADHD:** psychiatric condition other than ADHD 77.5%; Anxiety 23.6%; stress-related disorder 8.99%; depression life time 8.99%; OCD 6.74%; substance/ alcohol misuse 6.74%; eating disorder 2.25%; bipolar disorder 0%; psychosis 0%. **Non-ADHD:** psychiatric condition other than ADHD 59%; Anxiety 20.72%; stress-related disorder 10.76%; depression life time 7.97%; OCD 3.19%; substance/ alcohol misuse 2.39%; eating disorder 3.19%; bipolar disorder 0.8%; psychosis 0%.
	Neurodevelopmental/learning disorders	**ADHD:** Language disorder 37.08%; tic disorder 22.47%; oppositional defiant disorder 12.36; conduct disorder 7.87%; autism 1.12%, total IQ <70: mean 4 (SD 4.49). **Non-ADHD:** Language disorder 23.9%; tic disorder 11.6%; oppositional defiant disorder 1.2%; conduct disorder 0.8%; autism 1.99%; total IQ <70 mean 12 (SD 4.78).
Pettersson (2018)[84]	Age - Mean (SD; range)	**ADHD:** 28.18 (9.09; not reported); **Non-ADHD:** 32.75 (10.61; not reported)
	Sex (% male)	**ADHD:** 53.3%; **Non-ADHD:** 52.1%
	Occupation (employment type %)	**ADHD:** full time work/ studying 56.7%; part-time work/ studying 15%; unemployment/ vocational training 21.7%; long-term sick leave/ disability pension 6.7%. **Non-ADHD**: full time work/ studying 41.7%; part-time work/ studying 22.9%; unemployment/ vocational training 16.7%; long-term sick leave/ disability pension 18.8%.
	Education – Mean years (SD)	**ADHD:** 11.72 (1.85); **Non-ADHD:** 12.32 (1.60)
	Mental health disorders	**ADHD:** Beck Depression Inventory: mean 17.25 (SD 12.70); Beck Anxiety inventory mean 11.70 (SD 10.29); Mental health diagnoses - Axis 1 diagnosis (one or more) 50%; Axis II diagnosis (one or more) 16.7%. Distribution of Axis I and II diagnoses: Mood disorder 25%; Anxiety disorder 43.3%; Other Axis I disorder 16.7%; Axis II Cluster A disorder 5%; Axis II Cluster B disorder 8.3%; Axis II Cluster C disorder 10%. Estimated IQ: mean 91.52 (SD 12.31). **Non-ADHD:** Beck Depression Inventory: mean 23.83 (SD 12.87); Beck Anxiety inventory mean 17.96 (SD 11.98); Mental health diagnoses: Axis 1 diagnosis (one or more) 83.3%; Axis II diagnosis (one or more) 45.8%. Distribution of Axis I and II diagnoses: Mood disorder 43.8%; Anxiety disorder 68.8%; Other Axis I disorder 47.9%; Axis II Cluster A disorder 12.5%; Axis II Cluster B disorder 8.3%; Axis II Cluster C disorder 31.2%; Estimated IQ: 98.96 (SD 13.74).
Rufo-Campos(2012)[65]	No Progress-Plus information reported (conference abstract)	
Seesjarvi (2022)[77]	Age - Mean (SD; range)	**ADHD:** 10yr 4 month (1yr1month; not reported); **Non-ADHD:** 10yr 9month (1yr1month; not reported)
	Sex (% male)	Unclear
	Education (Mean (SD) Parental Education: 1 Comprehensive school, 2 high school/vocational school, 3 university degree or equivalent)	**ADHD:** 2.4 (0.6); **Non-ADHD:** 2.7 (0.5)
	Socioeconomic status	**ADHD:** 3.7 (1); **Non-ADHD:** 4 (1)

Study Details	Progress Plus Item	Details
	(Mean (SD) Parental Income before tax per adult: 1: less than 1500eur/m, 2: 1500-2200eur/m, 3: 2200-3000eur/m, 4: 3000-4000eur/m, 5: over 4000eur/m)	
	Neurodevelopmental/learning disorders	**ADHD:** conduct disorder n=3; oppositional defiant disorder n=4; OCD n=1; Tourette's n=1; provisional tic disorder n=1. **Non-ADHD:** exclusion criteria was any mental or behavioural disorder.
Sharma (2009)[64]	Age - Mean (SD; range)	Only range reported: 5-15 years.
Soderstrom (2014)[76]	Age - Mean (SD; range)	**ADHD:** 32.46 (8.99; not reported); **non-ADHD:** 30 (9.76; not reported)
	Sex (% male)	**ADHD (n=41):** 43.9%: **non-ADHD (n=20):** 40%
	Mental health disorders	**Total sample (n=61):** 63.9% had previously had contact with psychiatric services and had one or more psychiatric diagnoses. **ADHD (n=41):** axis I or axis II (cluster B diagnoses) 56.1%, of which: mood disorders 39%; anxiety disorders 31.7%; axis II cluster B disorders 4.9%; substance dependence disorders 7.3%. **Non-ADHD (n=20):** axis I or axis II (cluster B diagnoses) 80%, of which: mood disorders 45%; anxiety disorders 60%; axis II cluster B disorders 5%; substance dependence disorders 5%.
Stevanovic (2023)[41]	Age - Mean (SD; range)	**Total sample (n=1274) -** 13.5 (3.2; not reported)
	Sex (% male)	**Total sample (n=1274) -** 59.9%
	Neurodevelopmental/learning disorders	**Total sample (n=1274)**. **ADHD:** ASD 31.9%; another mental behavioural or neurodevelopmental disorder other than ASD 31.6%. **Non-ADHD:** any mental behavioural or neurodevelopmental disorder other than ADHD 81.8%; no diagnosis assigned/ clinical controls 18.2%. Intellectual difficulties: 32 people (excluded from analysis).
Tallberg (2019)[68]	Age – Median (median 1st-3rd quartiles)	**ADHD**: 12.5 (9.6-14.4); **Non-ADHD:** 11.2 (9.6-13.0).
	Sex (% male)	**ADHD**: 71%; **Non-ADHD**: 63%.
	Mental health disorders	**ADHD**: Not reported. **Non-ADHD**: Internalized problems such as mood disorder or anxiety disorder n=12.
	Neurodevelopmental/learning disorders	**ADHD**: % comorbid disorders not reported; Wechsler Intelligence Scale for Children IQ mean 87.15 CI 74.58-99.72. **Non-ADHD:** Autism spectrum disorders n=5; tic disorders n=3; language impairments or learning disorders n=12; internalized problems such as mood disorder or anxiety disorder; no diagnostic criteria n=14; Wechsler Intelligence Scale for Children IQ: mean 91.86 CI 78.59-105.13. "Two cases had full scale IQ just below 70, but with uneven cognitive profiles"
Ulberstad (2020)[79]	Age - Mean (SD; range)	**ADHD:** 27.58 (12.12); **Control**: 26.16 (9.55). **Total sample:** Range 12-60.
	Sex (% male)	**ADHD:** 52.2%; **Control**: 43.8%

Study Details	Progress Plus Item	Details
Zulueta (2019)[75]	Age - Mean (SD; Range)	**ADHD-combined:** 9.78 (2.65; not reported). **ADHD-inattentive:** 10.62 (2.79; not reported). **Control:** 9.08 (2.66; not reported).
	Sex (% male)	**ADHD-combined:** 76.9%; **ADHD-inattentive:** 69.5%; **Control:** 59.8%
	Neurodevelopmental/learning disorders	**IQ Mean (SD) – ADHD-combined:** 101.46 (SD 10.77); **ADHD-inattentive:** 98.78 (10.16); **Control:** 101.44 (10.55). Controls had no other behavioural disorder and minimal symptoms of ADHD reported on parent and teacher rating scales.

Table 43 Results for DTA studies included for objective 1

Study Details	Index Test	Measure & *Subgroup*	Threshold	Ref stand	TP	FP	FN	TN	Sens	Spec	AUC (95% CI)
Adamou(2022)[83]	QbTest (12-60)	Overall	1.5	DSM-5	27	18	11	13	0.71	0.42	NR
Bijlenga(2019)[80]	QbTest (12-60) + Clinical judgment	QBHyperactivity + Inattention	1.5	DSM-4-	88	10	9	102	0.91	0.91	NR
	QbTest (12-60)	QBHyperactivity + Inattention		DSM-5	54	19	43	93	0.56	0.83	NR
Brunkhorst-Kanaan(2020)[70]	QbTest (12-60)	QBImpulsivity	1.5	DSM-5	NR						0.54(0.52, 0.56)
		QBInattention	1.5		NR						0.56(0.54, 0.57)
		QBActivity	2.35		45	5	49	15	0.48	0.75	0.65(0.63, 0.67)
		QBActivity	1.5		64	10	30	10	0.68	0.5	
		QBActivity	2.95		26	2	68	18	0.28	0.90	
Edebol(2013)[81]	QbTest (12-60)	Overall	NR	DSM-4	47	35	8	167	0.85	0.83	NR
Edebol(2011)[78]	QbTest (12-60)	Overall; *All controls combined*	NR	DSM (version NR)	46	73		180	0.87	0.71	NR
		Overall; *Disconfirmed ADHD Only**				17		12	0.87	0.41	NR
		Overall; *Bipolar group*				29		16	0.87	0.36	NR
		Overall; *Healthy controls*				27		152	0.87	0.85	NR
Edebol(2011)[86]	QbTest (12-60)	Overall	>1.3	DSM-4	10	3	2	4	0.83	0.57	NR
Emser(2018)[85]	QbTest (12-60) + Clinical judgment	Overall	NR	DSM-4	31	9	7	29	0.82	0.76	NR
	QbTest (6-12) + clinical judgement	Overall			24	7	6	23	0.80	0.77	NR
Groom(2016)[82]	QbTest (12-60) + Clinical judgment	Overall	NR	DSM-5	30	4	2	21	0.94	0.84	0.87
Hamadache(2021)[29]	QbMini	QBActivity; *Healthy controls*	NR	DSM-4	NR						0.800
		QBActivity; *SLI group control**									0.506
		QBInattention; *Healthy controls*									0.670
		QBInattention; *SLI group**									0.524
		QBImpulsivity; *SLI group**									0.594
		QBImpulsivity; *Healthy controls*									0.589
Hollis(2018)[18]	QbTest (6-12) or QbTest (12-60) + clinical judgement	Overall	NR	DAWBA	37	26	6	17	0.86	0.40	NR
	Clinical judgement alone	Overall	NR	DAWBA	49	16	2	9	0.96	0.36	NR

Study Details	Index Test	Measure & *Subgroup*	Threshold	Ref stand	TP	FP	FN	TN	Sens	Spec	AUC (95% CI)
Hult(2018)[69]	QbTest (6-12)	QBActivity: *Total sample*	1.25	DSM-4	78	15	46	43	0.63	0.74	0.74 (0.66-0.82)
		QBActivity: *ADHD combined subgroup*			59	15	29	43	0.67	0.74	0.74 (0.66-0.83)
		QBActivity: *ADHD inattentive subgroup*			18	15	12	43	0.60	0.74	0.73 (0.63-0.84)
		QBImpulsivity: Total sample			52	16	72	42	0.42	0.72	0.62 (0.53-0.70)
		QBImpulsivity: *ADHD combined subgroup*			39	16	49	42	0.44	0.72	0.62 (0.53-0.71)
		QBImpulsivity: *ADHD inattentive subgroup*			11	16	19	42	0.37	0.72	0.62 (0.50-0.74)
		QBInattention: *Total sample*			60	10	64	48	0.48	0.83	0.76 (0.69-0.84)
		QBInattention: *ADHD combined subgroup*			45	10	43	48	0.51	0.83	0.77 (0.69-0.85)
		QBInattention: *ADHD inattentive subgroup*			14	10	16	48	0.47	0.83	0.76 (0.66-0.86)
Johansson(2018)[72]	QbTest (12-60)	QBInattention	NR	K-SADS-PL interview					0	0	0.59
		QBImpulsivity							0	0	0.58
		Overall			60	103	29	145	0.67	0.58	0.58
		QBActivity							0	0	0.49
Pettersson(2018)[84]	QbTestPlus	QBActivity	>1.5	DSM-4	46	27	14	21	0.77	0.44	0.664
		QBInattention	>1.5	DSM-4	35	16	25	32	0.58	0.67	0.673
		QbReactionTimeVariance	>1.5	DSM-4	26	12	34	36	0.43	0.75	0.674
		QbOmissionerrors	>1.5	DSM-4	44	21	16	27	0.73	0.56	0.725
	Conners' Continuous Performance Test II	CPTIICom	>1.5	DSM-4	20	4	40	44	0.33	0.92	0.741
		CPTIIVar	>1.5	DSM-4	16	7	44	41	0.27	0.85	0.706
Rufo-Campos(2012)[65]	Nesplora Kids (AULA)	Overall	NR	NR	Overall accuracy 93.5%						
Seesjarvi(2022)[77]	EPELI	Overall	46.5	ICD-10	29	17	9	21	0.76	0.55	0.70(0.59, 0.82)
		EPELITaskEfficacy	0.29		25	4	13	34	0.66	0.89	0.83(0.74, 0.92)
		EPELINavigationEfficacy	0.06		29	13	9	25	0.76	0.66	0.75(0.64, 0.86)
		EPELIControllerMotion	68,588.85		27	13	11	25	0.71	0.66	0.73(0.62, 0.85)
		EPELIActions	463		23	4	15	34	0.61	0.89	0.78(0.68, 0.89)
	Continuous Performance Task	CPT omission errors	3.5		19	8	19	30	0.5	0.79	0.70(0.57, 0.82)
		CPT Reaction time variability	150.3		33	9	5	29	0.87	0.76	0.85(0.76, 0.94)
		CPT comission errors	13.5		30	19	8	19	0.79	0.5	0.70(0.58, 0.82)

Study Details	Index Test	Measure & *Subgroup*	Thres hold	Ref stand	TP	FP	FN	TN	Sens	Spec	AUC (95% CI)
Sharma(2009)[64]	QbTest (6-12) or QbTest (12-60)	Overall	NR	NR	27	4	1	17	0.96	0.81	NR
Soderstrom(2014)[76]	QbTest (12-60)	QBActivity	1.5	DSM-4	28	7	13	13	0.68	0.65	0.666
		QBImpulsivity			24	4	17	16	0.59	0.80	0.683
		QBInattention			15	0	26	20	0.37	1	0.693
Stevanovic(2023)[41]	QbTest (6-12)	QBActivity	1.5	Clinic's standard diagnostic procedure	73	4	264	85	0.22	0.96	0.59(0.54, 0.64)
		QBInattention			168	19	171	68	0.5	0.78	0.64(0.59, 0.69)
		QBImpulsivity			90	6	252	78	0.26	0.93	0.59(0.54, 0.64)
	QbTest (12-60)	QBActivity			143	23	218	118	0.40	0.84	0.62(0.57, 0.66)
		QBInattention			124	24	239	115	0.34	0.83	0.58(0.54, 0.63)
		QBImpulsivity			117	19	249	117	0.32	0.86	0.59(0.55, 0.63)
Tallberg(2019)[68]	QbTest (6-12)	QbActivity	NR	DSM-4	45	20	35	18	0.56	0.47	0.48(0.36, 0.61)
		QbInattention			43	17	37	21	0.54	0.55	0.59(0.46, 0.72)
		QbImpulsivity			38	11	42	27	0.48	0.71	0.60(0.49, 0.72)
	Conners CPT II confidence index	NR			70	18	10	20	0.88	0.53	0.73(0.62, 0.84)
Ulberstadt(2020)[79]	QbCheck	Overall	NR	DSM-5	57	15	12	58	0.83	0.79	NR
		QbCheck Reaction time			NR						0.73
		QbCheck Commission errors									0.74
		QbCheck Omission errors									0.75
		QbCheck Microevents									0.80
		QbCheck Reaction time variability	NR	DSM-5							0.81
Zulueta(2019)[75]	Nesplora Kids (AULA)	Overall	NR	DSM-5	145	48	68	146	0.68	0.75	NR

*Data selected for synthesis where multiple control groups were available for a single study

Table 44 Detailed QUADAS-2 assessment showing judgements and rational for risk of bias and concerns regarding applicability for DTA studies included for objective 1

Study details	Risk of bias																Concerns regarding applicability				
	Consecutive/ random	Case-control avoided	No inappropriate excl	Patient selection bias	Index test blinded	Pre-specified	Index test bias	Ref stand appropriate	Blinded ref stand	Ref stand bias	Time interval	All received ref stan	Same ref stand	All included in analysis	Patient flow bias	Overall bias	Rationale Bias	Patient applicability	Ref stand applicability	Index applicability	Overall Applicability	Rationale
Adamou (2022)[83]	?	✓	✓	☺	✓	✓	☺	✓	?	?	✓	✓	✓	✗	☺	?	Unclear whether ref standard interpreted blind to QbTest results. 2 patients excluded from analysis but considered unlikely to have impacted results	☺	☺	☺	☺	No concerns
Bijlenga (2019)[80] *Qb test alone*	✗	✗	✓	☹	?	✓	?	✓	✓	☺	?	✓	✗	✗	☹	☹	Two-gate design – matched on age and gender. Control group received different reference standard. High proportion of drop-outs (25/234).	☹	☺	☺	☹	Two-gate design
Qb Test + clinical					?	?	?										No information on threshold					
Brunkhorst-Kanaan (2020)[70]	?	✓	✓	☺	?	✓	☺	✓	?	☺	?	✓	✓	✓	☺	☺	No concerns – no explicit information on blinding but QbTest conducted in separate appointment so appears unlikely that this would have influenced reference standard.	☺	☺	?	?	Limited details on test conduct & interpretation
Edebol (2013)[81]	✗	✗	✓	☹	✓	✓	☺	✓	?	☺	?	✓	✗	✗	☹	☹	Two-gate design. 4/55 ADHD group excluded from analysis.	☹	☺	☺	☹	Two-gate design
Edebol (2011)[86]	?	✓	✓	☺	✓	✓	☺	✓	✓	☺	✓	✓	✓	✓	☺	☺	No concerns	☺	☺	☺	☺	No concerns
Edebol (2012)[78]	✗	✗	✓	☹	?	✓	☺	?	?	?	?	?	✗	✓	☺	☹	Four-gate design. Limited details on reference standard.	☹	?	☺	☹	Four-gate design Limited details on reference standard

Study details	Risk of bias																Concerns regarding applicability				
	Consecutive/ random	Case-control avoided	No inappropriate excl	Patient selection bias	Index test blinded	Pre-specified	Index test bias	Ref stand appropriate	Blinded ref stand	Ref stand bias	Time interval	All received ref stan	Same ref stand	All included in analysis	Patient flow bias	Overall bias	Rationale Bias	Patient applicability	Ref stand applicability	Index applicability	Overall Applicability	Rationale
Emser (2018)[85]	✗	✗	✓	☹	?	?	?	✓	?	☺	?	✓	✗	✓	☺	☹	Case-control design. No information on threshold for Qb-Test + clinical assessment. No information on blinding of ref standard. Control group received different reference standard.	☹	☺	?	☹	Case-control design. Limited details on test conduct & interpretation
Groom (2016)[82]	✗	✗	✓	☹	?	?	?	✓	?	☺	✓	✓	✓	✗	☹	☹	Case-control design. No information on blinding of QbTest to case/control status. No detail on threshold. High proportion of drop-outs (5/37 in ADHD group).	☹	☺	?	☹	Case-control design. Limited details on test conduct & interpretation
Hamadache (2021)[29]	✗	✗	✓	☹	?	✓	☹	✓	✓	☺	?	✓	✗	?	☺	☹	Three-gate design. Limited details on QbMini. ROC analysis only so no thresholds.	☹	☺	?	☹	Three-gate design. Limited details on test conduct & interpretation
Hollis (2018)[18]	✓	✓	✗	☹	✓	?	☺	?	✓	☹	✓	?	✓	✓	☺	☹	Participants eligible for DTA sub-study if diagnostic decision had been made at 6 months (QbOpen eligible sample n=94/123; QbBlind n=76/127) Ref standard diagnosis made using limited data for around 50% participants..	☺	☺	☺	☺	No concerns
Hult (2015)[69]	✓	✓	✓	☺	?	✓	☺	✓	✓	☺	✓	✓	✓	✓	☺	☺	No concerns	☺	☺	☺	☺	No concerns

Study details	Risk of bias																Concerns regarding applicability				
	Consecutive/ random	Case-control avoided	No inappropriate excl	Patient selection bias	Index test blinded	Pre-specified	Index test bias	Ref stand appropriate	Blinded ref stand	Ref stand bias	Time interval	All received ref stan	Same ref stand	All included in analysis	Patient flow bias	Overall bias	Rationale Bias	Patient applicability	Ref stand applicability	Index applicability	Overall Applicability	Rationale
Johansson (2018)[72]	✓	✓	✓	☺	?	?	?	?	?	?	?	✓	✓	✗	☹	☹	Reference standard K-SADS-PL – not ADHD specific and so may not correctly diagnose ADHD. High proportion of participants excluded from 2x2 table.	☹	?	?	☹	Participants enrolled if at least one of twin pairs had pre-specified neuro-developmental disorders. Unlikely to be reflective of population with symptoms of ADHD.
Pettersson (2015)[84]	✓	✓	✓	☺	?	✓	☺	✓	?	?	?	✓	✓	✓	☺	?	Unclear if reference standard blind to QbTest result.	☺	☺	☺	☺	No concerns
Rufo-Campos(2012)[65]	✗	✗	?	☹	?	?	?	?	?	?	?	?	?	?	?	☹	Two-gate design; no details about conduct/ interpretation of index test, reference standard, or flow and timing	☹	?	?	☹	Two-gate design. Limited details on index test conduct & interpretation; no details about reference standard
Seesjarvi (2022)[77]	✗	✗	✗	☹	?	?	?	✓	✓	☺	?	✗	✗	✗	☹	☹	Two-gate design; patients with other listed comorbidities excluded from cases and controls; controls matched to cases. No information on whether Epeli test interpreters were blinded to diagnosis; high proportion excluded from 2x2 table.	☹	☺	?	☹	Limited details on test conduct & interpretation

Study details	Risk of bias																	Concerns regarding applicability				
	Consecutive/ random	Case-control avoided	No inappropriate excl	Patient selection bias	Index test blinded	Pre-specified	Index test bias	Ref stand appropriate	Blinded ref stand	Ref stand bias	Time interval	All received ref stan	Same ref stand	All included in analysis	Patient flow bias	Overall bias	Rationale Bias	Patient applicability	Ref stand applicability	Index applicability	Overall Applicability	Rationale
Sharma (2009)[64]	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	Limited information on patient selection (selected "semi-randomly" from database). Appropriateness of ref standard unclear; not clear if ref standard interpreters blinded to index test; not clear if all received same ref standard.	?	?	?	?	Very limited details on patient population, reference standard and patient flow.
Soderstrom (2014)[76]	?	✓	✓	☺	✓	✓	☺	✓	✗	☹	?	✓	✓	✓	☺	☹	Clinicians aware of QbTest results when interpreting reference standard.	☺	☺	☺	☺	No concerns
Stevanovic (2023)[41]	✗	✓	✓	☺	?	✓	☺	?	?	☹	?	✓	✗	✗	☹	☹	Unlikely that ref standard interpreted blind to index test; insufficient details on reference standard but was based on clinic records not DSM criteria. High proportion of drop-outs.	☹	☹	☹	☹	Children referred for evaluation of various neuropsychological conditions (not just ADHD). Test conduct did not follow manufacturers instructions (used only second part of QbTest to calculate scores).

Study details	Risk of bias																Concerns regarding applicability				
	Consecutive/ random	Case-control avoided	No inappropriate excl	Patient selection bias	Index test blinded	Pre-specified	Index test bias	Ref stand appropriate	Blinded ref stand	Ref stand bias	Time interval	All received ref stan	Same ref stand	All included in analysis	Patient flow bias	Overall bias	Rationale Bias	Patient applicability	Ref stand applicability	Index applicability	Overall Applicability	Rationale
Tallberg (2019)[68] - accuracy	✗	✓	✓	☺	?	✓	?	✓	?	?	?	✓	✓	✗	☹	☹	High proportion of missing data. Unclear if ref standard was blinded to QbTest; was not blinded to other tests evaluated (including CPT).	?	☺	?	?	Children had screened positive for ADHD and so were referred for further evaluation – unclear what screening involved and if were representative of our study population.
Ulberstadt (2020)[79]	✗	✗	?	☹	?	?	?	✓	✓	☺	?	✓	✗	✗	☹	☹	Two-gate design. Participants performed test at home; unclear who interpreted the test. 7/149 patients were not included in 2x2 table.	☹	☺	?	☹	Two-gate design. Limited details on test conduct & interpretation
Zulueta (2019)[75]	✗	✗	✓	☹	?	?	?	✓	✓	☺	?	✓	✓	✓	☺	☹	Two-gate design. No information on test interpretation or threshold.	☹	☺	?	☹	Two-gate design. Limited details on test conduct & interpretation

Table 45 QUADAS-C assessment showing judgements and rationale for risk of bias for comparative DTA studies included for objective 1

Study	Test A	Test B	Design	Patient	Index test	Ref standard	Flow and timing	Overall	Rationale
Bijlenga (2019)[80]	QbTest Alone	QbTest + clinical	Fully paired	☹	?	☺	☹	☹	Two-gate design. No information on threshold. No information on blinding between tests. High proportion of missing data for both tests.
Hollis (2018)[18]	QbTest + Clinical	Clinical Alone	Randomised	☺	☺	☹	☹	☹	Ref standard diagnosis made using limited data for around 50% participants as either parent or teacher assessment missing. High proportion of missing data for both tests as those without diagnosis at 6 months excluded.
Pettersson (2018)[84]	QbTest	CPTII	Fully paired	☺	?	?	☺	?	No information on blinding between tests or if reference standard blinded to test results.
Seesjarvi (2022)[77]	EF Sim	CPT?	Fully paired	☹	?	☺	☹	☹	Two-gate design; patients with other listed comorbidities excluded from cases and controls; cases matched to controls. No information on blinding to reference standard or between tests. high proportion excluded from 2x2 table
Tallberg (2019)[68] - accuracy	QbTest	CPTII	Fully paired	☺	?	?	☹	☹	No information on blinding to reference standard or between tests.

Table 46 Baseline Details for RCTs included for objective 1

Study Details	Participants	Group 1	Control
Author (Year) Chitsabesan (2022)[74] **Study Name** FACT **Country** England **Language** English **Setting** Young Offenders Institution (YOI) **Study design** Single-centre feasibility RCT **Funding** Non-industry	**Population:** ADHD diagnosis in boys aged 15-18 years **Inclusion Criteria:** Boys aged 15-18 years from a YOI who had any ADHD symptom from the Comprehensive Health Assessment Tool. **Exclusion Criteria:** Being on remand; not speaking English; previous/ current ADHD diagnosis; risk to researcher/ staff; unable to give informed consent (16yr+) or no guardian consent (under 16yr). **Number participants included (analysed):** 60 (47 at 3m, 19 at 6m) **Age** QbTest - age 16: 20%; 17: 26.7%; 18: 50%; missing: 3.3%. Control - age 16: 10%; 17: 36.7%; 18: 53.3%; missing: 0%. **Sex (% male)** 100	**QbTest and usual care (n=30 randomised; 20 completed test):** QbTest completed prior to first assessment by neurodevelopmental lead. Information from QbTest, plus clinical information, used to inform diagnostic decision.	**Usual care (n=30):** Assessed by neurodevelopmental lead. If potential ADHD symptoms present, then also assessed by assistant mental health practitioner (questionnaires, developmental history and observation). Third assessment by neurodevelopmental lead for diagnostic decision.

Study Details	Participants	Group 1	Control
Author (Year) Hollis (2018)[18] **Study Name** AQUA trial **Country** England **Language** English **Setting** Secondary care/ community: 10 child and adolescent mental health services (CAMHS) or community paediatric clinics **Study design** RCT with embedded qualitative evaluation and accuracy data **Funding** Non-industry	**Population** ADHD diagnosis in children aged 6-17 years **Inclusion Criteria** Children aged 6-17 years referred for their first ADHD assessment **Exclusion Criteria** Previous or current ADHD diagnosis; non-fluent in English; suspected moderate/ severe intellectual disability **Number participants included (analysed)** 267 (250) **Age** QbOpen(n=123): Mean 9.5; range 6.0-17.4; SD 2.8 QbBlind (n=127): Mean 9.4; range 5.9-16.2; SD 2.8 **Sex (% male)** **QbOpen:** 77%; **QbBlind:** 80%.	**QbOpen (n=123):** Usual care, in addition to QbTest (7-12 years) or QbTestPlus (12+ years), with Qb results shared with clinician to inform diagnostic decision, alongside clinical assessment. Usual care varied between sites but typically included interview with child and their family, and one standardised informant-based behavioural assessment measure.	**QbBlind (n =127):** Same as Group 1, but QbTest/ QbTestPlus results were withheld from clinician.

Table 47 Results from RCTs included for objective 1

Study	Outcome	Details	**Group 1:** QbTest + usual care		**Group 2** vs. usual care		**Effect measure – estimate (95% CI), p value**
			n	**No. Events**	**n**	**No. Events**	
Chitsabesan (2022)[74]	Time to assessment (*n=20 who completed the QbTest)*	Median no. days between randomisation and QbTest	20	Median (IQR) = 42 (26-93). Min=1; max=195	NR	NR	NR
	Impact on clinical decision making	Diagnostic decision made (all decisions were exclusion of ADHD diagnosis)	30	8	30	6	NR
	Morbidity	SDQ baseline: Close to average	30	7	30	5	NR
		SDQ baseline: Slightly raised	30	4	30	8	NR
		SDQ baseline: High	30	2	30	5	NR
		SDQ baseline: Very High	30	16	30	12	NR
		SDQ baseline: Missing	30	1	30	0	NR
		SDQ 3m: Close to average	23	2	24	4	NR
		SDQ 3m: Slightly raised	23	0	24	5	NR
		SDQ 3m: High	23	4	24	1	NR
		SDQ 3m: Very High	23	7	24	7	NR
		SDQ 3m: Missing	23	17	24	13	NR
		SDQ 6m: Close to average	9	2	10	3	NR
		SDQ 6m: Slightly raised	9	0	10	4	NR
		SDQ 6m: High	9	0	10	1	NR
		SDQ 6m: Very High	9	7	10	1	NR
		SDQ 6m: Missing	9	21	10	21	NR

Study	Outcome	Details	**Group 1:** care + QbTest or QbTestPlus, with test results available to clinician)		**Group 2** QbBlind: (Usual care + QbTest or QbTestPlus, with test results withheld from clinician)		**Effect measure – estimate (95% CI), p value**	**p-value**
			n	**No. Events**	**n**	**No. Events**		
Hollis (2018)[18]	Impact on clinical decision making	Diagnostic decision (confirming or excluding ADHD diagnosis) made	123	94	127	76	OR 2.43 (1.34-4.39)	p=0.003
	Diagnostic status	ADHD confirmed	123	69	127	65	RRR = 2.14 (1.00-4.59),	p=0.049
		ADHD excluded	123	25	127	11		
		No decision made (dropped out or discharged from clinic)	123	29	127	51		
	Diagnostic confidence:	Possible/ Uncertain	122	16	121	29	OR 1.77 (1.09-2.89),	p=0.022
		Probable	122	32	121	34		
		Definitely	122	74	121	58		
	Stability	Stability in diagnosis (any change in diagnosis from first confirmed diagnosis throughout study)	123	Kappa (95% CI) = 1 (1-1)	127	Kappa (95% CI) = 0.90 (0.7-1)	(χ2(1)=0.01,)	p=0.32
	Time to diagnostic decision	Number of minutes spent at clinic appointments until diagnosis	123	Mean (SD) = 141.97 (53.84) Observed median survival time (95% CI) = 150 (140-155)	127	Mean (SD) = 152.83 (75.88) Observed median survival time (95% CI) = 165 (150-180)	Time ratio: 0.85 (0.77-0.93),	p=0.001
		Number of days to diagnostic decision	123	Mean (SD): 82.54 (49.53) Observed median survival time (95% CI) = 96 (85-99)	127	Mean (SD): 83.94 (58.14) Observed median survival time (95% CI)= 108 (91-140)	Time ratio: 0.90 (0.73-1.10),	p=0.285
		Number of clinic appointments until diagnosis	123	Mean (SD): All participants: 2.69 (0.85) Those with diagnostic decision: 2.82 Those who dropped out or were discharged without a diagnosis: 2.28	127	Mean (SD): All participants: 2.72 (0.91) Those with diagnostic decision: 2.76 Those who dropped out or were discharged without a diagnosis: 2.67	NR	
		No. consultations to diagnostic decision (confirming or excluding ADHD diagnosis) by group over six-months, n=250	123	-	127	-	HR 1.44 (1.04-2.01)	p=0.029
		No. consultations to diagnostic decision (confirming or excluding ADHD diagnosis) by group over six-months, in n=198 aged 6-12 years (**using QbTest in intervention group)**	NR	-	NR	-	HR 1.84 (1.23 to 2.68),	p=0.001

Study	Outcome	Details	**Group 1:** care + QbTest or QbTestPlus, with test results available to clinician)		**Group 2** QbBlind: (Usual care + QbTest or QbTestPlus, with test results withheld from clinician)		**Effect measure – estimate (95% CI), p value**	**p-value**
			n	**No. Events**	**n**	**No. Events**		
		No. consultations to diagnostic decision (confirming or excluding ADHD diagnosis) by group over six-months, in n=52 aged >12 years (**using QbTest(12-60) in intervention group)**	NR	-	NR	-	HR 0.82 (0.37-1.80),	p = 0.618
	Costs	Cost of clinic appointments	123	Mean (SD): £87.62 (£40.45)	127	Mean (SD): £90.06 (£41.19)	-	

Table 48 Risk of bias assessment for RCTs included for objective 1

RoB2 assessment for the AQUA trial – the only RCT included for objective 1 that was not a feasibility trial.

Study Details	Outcome	Domain						Rationale
		1	2	3	4	5	Overall	
Hollis(2018)[18]	Diagnostic decision (confirming or excluding ADHD diagnosis) made OR 2.43 (1.34-4.39)	☺	☺	☺	☺	☺	☺	Appropriate randomisation and allocation concealment; participants blinded to allocation, clinicians not blinded, but it seems unlikely deviations took place due to trial context; appropriate measurement of the outcomes; pre-registered protocol, however potential for selective reporting due to HRQoL pre-specified but data not reported. Outcome not impacted by censoring/withdrawals
	Diagnostic status	☺	☺	☺	☺	☺	☺	Outcome not impacted by censoring/withdrawals
	Diagnostic confidence	☺	☺	☺	☺	☺	☺	Outcome not impacted by censoring/withdrawals
	Stability of diagnosis	☺	☺	☺	☺	☺	☺	Outcome not impacted by censoring/withdrawals
	No. consultations to diagnostic decision	☺	☺	☹	☺	☺	☹	Large proportion of participants (80/250) were censored from the analysis as they dropped out or were discharged from the clinic and so did not have a diagnosis at 6 months. This was a particular problem for time-to-event outcome data where the analysis assumed that participants were uninformatively censored and so had equivalent outcomes to those for whom full follow-up data were available.
	Number of minutes spent at clinic appointments until diagnosis	☺	☺	☹	☺	☺	☹	
	Number of clinic appointments until diagnosis	☺	☺	☹	☺	☺	☹	
	Number of days to diagnostic decision	☺	☺	☹	☺	☺	☹	
	Cost of clinic appointments	☺	☺	?	☺	☺	?	Unclear how costs calculated and so not clear how censored individuals contributed to this outcome

1: Randomisation process; 2: deviation from intended intervention; 3: missing outcome data; 4: measurement of the outcome; 5: selective outcome reporting

Table 49 Baseline Details for implementation studies that contribute data on process measures for objective 1

Study Details	Participants	Interventions and confounders
Author (Year) Hall (2016)[87] **Study Name** Not reported **Study Location** Kent, UK **Language** English **Setting** Community paediatric ADHD clinic **Study design** Uncontrolled before-after implementation study **Funding** Non-industry	**Population** Children and adolescents diagnosed with ADHD in community paediatric clinic **Sample selection and inclusion criteria** Patient files selected using random number generator. Case notes included if case had received primary diagnosis of ADHD; for the post-test implementation evaluation cases were only included if they had received a QbTest was part of diagnostic assessment. If a file was excluded, next available file was selected. **Exclusion Criteria** Not reported **Number participants included (analysed)** 80 (80) **Age** Pre-QbTest group: Mean 8.1; SD 2.4; Range 4.5-14.6 QbTest group: Mean 9.2; SD 2.3; Range 6.2-13.10 **PROGRESS Plus criteria reported by study** • **Sex (% male):** Pre-QbTest group: 80%; QbTest group: 70%; • **Neuro-developmental:** No. participants with secondary diagnosis - Pre-QbTest group: ASD 6; ASD and tic disorder 2; ASD and dyspraxia 2; ASD and OCD 1; oppositional defiance disorder 1; sensorineural deafness 1; mild epilepsy 1; Tourette's syndrome 1. QbTest group: ASD 7, Tourette's syndrome 1, sensory processing disorder 1, mild speech and language disorder 1, emotional difficulties1, dyslexia 1, learning difficulties 1. **Note: study results were not stratified by PROGRESS-Plus criteria.**	**Group 1 (pre-test implementation):** Standard ADHD assessment (n=40) **Group 2 (post-test implementation):** QbTest (6-12) or QbTest (12-60) + standard ADHD assessment (n=40) **Confounders**: authors state that "During this time period, there was no change to the assessment process, except the QbTest. Methods of acquiring parent and teacher information, and the quantity and quality of information, remained unchanged, as did members of the clinical and administration team."

Study Details	Participants	Interventions and confounders
Author (Year) Vogt (2011)[88] **Study Location** Berkshire, UK **Language** English **Setting** Child and adolescent mental health services (CAMHS) **Study design** Uncontrolled before-after implementation study **Funding** Not reported	**Population** Children and adolescents referred for ADHD assessment in CAMHS **Sample selection and inclusion criteria** Notes of 108 patients referred for ADHD to CAMHS clinic over 2 year period – 1 year before (2006-7) and 1 year after implementation of QbTest (2007-2008). Unclear whether all children assessed during eligible time periods enrolled or selected sub-sample. **Exclusion Criteria** Not reported **Number participants included (analysed)** 108 (108) **Age** Pre-QbTest group: Mean 9; mode 10; median 9 QbTest group: Mean 10.5; mode 8; median 10 **PROGRESS Plus criteria reported by study** None reported	**Group 1 (pre-test implementation):** Standard ADHD assessment (n=46) **Group 2 (post-test implementation):** QbTest (6-12) or QbTest (12-60) + standard ADHD assessment (n=62) **Confounders**: same child and adolescent psychiatrists conducted the assessments for both groups using the same protocol.

Study Details	Participants	Interventions and confounders
Author (Year) Sharma (2022)[66] **Study Location** Swindon, UK **Language** English **Setting** Hospital paediatric clinic **Study design** Uncontrolled before-after implementation study **Funding** Not reported	**Population** Children and adolescents referred for ADHD assessment in hospital paediatric clinic **Sample selection and inclusion Criteria** Patients assessed for ADHD between Jul 2020-Jan 2022 in hospital paediatric clinic, who had been referred for ADHD/ non-specific behavioural problems/ ASD. Unclear how patients were selected **Exclusion Criteria** Any patient who had not completed an ADHD assessment in the timeframe or whose assessment resulted in inconclusive determination. **Number participants included (analysed)** 40 (40) **Age** All participants: Mean 11.7 (SD 2.4) **PROGRESS Plus criteria reported by study** None reported	**Group 1 (pre-test implementation):** Standard ADHD assessment (n=20) **Group 2 (post-test implementation):** QbTest (6-12) or QbTest (12-60) + standard ADHD assessment (n=20) **Subgroups:** ADHD cases – those referred for ADHD Complex cases – those originally referred for non-specific behavioural difficulties or ASD **Confounding factors**: none reported

Study Details	Participants	Interventions and confounders
Author (Year) Humphreys (2018)[71] **Study Location** East Midlands, UK **Language** English **Setting** Community paediatric mental health settings in 3 NHS Trusts **Study design** Audit **Funding** Industry and non-industry: QbTech and East Midlands Academic Health Science Network	**Population** Children and adolescents referred for ADHD assessment in community paediatric mental health settings **Sample selection Inclusion Criteria** Selection of children (method of selection not reported) referred for ADHD assessment in community paediatric mental health settings, before and after implementation of QbTest **Exclusion Criteria** Not reported **Number participants included (analysed)** Unclear - 20-30 cases before QbTest implementation and 20-30 cases after test implementation, from each of the three Trusts. **Age** 5-16 years **PROGRESS Plus criteria reported by study** None reported	**Group 1 (pre-test implementation):** Standard ADHD assessment (60-90) **Group 2 (post-test implementation):** QbTest (6-12) or QbTest (12-60) + standard ADHD assessment (n=60-90) **Confounding factors**: none reported; authors note that the post-implementation group is after introduction of the QbTest and pathway re-design in two sites.

Study Details	Participants	Interventions and confounders
Author (Year) McKenzie (2022)[31] **Study Name** Focus ADHD **Study Location** England (sites throughout the country) **Language** English **Setting** CAMHS and paediatric sites (total of 20 sites) **Study design** Audit **Funding** Industry and non-industry: QbTech and Academic Health Science Networks in England	**Population** Children and adolescents referred for ADHDin CAMHS and paediatric sites **Inclusion Criteria** Selection of children referred for ADHD assessment in in CAMHS and paediatric sites across England, before and after implementation of QbTest. 61 potential sites identified; usable data obtained from 21 sites. Unclear how each site selected cases to report on. One site used test only for complex cases. **Exclusion Criteria** Not reported **Number participants included (analysed)** 1098 cases - this consists of 549 (10-30 cases per site) before QbTest implementation and 549 (10-30 cases) after test implementation, from each of the 21 included sites. **Age** 6-18 years **PROGRESS Plus criteria reported by study** None reported	**Group 1 (pre-test implementation):** Standard ADHD assessment (n=549) **Group 2 (post-test implementation):** QbTest (6-12) or QbTest (12-60) + standard ADHD assessment (n=549) **Subgroups**: CAMHS vs Paediatric sites Also report stratified data based on number of cases referred per site, and large vs small test volume – stratified data not extracted for these **Confounding factors**: QbTest implementation occurred from April 2019 to March 2022 and so overlaps with COVID-19 pandemic (from March 2020)

Table 50 Results data on process measures from implementation studies that contributed to objective 1

Study	Outcome	Details	**Group 1:** Standard ADHD assessment (pre-implementation)		**Group 2:** QbTest (6-12) or QbTest (12-60) + Standard ADHD assessment (post-implementation)		**Effect measure – estimate (95% CI)**	**p-value**	**Other reported details**
			n	**No. Events**	**n**	**No. Events**			
Hall (2016)[87]	Number of consultations to ADHD diagnosis	Number of consultations until ADHD diagnosis (mean, min, max)	40	Mean 3.05 (min 1, max 7)	40	Mean 2.18 (min 1; max 4)	Poisson regression incidence rate ratio (95% CI) 0.71 (0.54, 0.94)	P = 0.02	
	Reasons for delay in diagnosis	Clinician-reported reasons for delay in diagnosis, in those where =>5 consultations were needed to make a diagnosis (all in pre-QbTest group)	For 4/6 (66.6%) of cases, inconclusive or discrepancy outcomes from clinical rating scales were cited as the primary reason for delay, one case (17.0%) cited complex comorbidities and one (17.0%) clinician reluctance to make a diagnosis.)		-	-	-	-	
	Consultation cost	Total cost spent on ADHD assessment for all 40 cases combined	40	£13,176	40	£10,636	Saving = £2,540	-	Cost of a consultation within the Trust at the time of audit = £108.00. A single QbTest cost the Trust £31.00 (cost of the test as a proportion of the lease fee, and a 30 min nurse-led

Study	Outcome	Details	**Group 1:** Standard ADHD assessment (pre-implementation)		**Group 2:** QbTest (6-12) or QbTest (12-60) + Standard ADHD assessment (post-implementation)		**Effect measure – estimate (95% CI)**	**p-value**	**Other reported details**
			n	**No. Events**	**n**	**No. Events**			
									appointment to conduct the test).
Vogt (2011)[88]	Diagnoses revised to ADHD+ in those with a diagnosis rejected at initial assessment at 1-year follow-up	-	19	7	19	0	-	p=0.0035	
	Outcomes of those with ADHD at 1 year follow-up	ADHD diagnosis changed	27	1	43	1	-	p=0.24	
		Continuing on medication		13		28			
		Discontinued medication		9		9			
		Medication trial		22		38			
		Lost to follow-up		3		4			
Sharma (2022)[66]	Number of contacts to diagnosis	**All participants**	20	Mean 2.7 (SD 0.7)	20	Mean 2.4 (SD 0.8)	-	p>0.05	-
	Number of months to diagnosis	All participants	20	Mean 6.5 (SD 3)	20	Mean 5.5 (SD 1.8)	-	p>0.05	-
	ADHD confirmed diagnosis rate	All participants	20	90.6%	20	87.5%	-	p>0.05	-
	Number of months to diagnosis	ADHD cases (those referred for ADHD)	NR	NR	NR	Mean 5.6 (SD 1.7)	-	-	-

Study	Outcome	Details	**Group 1:** Standard ADHD assessment (pre-implementation)		**Group 2:** QbTest (6-12) or QbTest (12-60) + Standard ADHD assessment (post-implementation)		**Effect measure – estimate (95% CI)**	**p-value**	**Other reported details**
			n	**No. Events**	**n**	**No. Events**			
	Number of months to diagnosis	Complex cases (those originally referred for non-specific behavioural difficulties or ASD)	NR	NR	NR	Mean 5.5 (SD 2.7)	-	-	-
Humphreys (2018)[71]	Number of appointments to diagnostic decision	-	60-90	Range of 3-8 appts	60-90	Reduction compared to control of between (on average) 0.24 and 1.04 appts per child. In two trusts, a diagnosis was often reached at the first contact with paediatrician.	-	-	-
	Number of days to diagnostic decision	-	60-90	Average ranged from 161-453 (approx. 5-15 months)	60-90	Average ranged from 15-252 (approx. 2w-8.5 months)	-	-	The authors note for this outcome that the post-implementation group is after introduction of the QbTest AND pathway re-design in two sites.
	Number of days from assessment to commencing medications	-	60-90	Range 42-179 days	60-90	Range 15-96 days			

Study	Outcome	Details	Group 1: Standard ADHD assessment (pre-implementation)		Group 2: QbTest (6-12) or QbTest (12-60) + Standard ADHD assessment (post-implementation)		Effect measure – estimate (95% CI)	p-value	Other reported details
			n	No. Events	n	No. Events			
	Release of clinical time required to reach a diagnostic decision	-				Range 20% to 33% reduction			
McKenzie (2022)[31]	Number of clinical appointments	**All sites**	549	Mean 3.22 (range 1-50)	549	Mean 2.85 (Range 1-32)	Percent change: 11.5% decrease	NR	Data in this study likely affected by COVID-19 for all Group 2 data and comparison between groups 2 and 1
	Number of days from initial referral to diagnosis	**All sites**	549	Mean 452 (Range 15-3276)	549	Mean 507 (Range 43-1281)	Percent change: 12.2% increase	p<0.01	
	Number of days to reach diagnostic decision	**All sites**	549	Mean 117 (Range 0-1570)	549	Mean 129 (Range 0-1378)	Percent change: 10.3% increase	NR	
	Number of school observations utilised		549	120	549	49	Percent change: 17% decrease		
	Number of ADHD diagnoses		549	445	549	418	Percent change: 5% decrease		
	Number of clinical appointments	**CAMHS services**	326	Mean 4.13 (Range 1-50)	326	Mean 3.75 (Range 1-32)	Percent change: 9.2% decrease		

Study	Outcome	Details	**Group 1:** Standard ADHD assessment (pre-implementation)		**Group 2:** QbTest (6-12) or QbTest (12-60) + Standard ADHD assessment (post-implementation)		**Effect measure – estimate (95% CI)**	**p-value**	**Other reported details**
			n	**No. Events**	**n**	**No. Events**			
	Number of days from initial referral to diagnosis	**CAMHS services**	326	Mean 442 (Range 18-1161)	326	Mean 566 (Range 43-1821)	Percent change: 28.1% increase		
	Number of days to reach diagnostic decision	**CAMHS services**	326	Mean 119 (Range 0-888)	326	Mean 135 (Range 0-1378)	Percent change: 13.4% increase		
	Number of clinical appointments	**Paediatric clinics**	194	Mean 2.01 (Range 1-15)	194	Mean 1.63 (Range 1-4)	Percent change: 18.9% decrease		
	Number of days from initial referral to diagnosis	**Paediatric clinics**	194	Mean 444 (Range 15-3276)	194	Mean 367 (Range 1494)	Percent change: 17.3% decrease		
	Number of days to reach diagnostic decision	**Paediatric clinics**	194	Mean 130 (Range 0-1570)	194	Mean 138 (Range 0-1036)	Percent change: 6.2% decrease		

Table 51 ROBINS-I Risk of bias of implementation studies that contribute process measure data for objective 1

Study Details	Domain*								Rationale
	1	2	3	4	5	6	7	Overall	
Hall(2016)[87]	☹	☺	☺	☺	😐	😐	😐	☹	Confounders not controlled for and potential for confounding of the effect of the intervention; only people who had final diagnosis within timeframe selected; outcome measure could have been influenced by knowledge of intervention received; no protocol. Note: selection of participants was random, hence exclusion of participants was covered under the missing data domain.
Sharma(2022)[66]	?	☹	☺	?	☺	😐	😐	☹	Conference abstract with no information about whether confounders were controlled for, or about bias due to deviations from intended interventions; participants excluded if assessment inconclusive or did not receive diagnosis in timeframe; outcome measure could have been influenced by knowledge of intervention received; no protocol.
Humphreys(2018)[71]	☹	?	☺	😐	?	😐	😐	☹	Confounders not controlled for and potential for confounding of the effect of the intervention; no information about participant selection; potential for bias due to deviations from intended interventions due to two sites having a pathway redesign after introduction of QbTest; no information about missing data (authors confirmed not only ADHD+ cases selected); outcome measure could have been influenced by knowledge of intervention received; no protocol.
McKenzie(2022)[31]	☹	?	☺	☺	☺	😐	😐	☹	Confounders not controlled for and potential for confounding of the effect of the intervention (COVID-19 only confounder mentioned which the authors say would have impacted on the analysis); little information on participant selection; outcome measure could have been influenced by knowledge of intervention received; no protocol.
Vogt(2011)[88]	☹	?	☺	☺	☺	😐	😐	☹	Confounders not controlled for and potential for confounding of the effect of the intervention; no information about participant selection; outcome measure could have been influenced by knowledge of intervention received; no protocol.

*1: Confounding (potential confounders for all studies: Age at the point of seeking referral for ADHD; Sex; Comorbidities - e.g. Autism, anxiety; Nature and severity of symptoms at presentation – e.g. predominantly inattentive or hyperactive; Socioeconomic status; Ethnicity and for McKenzie (2022) also COVID-19 pandemic); 2: Selection of participants; 3: Classification of interventions; 4: Deviations from intended interventions; 5: Missing data; 6: Measurement of the outcome; 7: Selection of the reported result.
Note: Sad face= serious risk of bias; smiling face= low risk of bias, question mark= no information.

Table 52 Results data on process measures for DTA studies that contribute data for objective 1

Study details	Number patients with unavailable test result (%)	Details of missing results	Action taken post-test failure
Ulberstadt (2020)[79] Test: QbCheck	7/ 149 (5%)	Seven participants failed to complete the test. Two had technical problems with camera; four ended the test in the middle of the session for unknown reasons; one intentionally did not follow through the test. Six of the non-completers belonged to the ADHD group; one belonged to the healthy controls group.	Not reported - the participants were excluded from analyses
Bijlenga (2019)[80] QbTest (12-60)	25/ 234 (11%)	Two female ADHD patients (aged 63 and 73) did not perform QbTest because they did not understand the task. Twenty-three participants (seven ADHD; 16 healthy controls) were invalid due to being extreme outliers, not following instructions, technical errors, aborted test (data not stratified by reasons given).	
Groom (2016)[82] QbTest (12-60)	4/ 84 (5%)	Non-completion of the test by three people in the ADHD group. Failure to complete QbTest by one person in ASD group (no further information).	
Seesjarvi (2022)[77] Group 1: EPELI	22/ 115 (19%)	Five children with ADHD and 17 controls had technical failures or human error (scenarios accidentally presented in different order). (Data not stratified by reason given)	

Table 53 Baseline data for studies that reported on patient/ clinician carer views of sensor CPTs for ADHD diagnosis

Study Details	Study component	Participants and methodology
Author (Year) Chitsabesan (2022)[74, 110] **Study Name** FACT **Country** England **Language** English **Setting** Young Offenders Institution (YOI) **Study design** Interview and survey components of FACT feasibility RCT **Funding** Non-industry **Sensor CPT** QbTest + standard assessment	Interviews with young people	**Participants:** 6 adolescent boys in a YOI who participated in the FACT trial in the QbTest group. **Sampling strategy:** Purposive sampling used to select people considering age, completion of QbTest and scores on the "Qb Opinion Questionnaire". Unclear how many people were invited to participate in the interviews. **Data collection:** Semi-structured interviews completed 3 months into the FACT trial, about acceptability of QbTest. At the time of interview, not all people had received the result of the test/ ADHD assessment. **Analysis:** Thematic analysis, using inductive approach.
	Interviews with staff from the YOI and the research assistant	**Participants:** 1 research assistant and 5 staff members from the YOI who used QbTest in the FACT trial. **Sampling strategy:** All staff and the one researcher who used the QbTest in the trial were invited to participate. **Data collection:** Semi-structured interviews completed at the end of the FACT trial, about the acceptability and feasibility of administering and implementing QbTest within usual practice, barriers and facilitators to use, and reasons for non-completion. **Analysis:** Thematic analysis, using inductive approach.
	Survey to young people	**Participants:** 10 adolescent boys in a YOI who participated in the FACT trial in the QbTest group. **Sampling strategy:** All 20 young people who completed QbTest in FACT trial invited to complete survey; 10 responded. **Data collection:** "Qb Opinion Questionnaire" completed at 3 months. The survey contains 12 items e.g. "the QbTest results were difficult to understand" and the young person rates each item on a 5-point scale. **Analysis:** Descriptive analysis

Study Details	Study component	Participants and methodology
Author (Year) Hall (2017)[109] **Study Name** AQUA trial **Country** England **Language** English **Setting** Secondary care/ community: 10 child and adolescent mental health services (CAMHS) or community paediatric clinics **Study design** Qualitative sub-study of AQUA trial **Funding** Non-industry	Interviews with clinicians	**Participants:** 10 clinician leads (20% male) from each of the 10 sites involved in the AQUA trial. **Sampling strategy:** The clinical lead for the AQUA trial at each of the 10 sites was invited to interview (all accepted). **Data collection:** Semi-structured interviews conducted by a trained researcher regarding opinions of QbTest. **Analysis:** Thematic analysis, using an inductive, reflexive approach.
	Interviews with families	**Participants:** 20 families from the AQUA trial (the main care-giver was the primary interviewee but where possible the young person was encouraged to participate with their parent – all young people had been in the "QbOpen" group). Sample characteristics: • Child mean age 10.7 years (SD 2.9; Range 9-18). • 75% male • Confirmed primary diagnosis - ADHD 55%; not ADHD 25%, unconfirmed 25%. Comorbidities – ASD 5%; Conduct Disorder and Oppositional Defiance Disorder 0%; Tourette's/Tics 5%; Attachment Disorder 0%; Learning Difficulties 0%; Anxiety and Depression 0%. **Sampling strategy:** Two families per site who had participated in the AQUA trial "QbOpen" group were invited to interview. Thirty-eight families were invited to interview and 18 declined to participate. Refusing families were replaced with the next family until two families from each site were enrolled. **Data collection:** Semi-structured interviews conducted by a trained researcher regarding opinions of QbTest. **Analysis:** Thematic analysis using an inductive, reflexive approach.

Study Details	Study component	Participants and methodology
Sensor CPT Usual care + QbTest (6-12 and 12-60), with test results available to clinician ("QbOpen")	Survey to clinicians and families	**Participants:** 10 clinician leads (20% male) from each site in the AQUA trial, and 76 families from the AQUA trial. The following details were reported for the families only: • Child mean age 10.2 years (SD 2.9; Range 7-18). • 79% male • Confirmed primary diagnosis - ADHD 46%; not ADHD 14%, unconfirmed 39%. Comorbidities – ASD 5%; Conduct Disorder and Oppositional Defiance Disorder 4%; Tourette's/Tics 1%; Attachment Disorder 1%; Learning Difficulties 3%; Anxiety and Depression 1%. **Sampling strategy:** All participants and the 10 lead clinicians from the trial invited to participate; 10 clinicians and 76 families responded. **Data collection:** Quantitative online survey. Clinician questions centred on how best to administer QbTest, understanding results and communicating with families. Family questions focused on utility of QbTest in understanding symptoms and decisions, and experience of completing test. **Analysis:** Descriptive analysis.
Author (Year) McKenzie (2022)[31] **Study Name** Focus ADHD **Study Location** England (sites throughout the country) **Language** English	Interviews with healthcare staff	**Participants:** 21 healthcare staff involved in implementation of QbTest at their site, or conducting the test/ interpreting test results, in the Focus ADHD study. **Sampling strategy:** All sites were invited to participate - they aimed to include participants with different roles in the test implementation process, including those who delivered the test, interpreted the test and managers who were responsible for implementing the test at their site. **Data collection:** Semi-structured interviews conducted to explore experience of using test, adoption of test at their site and sustainability of its use. **Analysis:** Thematic analysis, analysed using the non-adoption, abandonment, scale-up, spread, sustainability (NASS) framework.

Study Details	Study component	Participants and methodology
Setting CAMHS and paediatric sites **Study design** Qualitative interview and survey components of an uncontrolled before-after implementation study **Funding** Industry and non-industry: QbTech and Academic Health Science Networks in England **Sensor CPT** QbTest (6-12) or QbTest (12-60) + standard ADHD assessment	Survey for healthcare professionals (HCPs)	**Participants:** 65 HCPs who attended audit training in the Focus ADHD study. **Sampling strategy:** All HCPs who attended audit training in the Focus ADHD study invited (n=unknown), 65 responded. **Data collection:** Online survey about how best to administer the QbTest, understanding the results and communicating with families. **Analysis:** Descriptive analysis.
	Survey for patients and their families	**Participants:** 22 patients who had been assessed with QbTest (and their parents) in the Focus ADHD study. **Sampling strategy:** Survey distributed to all patient families via text/ email and clinicians/ key stakeholders asked to pass it on (n=unknown). 22 patients/ families responded. **Data collection:** Online survey about the utility of the QbTest in understanding symptoms and diagnostic decisions and the experience of completing the test. **Analysis:** Descriptive analysis.
Author (Year) Pellegrini (2020)[89] **Study Name** Not reported **Study Location** Ireland **Language** English	Focus groups with clinicians	**Participants**: 19 clinicians who were working in one of the three CAMHS teams selected for this research in Ireland, and who were involved in using the Qbtest as part of an ADHD assessment process. Professional disciplines included: administration, occupational therapy, nurses, psychology, psychiatry, social work and speech and language therapy. **Sampling strategy:** All clinicians in the study who were using QbTest were invited (n=unknown). **Data collection:** Three semi-structured focus groups were conducted (n=6; n=6; n=7), gathering information on their experiences with the QbTest. **Analysis:** Thematic analysis, using a six-step, reflexive process.

Study Details	Study component	Participants and methodology
Setting Irish Child and Adolescent Mental Health Services (CAMHS) – 3 CAMHS teams **Study design** Mixed methods study of real-world impact of test implementation **Funding** Not funded **Sensor CPT** QbTest + standard ADHD assessment	Survey to clinicians, service users and their families	**Participants:** 50 participants: 17 clinicians who had used QbTest in one of the three CAMHS involved in the study, 15 young people who had completed QbTest as part of ADHD assessment in one of the three CAMHS teams involved in the study, and their parent/guardians (n=18). **Sampling strategy:** Young people and their parents/guardians were recruited during ADHD assessment – the clinician made the family aware of the survey study. Clinicians were sent the survey via email by research staff. Number of people invited to participate not reported. **Data collection:** Quantitative survey on experience of using QbTest. The survey was based on a template provided by QbTech that had been used in the AQUA qualitative sub-study.[109] **Analysis:** Descriptive analysis.
Author (Year) Humphreys (2018)[71] **Study Name** Not reported **Study Location** East Midlands, UK **Language**	Survey to patients and families	**Participants:** 48 patients (children who had ADHD assessment using QbTest in CAMHS in the before-after study) and their families **Sampling strategy:** Surveys were distributed by clinic staff as paper version - 90 questionnaires distributed, 43% response rate (48 respondents). **Data collection:** Survey on their experience of using QbTest (the same survey used in the AQUA trial.[109]) **Analysis:** Descriptive analysis.

Study Details	Study component	Participants and methodology
English **Setting** Community paediatric mental health settings in 3 NHS Trusts **Study design** Survey component of an uncontrolled before-after implementation study **Funding** Industry and non-industry: QbTech and East Midlands Academic Health Science Network **Sensor CPT** QbTest (6-12) or QbTest (12-60) + standard ADHD assessment	Survey to staff	**Participants:** Staff who had used QbTest (n= unknown) **Sampling strategy:** Sampling strategy not reported. Number distributed not reported, 76% response rate. **Data collection:** Survey on their experience of using QbTest (the same survey used in the AQUA trial.[109]) **Analysis:** Descriptive analysis.
Author (Year) Peili Vision (NR)[90] **Study Name** Health Service Pilot **Study Location** Finland	Survey to teachers	**Participants:** 21 teachers of participating schools that used EFsim for students in the Health Service Pilot **Sampling strategy:** Not reported. Number of teachers invited to participate unknown. **Data collection:** Feedback questionnaire for evaluating the main aspects of how they felt the EFSim check went, containing 10 questions. Scores given on a scale of 1 to 5. **Analysis:** Descriptive analysis

Study Details	Study component	Participants and methodology
Language English **Setting** 18 schools in Finland **Study design** Pilot cohort study **Funding** Industry – test manufacturer (Peili Vision) **Sensor CPT** EFSim test + psychologist evaluation	[redacted]	[redacted]

Study Details	Study component	Participants and methodology
Author (Year) Ulberstadt (2020)[79] **Study Name** Not reported **Study Location** Germany, Sweden, USA **Language** English **Setting** Secondary care **Study design** Survey data from two-gate DTA study **Funding** Industry - authors employed by QbTech **Sensor CPT** QbCheck	Survey to patients	**Participants:** Patients who used QbCheck in the DTA study and who completed the survey (n=125; 59 ADHD and 69 healthy controls) **Sampling strategy:** All patients (142) from DTA study given survey, 125 completed it. **Data collection:** Survey about experience of using QbCheck – three questions assessed on a scale from 0 to 10 that assessed the usability of the test; one yes/no question about problems with using the test. **Analysis:** T tests (the dimensional variables) or chi-square test (the categorical variable) to compare the group with ADHD to the controls.

Study Details	Study component	Participants and methodology
Author (Year) Seesjarvi (2022)[77] **Study Name** Not reported **Study Location** Finland **Language** English **Setting** Secondary care **Study design** Survey data from two-gate DTA study **Funding** Non-industry (but authors developed test) **Sensor CPT** EPELI	Survey to patients	**Participants:** Children (some with ADHD; some healthy controls – n=not reported) who took part in the DTA study using EPELI test and completed the survey component **Sampling strategy:** Not reported. **Data collection:** Survey about use of EPELI test- shortened version of the Presence Questionnaire 3.0. **Analysis:** Descriptive analysis

Table 54 CASP checklist quality assessment of studies included for objective 1 that reported qualitative data on patient/ clinician carer views of sensor CPTs for ADHD diagnosis

CASP Checklist Questions	Quality assessment answers per study (answer options: yes, no, can't tell)			
	Chitsabesan (2022)[74]	Hall(2017)[109]	McKenzie (2022)[31]	Pellegrini (2020)[89]
Was there a clear statement of the aims of the research?	Yes	Yes	Yes	Yes
Is a qualitative methodology appropriate?	Yes	Yes	Yes	Yes
Was the research design appropriate to address the aims of the research?	Yes	Yes	Yes	Yes
Was the recruitment strategy appropriate to the aims of the research?	Yes	Yes	Yes	Yes
Was the data collected in a way that addressed the research issue?	Yes	Yes	Yes	Yes
Has the relationship between researcher and participants been adequately considered?	Can't tell	Yes	Can't tell	Yes
Have ethical issues been taken into consideration?	Yes	Yes	Yes	Yes
Was the data analysis sufficiently rigorous?	Can't tell	Yes	Can't tell	Yes
Is there a clear statement of findings?	Yes	Yes	Yes	Yes

Table 55 Quality assessment of studies included for objective 1 that reported survey data on patient/ clinician carer views of sensor CPTs for ADHD diagnosis

Questions (n=20)	Quality assessment answers per study (answer options: yes, no, not stated clearly)							
	Chitsabesan (2022)[74]	Hollis (2018)[109]	McKenzie (2022)[31]	Pellegrini (2020)[89]	Humphreys (2018)[71]	Peili Vision (NR)[90]	Ulberstadt (2020)[79]	Seesjarvi (2022)[174]
Was the problem or phenomenon under investigation defined, described, and justified?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the population under investigation defined, described, and justified?	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Were specific research questions and/or hypotheses stated?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were operational definitions of all study variables provided?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were participant inclusion criteria stated?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the participant recruitment strategy described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
Was a justification/ rationale for the sample size provided?	No	No	No	No	No	No	No	No
Was the attrition rate provided? (applies to cross-sectional and prospective studies)	Yes	Yes	Yes	Yes	No	No	Yes	No
Was a method of treating attrition provided? (applies to cross-sectional and prospective studies)	No	Yes	No	No	No	No	No	No
Were the data analysis techniques justified (i.e., was the link between hypotheses/ aims / research questions and data analyses explained)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Questions (n=20)	Quality assessment answers per study (answer options: yes, no, not stated clearly)							
	Chitsabesan (2022)[74]	**Hollis (2018)[109]**	**McKenzie (2022)[31]**	**Pellegrini (2020)[89]**	**Humphreys (2018)[71]**	**Peili Vision (NR)[90]**	**Ulberstadt (2020)[79]**	**Seesjarvi (2022)[174]**
Were the measures provided in the report (or in a supplement) in full?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was evidence provided for the validity of all the measures (or instrument) used?	No	No	No	No	No	No	No	No
Was information provided about the person(s) who collected the data (e.g., training, expertise, other demographic characteristics)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was information provided about the context (e.g., place) of data collection?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was information provided about the duration (or start and end date) of data collection?	No	Yes	No	No	No	No	No	No
Was the study sample described in terms of key demographic characteristics?	No	Yes	No	No	No	No	No	No
Was discussion of findings confined to the population from which the sample was drawn?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were participants asked to provide (informed) consent or assent?	Yes	Yes	Yes	Yes	Not stated clearly	Not stated clearly	Not stated clearly	Not stated clearly
Were participants debriefed at the end of data collection?	Not stated clearly	Not stated clearly	Not stated clearly	Yes	Not stated clearly	Not stated clearly	Not stated clearly	Not stated clearly
Were funding sources or conflicts of interest disclosed?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Table 56 Baseline Details for RCT included for objective 3

Study Details	Participants	Group 1	Control
Author (Year) Williams (2021)[111] **Study Name** QUOTA **Country** England **Language** English **Setting** Secondary care/ community: 5 CAMHS or community paediatric clinics **Study design** Parallel group, single-blind, feasibility multi-site RCT with embedded qualitative evaluation **Funding** Non-industry	**Population** ADHD medication management for people aged 6-15 **Inclusion Criteria** 6-17 years; referred to CAMHS/ community paediatric; clinical ADHD diagnosis; about to commence ADHD medication (methylphenidate/ lisdexamfetamine) **Exclusion Criteria** Non-fluent English; unable to provide written consent; suspected severe learning disability. **Number participants included (analysed)** 44 (44) **Age** Mean (SD): QbTest: 9.29 (2.81); Control: 9.22 (2.19). Full sample range: 6-15 years. **PROGRESS Plus criteria reported by study** • **Sex (% male): QbTest -** 95.24%. **Control -** 82.61% • **Ethnicity: QbTest -** White 76.19%; Bangladeshi 4.76%; Dual heritage 4.76%; Not given 4.76%; Other 4.76%; Pakistani 4.76%. **Control -** White 91.30%; Bangladeshi 0%; Dual heritage 0%; Not given 0%; Other 4.35%; Pakistani 4.35%; • **Neuro-developmental: QbTest** – ASD/ social communication/ speech/ speech difficulties 14.28%; Attachment disorder 0%; Conduct disorder 0%; Tic and neurological disorders 9.52%; Mood disorders 4.76%. **Control -** ASD/ social communication/ speech/ speech difficulties 21.75%; Attachment disorder; 4.35% Conduct disorder 8.70%; Tic and neurological disorders 0%; Mood disorders 0%.	**QbTest + treatment as usual (n=21):** Treatment as usual, in addition to QbTest completed at baseline, 2-4 weeks later (follow-up 1) and 8-12 weeks later (follow-up 2). At each time point, the clinician reviewed QbTest results with other clinical tools to monitor medication. Treatment as usual varied between sites. Participants received their site's standard usual care, but all sites were asked to contact participant twice by the end of the 12 weeks (to ensure level of contact consistent between groups).	**Treatment as usual (n=23):** Treatment as usual was as listed for Group 1 (usual care, without QbTest).

Table 57 Results from RCT included for objective 3

Table reports number of participants and no. of events in each group, unless stated otherwise.

Study	Comparison	Outcome	Details	Group 1		Group 2	
				n	No. Events	n	No. Events
Williams (2021)[111]	QbTest + treatment as usual vs. treatment as usual	Use of interventions e.g. ADHD medication	Change to type or dose of ADHD medication at follow-up 1 (2-4 weeks)	18	10	21	7
			Change to type or dose of ADHD medication at follow-up 2 (8-12 weeks)	17	7	19	9
			Medication adherence at follow-up 1: taken medication most/every day	8	8	9	8
			Medication adherence at follow-up 2: taken medication most/every day	8	7	9	9

Table 58 Results from qualitative sub-study of RCT included for objective 3

Study details	Outcome	Details	Results
Williams (2021)[111]	Impact on clinical decision making	Clinician-completed proforma (n=33) in the intervention arm (QbTest + treatment as usual)	• Across both follow-ups, 73% (24/33 responses) of clinicians reported that the QbTest was useful in determining treatment. 18% (6) were neutral, and 9% (3) stated it was not helpful. • More clinicians found the QbTest helpful at follow-up 1 (76.5%; 13/17), than follow-up 2 (68.8%; 11/16).
	Ease of use/acceptability - patients/carers	Interviews with the parents of eight children who took part in the trial (6 intervention; 2 control), about using the QbTest to monitor medication	• Needing to have multiple appointments for the QbTest means time out of school. Appointments before/after school or in the school holidays would be preferable but ultimately attending the appointments was considered beneficial. • QbTest was described by parents as increasing their confidence in the child's treatment. • Parents considered repeated QbTests useful in increasing confidence in ongoing medication decisions as well as a tool the clinicians used to communicate changes in ADHD symptoms. • Parents said the QbTest was not considered burdensome to children and young people, but some found it "boring". • QbTest has potential to aid communication – parents described how a visual representation of the child's symptoms helped them to better understand treatment impact.
	Ease of use/acceptability - clinicians	Interviews with five clinicians (from 4 of 5 clinic sites) from the trial, about using the QbTest to monitor medication. Four community paediatricians and one psychiatrist (all female).	• Objectivity of the QbTest appreciated by clinicians in comparison to informant measures traditionally used to monitor medication. • Clinic appointments often occur during working hours which has implications for children and their families. Running multiple QbTest appointments could increase these problems and it may be burdensome for children and young people. • Preference to only run multiple QbTests when it was perceived to add value. It was described as one of a suite of tools to monitor ADHD symptoms and clinicians felt the additional resources needed to carry out QbTests (staffing, clinic time, test interpretation) are not necessary in routine cases, but may be of use in trickier/ complex cases. • QbTest has potential to aid communication, helps parents to better understand treatment impact and give extra weight to clinician advice during consultations. Clinicians note this appears to help parents to be more accepting of treatment recommendations.
	Confidence of HCP in assessment		• QbTest was described by clinicians (and parents) as increasing their confidence in the child's treatment.

Table 59 Baseline Details for DTA study included for objective 3

Study Details	Setting and Population	Index test	Reference standard
Tallberg (2019)[68] **Design** One-gate **Country** Sweden **Funding** Non-industry	**Setting:** Secondary care **Population:** Children (age 9-14 years) **Inclusion criteria:** Children with ADHD from a Child and Adolescent Psychiatry clinic in southern Sweden (n=186) **Exclusion criteria:** None reported **Numbers:** 186 (56)	**Sensor CPT** QbTest (6-12)	**Reference standard** QbTest (6-12) + SNAP-IV

Table 60 Results for DTA study included for objective 3

Study Details	Index Test	Measure & *Subgroup*	Threshold	Ref stand	TP	FP	FN	TN	Sens	Spec	AUC (95% CI)
Tallberg(2019)[68]	QbTest (6-12)	QBInattention	Unsure	Unsure	41	4	9	6	0.82	0.60	NR
		QBActivity	Unsure	Unsure	38	6	12	4	0.76	0.40	NR

Table 61 Detailed QUADAS-2 assessment showing judgements and rational for risk of bias and concerns regarding applicability for DTA study included for objective 3

Study details	Risk of bias																Concerns regarding applicability				
	Consecutive/ random	Case-control avoided	No inappropriate excl	Patient selection bias	Index test blinded	Pre-specified	Index test bias	Ref stand appropriate	Blinded ref stand	Ref stand bias	Time interval	All received ref stan	Same ref stand	All included in analysis	Patient flow bias	Overall bias	Rationale Bias	Patient applicability	Ref stand applicability	Index applicability	Overall Applicability	Rationale
Talberg – dose titration	✗	✓	✓	☺	☺	✓	?	✗	✗	☹	✓	✓	✓	✗	☹	☹	Index test formed part of reference standard (improvement on SNAP-IV or decrease on QbTest). High proportion of drop-outs (130/186)	☺	☺	?	☹	Limited details on test conduct & interpretation

Table 62 CASP checklist quality assessment of study included for objective 3 and not objective 1 that reported qualitative data on patient/ clinician carer views of sensor CPTs for ADHD medication management/ titration

Study details: Williams (2021)[111]		
Question	**Answer (yes/ can't tell/ no)**	**Comments**
Was there a clear statement of the aims of the research?	Yes	Aims of the interviews are listed in the measures section as not the main aim of the feasibility trial
Is a qualitative methodology appropriate?	Yes	
Was the research design appropriate to address the aims of the research?	Yes	
Was the recruitment strategy appropriate to the aims of the research?	Yes	All intervention and control participants and clinicians were invited to take part (random subsample- see protocol)
Was the data collected in a way that addressed the research issue?	Yes	
Has the relationship between researcher and participants been adequately considered?	Can't tell	Not stated whether researcher examined own potential bias
Have ethical issues been taken into consideration?	Yes	
Was the data analysis sufficiently rigorous?	Yes	
Is there a clear statement of findings?	Yes	

Table 63 Quality assessment of study included for objective 3 and not objective 1 that reported survey data on patient/ clinician carer views of sensor CPTs for ADHD medication management/ titration

Questions	Williams (2021)[111]
Was the problem or phenomenon under investigation defined, described, and justified?	Yes
Was the population under investigation defined, described, and justified?	Yes
Were specific research questions and/or hypotheses stated?	Yes
Were operational definitions of all study variables provided?	Yes
Were participant inclusion criteria stated?	Yes
Was the participant recruitment strategy described?	Yes
Was a justification/ rationale for the sample size provided?	No
Was the attrition rate provided? (applies to cross-sectional and prospective studies)	Yes
Was a method of treating attrition provided? (applies to cross-sectional and prospective studies)	Yes
Were the data analysis techniques justified (i.e., was the link between hypotheses/ aims / research questions and data analyses explained)?	Yes
Were the measures provided in the report (or in a supplement) in full?	No
Was evidence provided for the validity of all the measures (or instrument) used?	No
Was information provided about the person(s) who collected the data (e.g., training, expertise, other demographic characteristics)?	Yes
Was information provided about the context (e.g., place) of data collection?	Yes
Was information provided about the duration (or start and end date) of data collection?	No
Was the study sample described in terms of key demographic characteristics?	Yes
Was discussion of findings confined to the population from which the sample was drawn?	Yes
Were participants asked to provide (informed) consent or assent?	Yes
Were participants debriefed at the end of data collection?	Can’t tell
Were funding sources or conflicts of interest disclosed?	Yes

Appendix 4

Synthesis of studies that reported on patient/ clinician carer views of sensor CPTs for ADHD diagnosis

Views around the helpfulness of the QbTest

Conceptual categories we identified regarding views around the helpfulness of the QbTest included contribution to ADHD diagnosis, communication with caregivers, and understanding of subjective experience.

Contribution to ADHD diagnosis

Findings from qualitative data

Clinicians interviewed in the qualitative sub-study of the AQUA trial reported that use of the QbTest led them to feel more confident in their diagnostic decision making.[109]

"I would move to the diagnosis more confidently and more quickly having evidence that something was wrong, you know objective evidence. …reduced the amount of the anxiety of uncertainty" - Healthcare professional on the use of QbTest[109]

Increased confidence in the diagnostic decision was also reported in interviews with healthcare staff in the Focus ADHD study, who commented that the increased confidence was derived from the fact that the data provided by the test is objective, rather than scales and surveys that give subjective data.[31] Focus groups with clinicians in CAMHS also revealed that the QbTest gave them increased confidence in their decisions.[89]

"I think it gives all clinicians a bit more confidence around making diagnosis, and I think for nurses, that's where its particularly helpful. Especially if they're nurse prescribers, because they have that responsibility of making the diagnosis and providing medication. So, they want it to be… they want to feel very, very sure that this is ADHD, that nothing is being missed." – Healthcare professional on using QbTest[31]

Despite the suggestion from studies that the QbTest could contribute positively to the ADHD diagnostic process, clinicians reported in focus groups that there is a need to establish where the QbTest falls on the ADHD assessment pathway.[89] Staff interviewed in the Focus ADHD study felt that the QbTest should be implemented early in the assessment pathway, and when this was done, the clinicians felt they had a clearer understanding of whether the young person had a profile indicative of ADHD.[31] In line with this, most clinicians and families interviewed in the AQUA sub-study felt that the QbTest should be conducted before the initial appointment with clinician. One family suggested doing QbTest in GP surgery as initial screen and clinicians were supportive of this. Whilst, some clinicians suggested using it only for complex cases.[109]

"I would then also even put a QbTest in as a precursor to the initial consultation so that at the time you see the child, they've had all the relevant questionnaires completed from home and school and a QbTest and you could probably make a diagnosis on the first appointment" - Healthcare professional on the use of QbTest[109]

Some clinicians and families interviewed in the AQUA sub-study questioned the validity of the clinical setting of the test and wondered if it is not representative of what happens e.g. in school.

"He behaves differently at home and school to what he would do in a clinical office sort of thing… And of course for that twenty minutes that he was seen he was on his best behaviour" – Healthcare professional on the use of QbTest[109]

Findings from quantitative data

Some respondents to the patient/ carer survey in the Focus ADHD study said that they think the QbTest should have been offered sooner.[31]

Diagnosis in complex cases

Findings from qualitative data

Interview findings from two studies suggested that the QbTest can be helpful in the diagnosis of individuals with comorbidities.[74, 109] Clinicians interviewed in the AQUA trial sub-study reported that the tests helped to discriminate ADHD from Autism Spectrum Disorder (ASD), anxiety, depression, and learning difficulties. Clinicians with more prior experience of using the QbTest were more positive in its abilities to help in the diagnosis of cases with co-morbidities than those with less experience.[175] In the FACT RCT, one staff member interviewed also said that the QbTest was helpful in the assessment of young people where there might be concerns about co-morbid diagnosis.[74]

"I very often use it for children that I suspect have got ASD comorbidity. I think it's very clear that there's a group of children with just pure ADHD who do a QbTest in one way, and then the group that's got some degree of autism or autistic traits do it very differently, and I think that's really helpful"- Healthcare professional on the use of QbTest[109]

In the Focus ADHD study, interviews with staff also found that the QbTest can be helpful in cases where there is contradictory information between home and school settings, or cases where the young person has limited corroborating information due to being home schooled or a 'looked after child'.[31]

"I think it works well with subtle presentations. Presentations maybe where there's a disagreement between school and home. Cases where there are parental disagreements. Cases where young people themselves are unsure." – Healthcare professional on the use of QbTest[31]

Clinicians interviewed in the AQUA trial sub-study reported that the QbTest was useful in differentiating ADHD subtypes, but there was no consensus as to which symptom domain was particularly valuable. Some clinicians specifically commented on the utility of the attention measure for girls with the inattentive subtype who can be hard to diagnose.[109] This was also highlighted in the Focus ADHD study - healthcare staff commented that the addition of the QbTest into the assessment process helped to identify individuals with subtle presentation of ADHD (e.g. girls or older adolescents) and those who mask their difficulties.[31]

"I think it can be helpful for picking out cases where there might be more subtle presentations, for example in girls or older adolescents." – Healthcare professional on the use of QbTest[31]

Findings from quantitative data

In two studies that surveyed healthcare professionals, there was no consensus as to whether the QbTest should be reserved for use in cases where there is a diagnostic uncertainty.[31, 71] However, in one of the studies,[31] some healthcare professionals did report that the test was most useful in certain patient groups including female patients, older children, cases where the parent or school does not agree with the clinician's decision, and in identifying patients for ASD assessment by being able to rule out ADHD. Survey data from healthcare staff in the Focus ADHD study concurred with the interview findings from this study; healthcare staff reported that the QbTest is useful in those with subtle presentations who mask their symptoms.[176]

Time to diagnostic decision

Findings from qualitative data

Qualitative data (mostly from healthcare professionals) from four studies suggested that the QbTest could be helpful in improving the time to diagnostic decision. Clinicians interviewed in the AQUA sub-study reported that the QbTest may help to reduce delays in diagnosis and treatment onset. They also noted that time and cost savings may be made by replacing the lengthy and difficult to access school observations with the QbTest.[109]

"What we did was because of QbTest results, I then stopped the school observations, so then we could confirm the diagnosis and go ahead with the medication"- Healthcare professional on the use of QbTest[109]

Families interviewed in the AQUA trial commented that there is a need for a quick decision to facilitate treatment initiation, particularly for children who were struggling in education, and to not prolong the emotionally overwhelming process. However, they also emphasized that they did not want the process to be rushed, and their child should not be "labelled" quickly.[109]

"I just wished it were more like I say I was in and out, just wished it were more appointments and a bit more time" - Parent of child who had used QbTest[109]

Staff interviewed in the FACT RCT also felt that the QbTest could help to improve waiting times.[74] Focus groups with 19 clinicians who had used the QbTest in CAMHS highlighted that the QbTest was perceived to have resulted in time savings and felt that it has the potential to streamline and improve the service.[89]

"…so on the ground level it's helping us with our picture of the child, but in the bigger picture of things, if we are dealing more efficiently and more correctly with each child, that's going to make the service more efficient and better for the next child coming in the door, so there's a bigger picture knock on effect happening with a tool like this…" - Healthcare professional on the use of QbTest[89]

These views were shared by some healthcare staff interviewed in the Focus ADHD study, who felt that the addition of the QbTest into the assessment process led to a faster and more efficient process, which in turn reduces cost.[31] Most sites in the Focus ADHD study found that QbTest implementation had resulted in fewer appointments by replacing the school observation, and that the quicker assessment pathway supported the young person in getting educational support quickly. Some sites also reported a reduction in re-referrals from caregivers who disagreed with a non-diagnosis decision.

"I see it as a way of reducing the amount of time children are waiting to be seen. And thus, reducing the number of follow-ups, thus reducing the number of times they have to come back to the hospital so it's an opportunity to save the patients and parents time." - Healthcare professional on the use of QbTest[31]

Findings from quantitative data

Some patients/ carers (n=not reported) surveyed in the Focus ADHD study reported that the QbTest helped to speed up the assessment process and to get a diagnosis.[31]

Communication with caregivers

Findings from qualitative data

Interview findings suggested that the QbTest helped to improve communication between clinicians and patients/ families. Clinicians and families interviewed in the AQUA trial sub-study felt that the output of the QbTest helped them to communicate to families information around diagnosis and medication effect. Specifically, clinicians reported that being able to show a comparison of the child's performance to a normative sample helped them to communicate the diagnostic decision to families, and they thought that this helped families to accept the decision.

"A lot of parents who previously would have probably shouted and screamed at you for not saying their child had ADHD will accept it if the computer is not showing the evidence" – Healthcare professional on using QbTest[109]

Mostly, families in the AQUA sub-study felt that clinicians explained the QbTest reports well and they were easy to understand, however some families felt that it was unclear how the report was being used to inform decision making.[109]

"I don't know if she explained, it felt like the QbTest had said it so that's what we're going with" – Parent of child who had used QbTest[109]

In two other studies, clinicians also felt the QbTest helped to improve communication with young people and their families, through improving clarity,[89] and through providing an objective and visual aspect to use to evidence and justify diagnostic decisions.[31] However, some clinicians in the latter study (Focus ADHD) commented that families could still struggle to accept a diagnostic decision.[31] This study did not interview parents/ carers.

"I think they offer a very visual result for the parents, […] especially the little chart that shows hyperactivity and stillness and the wild swinging round. So, I think that sort of aspect to it is really good to be able to communicate the diagnosis." – Healthcare professional on use of QbTest[31]

Findings also suggested that the implementation of the QbTest can help to improve communication between the clinician and school,[109] between clinical colleagues,[89] and between the person with ADHD and their family[109].

Findings from quantitative data

Survey data suggested that clinicians valued the QbTest for improving communication with the patient/ family. In line with the results from the AQUA sub-study interviews, all 10 clinicians surveyed reported that the QbTest helped to improve communication with patients and they all valued the QbTest in helping to explain why they had ruled out a diagnosis.[109] Likewise, the majority of clinicians surveyed in three other studies felt that the QbTest results improved the communication of diagnostic decision with the patient.[31, 71, 89]

However, the views of parents/ carers were more mixed as to whether the QbTest improved communication. Only 31/68 families in the AQUA sub-study said that the QbTest helped them to understand how the diagnosis was made, and answers were split regarding whether they thought the results of the test were difficult to understand. Families who received a diagnosis of ADHD were more likely to view the QbTest as useful for understanding how the diagnosis was made, than those who were not diagnosed.[109] Similarly, in the Focus ADHD study, only 10/22 patients/ carers surveyed felt that when the clinician talked through the QbTest results with them, it helped them to understand how they reached the diagnosis. The respondents did not have a strong opinion about whether

the results were difficult to understand (votes were split and many voted "neither agree/ disagree"), but some respondents noted in free text responses that they did not find the test helpful because the results were not properly explained to them.[31]

In two studies, parents/ carers provided a more positive view on the QbTest for aiding communication, with the majority of survey respondents reporting that the clinician talking through the results helped them to understand how their diagnosis had been made.[71, 89]

Understanding of subjective experience

Findings from qualitative data

Clinicians reported in focus groups that the test helped them to better understand the young person's subjective experience.[89] Additionally, one staff member interviewed as part of the FACT RCT reported that the QbTest helped the young person and the staff to better understand the young person's behaviours.[74]

"It feels as if it brings another layer into knowing some of the children" - CAMHS professional on the use of the QbTest[89]

Clinicians and families interviewed in the qualitative sub-study of the AQUA trial appreciated that the QbTest provided what they regarded as an objective and observable measure of symptoms.[109] This finding was echoed in focus groups with clinicians in Child and Adolescent Mental Health Services (CAMHS),[89] interviews with healthcare staff in the Focus ADHD study,[31] and by one staff member interviewed in the FACT RCT.[74]

"I think to be able to see something, it's that black and whiteness of it, to look at it and go yeah I can see that" - Parent on the use of the QbTest[109]

Findings from quantitative data

Findings from surveys with healthcare professionals were in line with the interview data in suggesting that the QbTest can help staff to better understand the patient's symptoms. In the AQUA trial sub-study, all 10 clinicians surveyed felt that the QbTest had helped them to better understand the patient's ADHD symptoms.[109] Likewise, most healthcare professionals surveyed in the Focus ADHD study agreed that the QbTest results were helpful in understanding their client's symptoms,[31] as did clinicians surveyed who had used the QbTest in CAMHS.[89].

Findings were more mixed from surveys with patients and carers. In the AQUA trial qualitative sub-study, only 35/ 73 families surveyed felt that it helped them to understand their child's symptoms better.[109] Likewise, only eleven out of 22 patients/carers surveyed in the Focus ADHD study felt that the QbTest helped them to understand their symptoms.[31] In a survey of 10 adolescent boys in a young offenders institute who used the QbTest in the FACT RCT, the majority of respondents reported that they neither agreed nor disagreed that the QbTest helped them to understand their ADHD symptoms or changes in their

symptoms.[74] Two studies reported more beneficial effects of the QbTest on level of understanding. In one study, 13/15 children/ adolescents reported that the QbTest helped them to understand their symptoms,[89] and in the other study, 41/48 children (and their families) felt that it helped them to understand their symptoms.[71]

Barriers to implementation of the QbTest

Conceptual categories we identified regarding views around barriers to the implementation of the QbTest included: practical barriers, other barriers, and acceptability to patients/ carers.

Practical barriers

Space

Findings from qualitative data

Interview data from three studies highlighted that a room is required to be able to administer the QbTest, and sometimes this is hard to arrange, which means the equipment may need to be moved between rooms.[31, 74, 109] Focus groups with clinicians in CAMHS highlighted concerns about managing environmental factors influencing the QbTest.[89]

"The main [challenges] were just the practical side, like the room space and things. It's really competitive to get rooms here so making sure it was booked well in advance." – Healthcare professional on the use of QbTest[31]

Findings from quantitative data

None reported.

Staffing

Findings from qualitative data

Clinicians in the AQUA sub-study said that use of the QbTest requires someone trained to administer the task and they thought it is best delivered by healthcare assistant, then interpreted by clinician. However, some healthcare professionals noted that it was important to observe the test to assess the validity of the results.[109] Similarly, in focus groups conducted with clinicians in another study, whilst some clinicians felt that hiring an administrator to administer the test would be helpful, others felt that observing a young person complete the QbTest provided extremely valuable information and this superseded the value that a team would receive from a QbTest administrator.[89] Staff interviewed in the Focus ADHD study highlighted issues with training needs and staff capacity,[31] and interviews with clinicians in one other study flagged the need for continued supervision and learning about the test.[89]

"If you're not aware of what's actually happening at that time, then I think it might be difficult… the actual observation, what's happening during that time, is very important" – Healthcare professional on the use of QbTest[109]

Findings from quantitative data
None reported.

Technology

Findings from qualitative data
Some clinicians in the AQUA trial had issues with technology (internet connection, access to printer) and lack of resources.[109] Likewise, focus groups with clinicians reported being intimidated by the technology and noted instances of QbTest reports disappearing, connectivity issues, and components of the test breaking.[89] Staff in the FACT RCT also reported concerns because of equipment and IT system needed,[74] and staff interviewed in the Focus ADHD similarly flagged issues with equipment and Wi-Fi, including challenges with finding a room with a Wi-Fi connection, accessing laptops and sharing passwords.[31]

"There was a lot of IT [Information Technology] governance issues to get it set up" - Healthcare professional on the use of QbTest[109]

Findings from quantitative data
None reported.

Other barriers

Findings from qualitative data
Funding was mentioned as a resource need in the Focus ADHD study.[31] Additionally, a lack of follow-up was highlighted in the AQUA sub-study. Some families interviewed felt abandoned by the service after diagnosis and those who received medication reported they should have been more closely monitored. Additionally, those who didn't receive medication were unclear of what options were available.[109] However, it is not clear how this relates to the QbTest as opposed to the general diagnostic process.

"Like I just feel like maybe my child by the doctors and stuff has been let down a bit by not being seen and just like he said he should have been seen really after the medication and he hasn't" -Parent of child who used QbTest[109]

Findings from quantitative data
None reported.

Acceptability to patients and caregivers

Findings from qualitative data
Two studies reported qualitative data concerning the acceptability of the QbTest. In the FACT RCT, some of the adolescent boys interviewed reported that they found the QbTest boring or felt exhausted by it and one person felt cross that they had to repeat the test. However, one person did report that they would recommend the test to others (no quotes provided).[74]

In the Focus ADHD study, interviews with healthcare staff highlighted that particular groups struggled to use the test. Some young people experienced sensory discomfort during the QbTest and some individuals with Autism also struggled with having the tight headband around their head. In some instances, the individual could adapt the test (e.g. to wear a hoodie underneath the headband), however these issues did prevent some individuals from completing the test. Staff also reported that some young people (particularly six year olds) struggled with anxiety during the test, due to the test itself and/or being without their caregivers. Additionally, some of the younger children struggled to follow the instructions and some older teenagers disengaged from the test and became disruptive. Further issues were raised about the language used in the assessment (e.g. use of the word "test" made people stressed), the length and repetitive nature of the test, the lack of representation of different ethnicities in the explanation video, and the requirement to choose biological sex before conducting the test.[31]

"A lot of our young people that come in for both an autism and an ADHD assessment can experience difficulty with the plastic covering of the headband, because it's quite a sensory thing on the head and that can be quite uncomfortable. It's quite tight on the forehead and around the head." – Healthcare professional on the use of QbTest[31]

Findings from quantitative data

Four studies provided information about the acceptability of the QbTest from surveys to patients/ carers.[31, 71, 74, 89] Findings were mixed between studies, with some participants finding the QbTest difficult to complete, and others not having issues with the test.

In a survey of 10 adolescent boys assessed for ADHD in the FACT RCT (based in a young offenders institution), the majority (9/10) of respondents said that they found the QbTest assessment very stressful and that the task took too long. Additionally, eight out of ten respondents agreed that the task was difficult to complete.[74]

In contrast, in a survey of 48 children (and their families) who had used QbTest in CAMHS, the majority of respondents reported that the results were not difficult to understand and did not find the task difficult to complete.[71] Additionally, in a survey to 15 children/ adolescents who had used the QbTest in a study conducted in CAMHS, 67% did not find the task difficult to complete and most (93%) agreed that overall the experience of using the test was helpful. There was no clear consensus in this study on whether respondents found the stool/chair very uncomfortable or whether the QbTest results were difficult to understand.[89]

In the Focus ADHD study, there was no clear consensus on whether the QbTest was difficult to complete (3/22 said it was, 9 neither agree/ disagree, 10 strongly disagree/ disagree).[31] Although, some of the participants surveyed reported issues with the test, including that their child could not sit through the full test, the QbTest machine did not work in their

appointment, and that they felt the staff member delivering the test did not know what they were doing.

Two studies provided information from surveys about the acceptability of the QbTest for clinicians.[71, 89] In a survey of 17 clinicians who had used the QbTest in CAMHS, 13/17 clinicians agreed that the QbTest was easy to use. Additionally, all clinicians agreed that the test helps them to visualise and quantify symptoms, it is a great addition to other investigative techniques, and it is helpful to monitor the effects of treatment and to standardise assessment and treatment.[89] Whereas, in another study that involved a survey to clinicians in CAMHS (n=not reported), 30% of respondents found the results difficult to understand.[71]

QbCheck: One study provided survey data on the acceptability of the QbCheck, from a short survey given to 125 patients (56 with ADHD; 69 healthy controls) in a diagnostic test accuracy study.[79] The participants reported that they found the test easy to use, including performing the preparations before starting the test, and understanding and following the test rules during the test. The questions were scored on a scale of 0-10 with higher scores indicating higher ease of use, and mean values were all =>8.06. The most common reason for a score less than 8 was that the test took a long time, so it was hard to stay focused.

Patient/ carer/ clinician views of the EFSim Test

Two studies reported survey data for the EFSim test, mainly focusing on the acceptability of the test. As there are only two studies, which reported fairly limited data, we summarise them in turn, below.[77, 90]

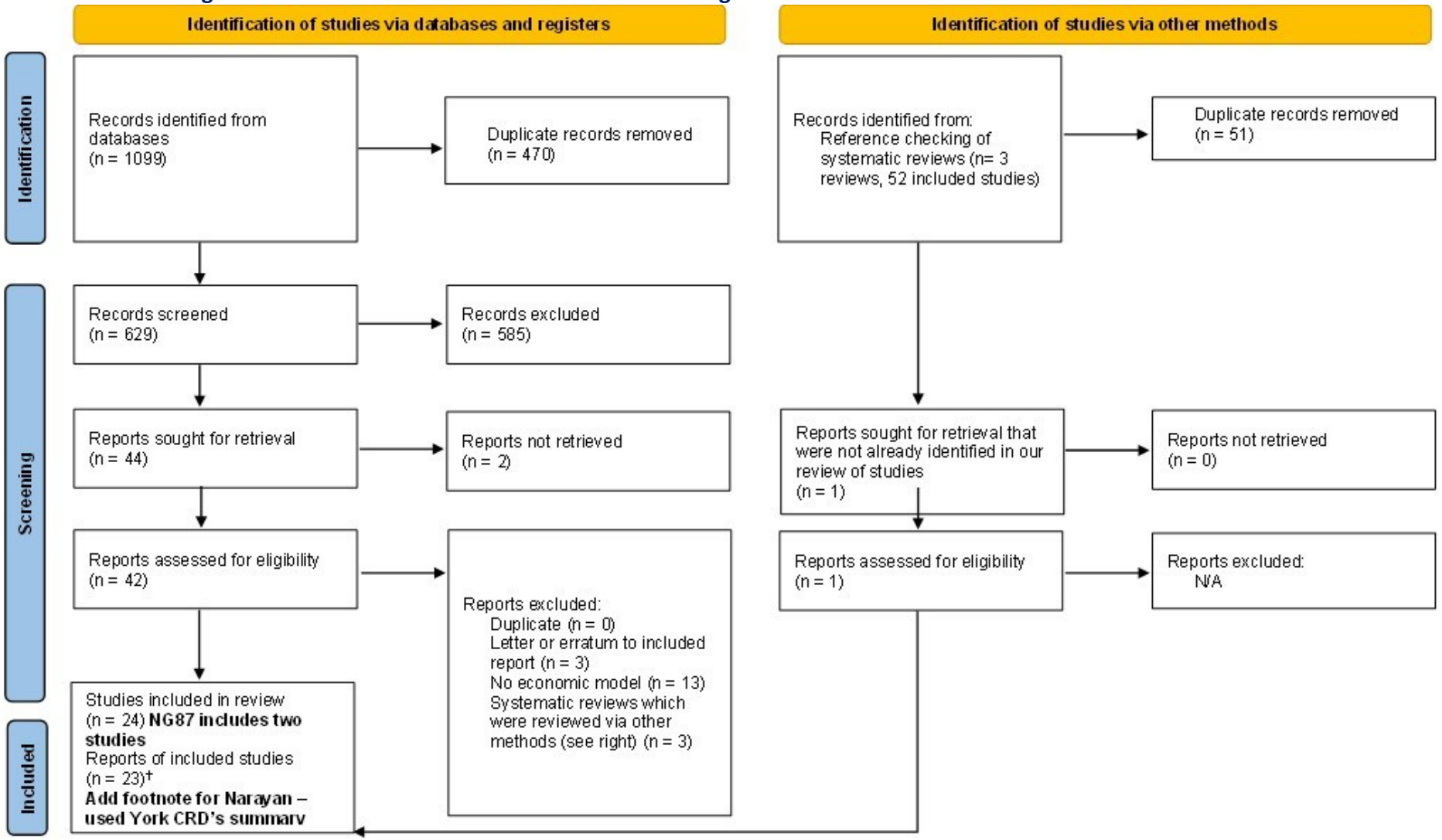
One study, run by the test manufacturer, surveyed 21 teachers of participating schools that had implemented the EFSim test for students in a pilot study. On average, the majority of the teachers found the test results usable and reported that they can support communication with guardians, and that they are helpful to identify executive functioning challenges in students that may otherwise go unnoticed.[90] [redacted]

The other study was a diagnostic test accuracy study of the EFSim test (previous version named EPELI) in children (some with ADHD, some healthy controls, n=not reported). The short survey was answered on a scale from 1 “no” to 7 “completely/ very much”. On average, children appeared to feel enthusiastic about the tasks (ADHD mean score 5 SD, 1.95; healthy control 5.45, SD 1.59), found them interesting (ADHD mean score 4.82, SD 2.17; healthy control 5.32, SD 1.54), and they put effort into their performance (ADHD mean score 5.87, SD 1.23; healthy control 6.21, SD 0.96).

Appendix 5

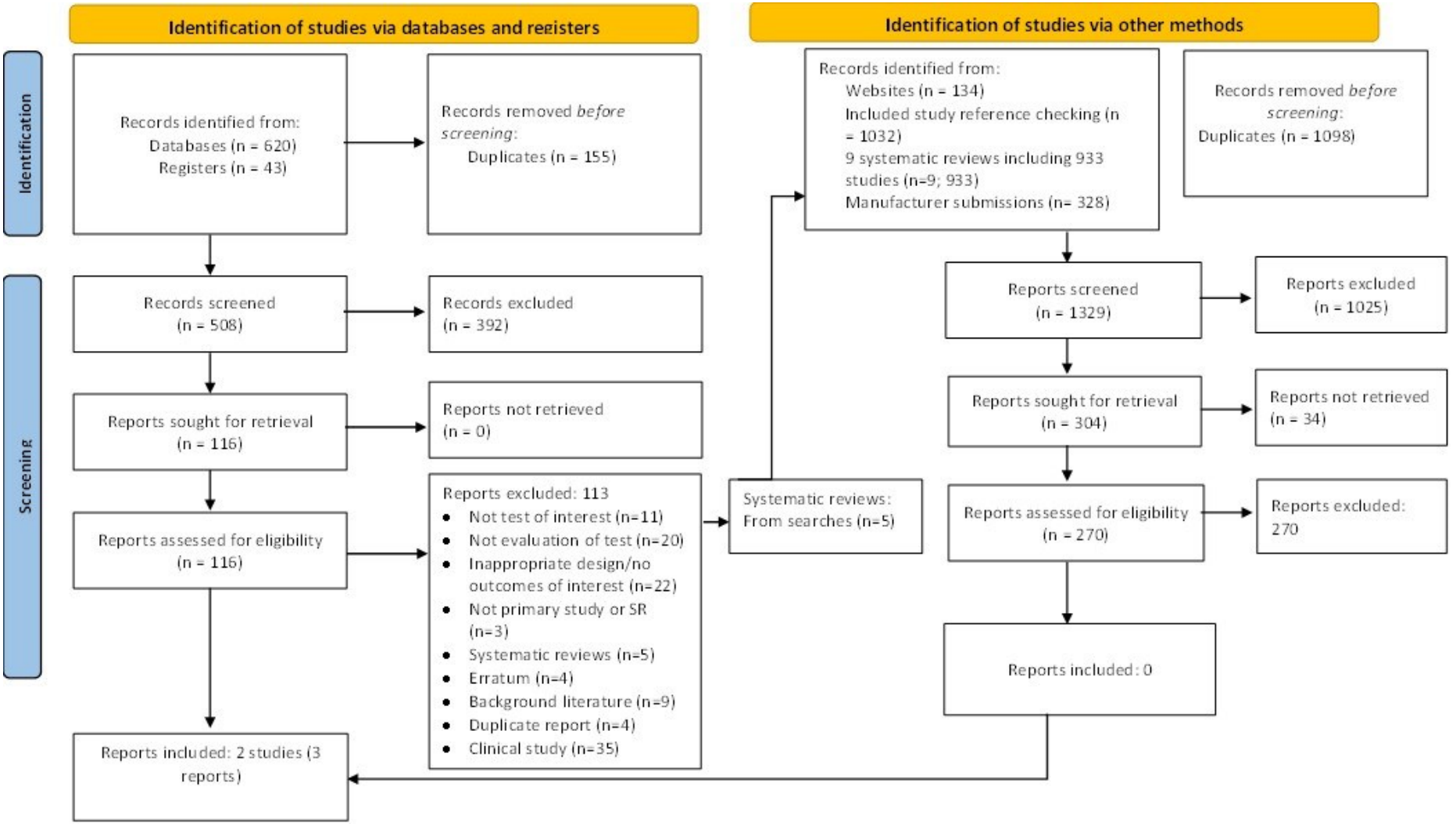
Review of economic models: PRISMA diagrams

Figure 22 PRISMA diagram for the review of economic models for diagnosis and treatment of ADHD



† We were unable to retrieve the full test for Naravan {ref} and instead used the York CRD review of this study {ref}

Figure 23 PRISMA diagram for the identification of economic evaluations of sensor CPTs for diagnosis of ADHD



Appendix 6

Quality assessment economic evaluations of sensor CPTs for the diagnosis of ADHD

Table 64 Quality assessment using the Drummond checklist[113] for the two economic evaluations of sensor CPTs for ADHD are given below. (NA=Not Applicable)

Drummond criteria	AQUA trial[18]	AHSN study*[71]
Study design		
1. The research question is stated	Yes	Yes
2. The economic importance of the research question is stated	Yes	Yes
3. The viewpoints of the analysis are clearly stated and justified	Yes	Yes
4. The rationale for choosing the alternative programmes or interventions compared is stated	Yes	Yes
5. The alternatives being compared are clearly described	Yes	Yes
6. The form of economic evaluation used is stated	Yes	Yes
7. The choice of form of economic evaluation is justified in relation to the questions addressed	Yes	Yes
Data collection		
8. The sources of effectiveness estimates used are stated	Yes	Yes
9. Details of the design and results of effectiveness study are given (if based on a single study)	Yes	Yes but more detail would be useful
10. Details of the method of synthesis or meta-analysis of estimates are given (if based on an overview of a number of effectiveness studies)	NA	NA
11. The primary outcome measure(s) for the economic evaluation are clearly stated	Yes	Yes
12. Methods to value health states and other benefits are stated	No, but EQ5DY data collected	Yes
13. Details of the subjects from whom evaluations were obtained are given	Yes	No or NA
14. Productivity changes (if included) are reported separately	NA	NA
15. The relevance of productivity changes to the study question is discussed	NA	Yes
16. Quantities of resources are reported separately from their unit costs	Yes	Yes but not very clearly
17. Methods for the estimation of quantities and unit costs are described -	Yes	Yes
18. Currency and price data are recorded	Yes	No
19. Details of currency or price adjustments for inflation or currency conversion are given	Yes	Yes
20. Details of any model used are given	NA	Yes
21. The choice of model used and the key parameters on which it is based are justified	NA	NA
Analysis and interpretation of results		

22. Time horizon of costs and benefits is stated	Yes	No (only in results and inconsistent)
23. The discount rate(s) is stated	Yes	Yes
24. The choice of rate(s) is justified	Yes	No
25. An explanation is given if costs or benefits are not discounted	Yes	NA
26. Details of statistical tests and confidence intervals are given for stochastic data	NA	No
27. The approach to sensitivity analysis is given	NA	Yes
28. The choice of variables for sensitivity analysis is justified	NA	No
29. The ranges over which the variables are varied are stated	NA	Yes
30. Relevant alternatives are compared	Yes	Yes
31. Incremental analysis is reported	ICER is reported	No
32. Major outcomes are presented in a disaggregated as well as aggregated form	No	Yes
33. The answer to the study question is given	Yes	Yes
34. Conclusion follow from the data reported	No because QbTest cost excluded from both arms	Yes
35. Conclusions are accompanied by the appropriate caveats	Yes	Yes

HealthTech Programme

Technologies for the assessment of attention deficit hyperactivity disorder (ADHD)

Section A: External Assessment Report - Comments collated table:

Any confidential sections of the information provided should be underlined and highlighted. Please underline all confidential information, and separately highlight information that is 'commercial in confidence' in blue and all that is 'academic in confidence' in yellow

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
1.	[redacted]	-	-	The recommendations for using the QbTest in adult ADHD diagnosis and management seem overly favourable, given the limitations in the available evidence, high risk of bias in existing studies, and reliance on paediatric data. **1. Limited Data for Adults** "We did not identify any studies in adults that reported information on time and number of appointments until diagnosis, and no studies with diagnostic accuracy data for sensor CPTs in combination with clinical assessment. Our main analyses are therefore only directly applicable for children and adolescents" . **2. Insufficient Evidence on Diagnostic Accuracy** "Estimates of sensitivity ranged from 67% (95% CI 57, 77%) to 87% (95% CI 75, 95%) with a summary estimate of 79% (95% CI 69, 86%). Estimates of specificity were slightly lower and ranged from 41% (95% CI 24, 61%) to 83% (95% CI 77, 88%) with a summary estimate of 60% (41, 76%)" . "One study (not shown on the plots) conducted in older adults and judged at low risk of bias, only provided data for a combination of scores across the QbActivity and QbInattention subcategories. Estimated sensitivity was 56% (95% CI 45, 66%) and specificity was 83%" .	We should clarify that the place of the EAG report is not to make recommendations, but to present the clinical and cost-effectiveness data, including a discussion of the limitations of the evidence. It is the committee that make the recommendations. As highlighted here, the EAG are clear about the limitations in the evidence in their report.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				2. Cost-Effectiveness Assumptions "Our overall conclusions were robust to most of our modelling assumptions. However, if the state costs for responders / non-responders on treatment were assumed to be higher, then QbTest in addition to clinical assessment would not be cost-effective, due to the higher proportion who initiate treatment and incur the higher costs" . **4. Medication Management Data** "There are no specific studies identified that evaluated the QbTest or other sensor CPTs for medication management in adults" . **5. Potential Overestimation of Benefits** "Clinicians felt the test increased confidence in clinical decision making, and both clinicians and families felt it may reduce the time to diagnostic decision. Although, some families felt that the test results were not properly explained to them and did not help them to understand symptoms or how diagnoses were made. Barriers to implementation included staffing, training, and technology requirements" . "Estimates of sensitivity and specificity were derived from the models; details on how this was done were not reported" . **6. Recommendations vs. Evidence** "The key source of evidence on effectiveness of sensor CPTs was the AQUA trial which evaluated QbTest (6-12) (in children 7-12years) and QbTest (12-60) (for adolescents 12-17 year olds)" . "We found that QbTest in addition to clinical assessment is likely to be cost-effective, with	

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				incremental costs of £238.35 and incremental QALYs of 0.0385 per person evaluated for ADHD. The resulting incremental cost-effectiveness ratio (ICER) is £6183 per QALY gained, which is cost-effective at a willingness to pay (WTP) threshold of £20,000 per QALY. These findings were driven by reduced time waiting for assessment, reduced appointments until diagnosis, and a higher proportion receiving a diagnosis so that more patients with ADHD receive treatment benefits" .	
2.	Peili Vision Oy (ARVO)	3	Abstract	We thank you for the opportunity to comment on your review of the scope for diagnostic devices for ADHD. EFSim is an immersive simulation of everyday life. Unlike CPT, EFSim provides a simulated home-like environment where the user is required to perform realistic everyday life tasks in a setting where executive functioning difficulties are most likely to arise and appear, while CPT [which is characterised by extended periods of repetition of a single, non-realistic task] is removed from that context. The final scope of the assessment published in Nov 2023 outlines the assessment to be focusing on a variety of technologies for the assessment of ADHD. The importance was noted in combining measures of cognition and motor activity: final-scope (nice.org.uk) (page 2). Whilst the scope mentions CPT, it also explicitly uses several different tools for comparison. However, we note that the external assessment report has narrowed the scope and considers all the presented technologies as CPT/Sensor CPT.	We found it challenging to come up with a term to define all the tests of interest. In discussion with out clinical experts, sensor CPT seemed the most appropriate term. We have not narrowed the scope or changed the inclusion criteria in any way, we have simply used the term “sensor CPT” to refer to the test in the scope set out by NICE.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				EFSim is not a sensor CPT. EFSim is an immersive evaluation of cognition and motor activity. EFSim provides a more naturalistic assessment of executive functions which are core to accurately diagnosing, and effectively treating, ADHD. *"Naturalistic tasks are more sensitive to cognitive impairments in situations where more traditional tasks fail to detect them and could offer better predictive value for everyday functioning."* (Shallice & Burgess, 1991). Moreover, CPT tests can often be difficult for young people to sit through, which can be particularly difficult for impulsive individuals and result in a lower test completion rate. There is concern that mis-labelling EFSim as a CPT test could inadvertently conflate very different technologies with each other. For example, the repetitive nature of CPT is regarded as difficult for young people to sit through, which can be particularly difficult for impulsive individuals and can result in a lower test completion rate, despite impulsivity not being a clear indicator of ADHD. Naturalistic assessment does not have this issue.	
3.	Peili Vision Oy (ARVO)	3	Abstract	EFSim is an immersive simulation of everyday life. The simulation includes a home-like environment where the user performs everyday life tasks. Challenges within the home are one of the requirements for ADHD diagnosis. EFSim simulates the home environment as it is widely recognised as where ADHD symptoms typically represent themselves.	No response needed
4.	Peili Vision Oy (ARVO)	30	1.3.3	This section references us using Oculus GO, which is not the case. We would like to draw your attention to the following:	Apologies we took this information from the NICE scope. We do also refer to the web-based version of the test in this section. We did not

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				1) We have proposed the use of our web version which is not in VR (Virtual Reality) and purely requires access to a web browser via a standard computer/laptop. 2) Our VR product is currently only for the Pico HMD. We are not a VR only technology. The web version ('flat screen version') does not require the use of a VR headset.	identify any evaluations of this test that met our inclusion criteria.
5.	Peili Vision Oy (ARVO)	6	Scientific Summary	In this section the review did not recognize one scientific publication of EFSim Web version. In the research EFSim web is referred to as EPELI Flat Screen version. https://www.frontiersin.org/articles/10.3389/frvir.2023.1138240/full	We used the search term EPELI which would also have identified any studies using the term EPELI Flat screen. This study was not indexed in any of the databases that we searched and so was not identified by the searches. However, as it was reported in the Peili Vision manufacturer submission we retrieved the full text of this paper and screened this for inclusion. It was not included in the review as it "does not report on outcome of interest" (as shown in Table 39 of the EAG report). In addition we note that this study was conducted in typically developing children (not those with suspected ADHD) and so would also have been excluded for this reason.
6.	Peili Vision Oy (ARVO)	29	1.3	The summary of EFSim did not note the neurological performance indicator reports that Peili provides which is a key aspect of the pre and post diagnostic support that is offered as it allows individuals to get a much more tailored understanding of their executive functioning difficulties to	The information on the Peili vision test was taken from the final NICE scope.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				support parents and caregivers in delivering much more individualised support.	

7.	Peili Vision Oy (ARVO)	85	5	We provided our costings in our executive summary that was submitted as part of the scoping. However, these costs were not reviewed. We have reproduced them below:
				Delivery Model
				
				We propose utilising a dedicated healthcare assistant (HCA) within each Primary Care Network to deliver EFSim testing efficiently across all practices and schools in the PCN.
				
				The HCA would travel to each practice one day per month. They would provide EFSim assessments to all patients with suspected ADHD based on initial screening.
				
				This model allows easy access to EFSim testing across a PCN without needing full equipment and staffing at each practice.
				
				Estimated Costs:
				
				- Salary costs:
				  - Full-time HCA salary: £24,214 (AfC Band 3)
				  - Assuming 48 weeks/year and 8 sessions/day
				  - 1 day per practice per month = daily cost of £153
				- Facility costs:
				  - Room cost estimated at £2-3/hour
				  - At £2.50/hour for a 7.5 hour session = £18.75 per practice
					Please note that our remit and our model is to evaluate cost-effectiveness. It is not a cost-comparison. This means that we need data on the implications of EFSim for diagnostic performance (diagnostic accuracy, number of appointments, length of appointments, etc.) to include EFSim in the model. We did not identify any such data in our reviews, and so could not include EFSim in our cost-effectiveness model.
					
					We did not originally include a scenario using the per test cost estimated by the company. This was due to the proposed delivery model being very different to that of QbTest on which the effectiveness data was based. However, we apologise that we did not explain that in the report. We have now added an additional scenario 4(f), which uses the costs as estimated by the company, assuming 15 test per monthly practise session day, giving a per-test cost of £13.14. However, we stress that these results should not be interpreted as the cost-effectiveness of EFSim.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response

				- Administration costs:
				  - 10% of salary costs = £15.30 per session
				- Travel costs:
				  - Estimated at 50p/mile
				  - Average 10-mile round trip per practice
				  - £5 per session travel costs
				- Equipment costs:
				  - VR headset: £400 (amortised over 3 years)
				
				Total estimated cost per monthly PCN-wide clinic day:
				
				- Salary: £153
				- Room: £18.75
				- Admin: £15.30
				- Travel: £5
				- Equipment: £5
				- Total: £197.05 per day
				
				Fig. 3. Potential Cost Savings with EFSim Based on all of England. (Executive Summary)Assumptions
				Population: 56,550,138 (2021 Census data)
				Child population (age 5-18): 11,908,194 (ONS)
				Estimated (conservative estimate) ADHD Prevalence: 1.53% Expected number of ADHD cases; 1.53% x 11,908,194 = 182,341 - Assumptions:
				
				- 30% misdiagnosis rate
				- £700 savings per avoided misdiagnosis
				- £15 savings per appointment avoided
				- £10,400 lifetime cost savings per patient	

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
8.	Peili Vision Oy (ARVO)			Regarding the concerns raised by the reviewers about two-gated studies we note that NICE has historically shown preference away from RCTs. In the 2018 paper by Campbell et al it was noted that *"Between 2009 and 2015 a NICE committee considered 169 technologies, of which it selected 74 (44 percent) for full evaluation, based on the claims of benefit and the evidence available. An average of 7.5 claims were made per technology; the total number did not influence selection but presence of studies supporting all the claims ($p < .001$) or any of the claims ($p < .05$) had a positive influence, as did claims for quicker patient recovery ($p < .001$). A greater number of studies to support the claims made selection more likely ($p < .001$), as did cohort studies ($p < .05$) and surveys ($p < .05$)* ***but, unexpectedly, not randomized trials****."* The same paper also noted *"With regard to the types of studies and their influence on selection, randomized controlled trials were not associated with a greater likelihood of selection, based on our statistical analysis.* ***While this might suggest a bias against the normal hierarchy of evidence, it may well be because randomized trials of technologies are sometimes designed with outcomes and endpoints that are not the most relevant for an assessment of their value to patients or the service****, or they are designed without the most appropriate comparators. Lack of appropriate comparators in trials may sometimes have been based on choosing ones that are more costly or more likely to prove inferior, rather than the most commonly used alternative; or it may happen because trials were done outside the United Kingdom, where the most commonly used alternative technology is different."* (Campbell et al, 2018)	There is strong evidence that 2-gate designs, especially those that include a group of healthy controls, over-estimate accuracy compared to one-gate designs(1, 2) The information provided here is a comparison between RCTs and other sources of data and does not discuss two-gate designs and is very difficult to interpret out of context. RCTs remain the most robust form of evidence if conducted in the appropriate population, and evaluating the appropriate interventions and outcomes. If RCTs are not available or directly relevant to the research question then other sources of evidence may need to be used; but these will be at higher risk of bias than a well-conducted RCT. Note that an RCT cannot provide information on accuracy (unless an accuracy sub-study is included as with the AQUA trial) so to address issues of accuracy a DTA study will be required. The most robust design for a DTA study is a one-gate design. 1. Whiting P, Rutjes AW, Reitsma JB, Glas AS, Bossuyt PM, Kleijnen J. Sources of variation and bias in studies of diagnostic accuracy: a systematic review. Annals of internal medicine. 2004 Feb 3;140(3):189-202. 2. Whiting PF, Rutjes AW, Westwood ME, Mallett S, QUADAS-2 Steering Group. A systematic review classifies sources of bias and variation in diagnostic test accuracy studies.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
					Journal of clinical epidemiology. 2013 Oct 1;66(10):1093-104.
9.	Nesplora	3	Results	The results report the inclusion of only 2 studies referring to AULA test (named here as "Nesplora Kids"), where since 2014 to November 2023 (date which the systematic review states as the latest date for inclusion of studies), there are **8 original papers reporting the use of AULA as the main measure, one of them being the normative study with general population and another 6 specifically using AULA as a measure of the attentional profile with clinical samples of ADHD**. A simple search in PubMed using the terms "AULA AND "Virtual Reality"" shows this: https://pubmed.ncbi.nlm.nih.gov/?term=aula+AND+%22virtual+reality%22 **An additional original study was found using APA Psychinfo:** Zulueta, A., Díaz-Orueta, U., Crespo-Eguilaz, N., & Torrano, F. (2019). Virtual reality-based assessment and rating scales in ADHD diagnosis. *Psicología Educativa, 25*(1), 13–22. https://doi.org/10.5093/psed2018a18 **Additional sources for AULA**: Díaz-Orueta, U. (2017). Advances in Neuropsychological Assessment of Attention: From initial computarized continuous performance test to AULA. In Kane, R.L. y Parsons, T.D. (Eds), The Role of Technology in Clinical Neuropsychology (pp. 103-136). New York, EEUU: Oxford University Press (https://academic.oup.com/book/40883/chapter-abstract/348955773?redirectedFrom=fulltext). **This is a review study presenting the main psychometric**	All reports listed (except for one, detailed below) were identified by our searches and were screened for inclusion in the review. We have clearly documented reasons for exclusion in Appendix 2 as follows: AULA-**Advanced** Virtual Reality **Tool for the Assessment of Attention: Normative Study in Spain. Iriarte Y, Diaz-Orueta U, Cueto E, Irazustabarrena P, Banterla F, Climent G.** Exclusion reason: Does not report on one of the outcomes of interest (Table 35) AULAvirtualreality **test as an attention measure: convergent validity with Conners' Continuous Performance Test.Díaz-Orueta U, Garcia-López C, Crespo-Eguílaz N, Sánchez-Carpintero R, Climent G, Narbona J.** Exclusion reason: Does not report on one of the outcomes of interest (Table 35) **[Efficacy of lisdexamphetamine to improve the behavioural and cognitive symptoms of attention deficit hyperactivity disorder: treatment monitored by means of the** AULA **Nesplora** virtualreality **test]. Diaz-**

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				properties of AULA, including measures of sensitivity and specificity. **Reviews:** Diaz-Orueta, U., Blanco-Campal, A., Lamar, M., Libon, D. J., & Burke, T. (2020). Marrying Past and Present Neuropsychology: Is the Future of the Process-Based Approach Technology-Based?. *Frontiers in psychology*, *11*, 361. https://doi.org/10.3389/fpsyg.2020.00361 Parsons, T. D., Duffield, T., & Asbee, J. (2019). A Comparison of Virtual Reality Classroom Continuous Performance Tests to Traditional Continuous Performance Tests in Delineating ADHD: a Meta-Analysis. *Neuropsychology review*, *29*(3), 338–356. https://doi.org/10.1007/s11065-019-09407-6 Separately, **the report totally ignores studies related to Nesplora Aquarium**, not just the normative study (https://doi.org/10.1080/23279095.2019.1646745), but the ones detailed below specifically targeting ADHD populations as well as non-clinical individuals with ADHD symptomatology: Areces, D., García, T., Cueli, M., & Rodríguez, C. (2019). Is a Virtual Reality Test Able to Predict Current and Retrospective ADHD Symptoms in Adulthood and Adolescence?. *Brain Sciences, 9*(10), 274. https://doi.org/10.3390/brainsci9100274 Camacho-Conde, J. A., & Climent, G. (2022). Attentional profile of adolescents with ADHD in virtual-reality dual execution tasks: A pilot study. *Applied Neuropsychology,*	**Orueta U, Fernandez-Fernandez MA, Morillo-Rojas MD, Climent G.** Exclusion reason: Not an evaluation of the test (Table 35) **Efficacy of a Continuous Performance Test Based on** VirtualReality **in the Diagnosis of ADHD and Its Clinical Presentations. Areces D, Rodríguez C, García T, Cueli M, González-Castro P.** Exclusion reason: Does not report on one of the outcomes of interest (Table 35) **Analysis of cognitive and attentional profiles in children with and without ADHD using an innovative** virtualreality **tool. Areces D, Dockrell J, García T, González-Castro P, Rodríguez C.** Exclusion reason: Not an evaluation of the test (Table 35) **Comparison between two continuous performance tests for identifying ADHD: Traditional vs.** virtualreality**. Rodríguez C, Areces D, García T, Cueli M, González-Castro P.** Exclusion reason: Does not report on one of the outcomes of interest (Table 35)

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				Child, 11(1), 81–90. https://doi.org/10.1080/21622965.2020.1760103	**Postnatal arsenic exposure and attention impairment in school children. Rodríguez-Barranco M, Gil F, Hernández AF, Alguacil J, Lorca A, Mendoza R, Gómez I, Molina-Villalba I, González-Alzaga B, Aguilar-Garduño C, Rohlman DS, Lacasaña M.** Exclusion reason: Not an evaluation of the test (Table 40) **Data-driven profiles of attention-deficit/hyperactivity disorder using objective and ecological measures of attention, distractibility, and hyperactivity. Fernández-Martín P, Rodríguez-Herrera R, Cánovas R, Díaz-Orueta U, Martínez de Salazar A, Flores P.** Exclusion reason: Not an evaluation of the test (Table 35) **Zulueta, A., Díaz-Orueta, U., Crespo-Eguilaz, N., & Torrano, F. (2019). Virtual reality-based assessment and rating scales in ADHD diagnosis. *Psicología Educativa, 25*(1), 13–22. https://doi.org/10.5093/psed2018a18** This study is included in the review (Table 33) **Additional sources for AULA**: Díaz-Orueta, U. (2017). Advances in Neuropsychological Assessment of Attention:

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					From initial computarized continuous performance test to AULA. In Kane, R.L. y Parsons, T.D. (Eds), The Role of Technology in Clinical Neuropsychology (pp. 103-136). New York, EEUU: Oxford University Press (https://academic.oup.com/book/40883/chapter-abstract/348955773?redirectedFrom=fulltext). **This is a review study presenting the main psychometric properties of AULA, including measures of sensitivity and specificity.** Exclusion reason: Not a primary study or SR (Table 35) **Nesplora aquarium:** **Climent GR, Celestino Garcia, Trinidad Areces, Debora Mejias, Miguel Aierbe, Amaia Moreno, Marta Cueto, Eduardo Castella, Judit Feli Gonzalez, Mari. New virtual reality tool (Nesplora Aquarium) for assessing attention and working memory in adults: A normative study. Applied neuropsychology Adult 2021;28(4): 403-415** Exclusion reason: Does not report on one of the outcomes of interest (Table 35) **Areces, D., García, T., Cueli, M., & Rodríguez, C. (2019). Is a Virtual Reality Test Able to Predict Current and Retrospective ADHD Symptoms in Adulthood and Adolescence?.**

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					***Brain Sciences, 9*(10), 274. https://doi.org/10.3390/brainsci9100274** Exclusion reason: Does not report on one of the outcomes of interest (Table 35) **Camacho-Conde, J. A., & Climent, G. (2022). Attentional profile of adolescents with ADHD in virtual-reality dual execution tasks: A pilot study. *Applied Neuropsychology, Child, 11*(1), 81–90. https://doi.org/10.1080/21622965.2020.1760103** Exclusion reason: Not an evaluation of the test (Table 35) The following review was excluded at title and abstract stage (and therefore is not tabulated in the EAG report), as it is not a primary study or SR and does not mention any of the tests within scope in the title or abstract: **Diaz-Orueta, U., Blanco-Campal, A., Lamar, M., Libon, D. J., & Burke, T. (2020). Marrying Past and Present Neuropsychology: Is the Future of the Process-Based Approach Technology-Based?. *Frontiers in psychology*, *11*, 361. https://doi.org/10.3389/fpsyg.2020.00361**

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					Lastly, this review was not identified in our searches as the tests of interest were not named in title, abstract, or indexing. This review was also not provided in the submission pack by the manufacturer. We note that reviews were not eligible for inclusion, rather where they were identified, we checked the studies included for eligibility (See Table 37 of the EAG report). We have checked the studies included by Parsons *et al.,* and identified no additional studies or reports eligible for inclusion in our review. **Parsons, T. D., Duffield, T., & Asbee, J. (2019). A Comparison of Virtual Reality Classroom Continuous Performance Tests to Traditional Continuous Performance Tests in Delineating ADHD: a Meta-Analysis. *Neuropsychology review*, *29*(3), 338–356. https://doi.org/10.1007/s11065-019-09407-6**
10.	Nesplora	4	Results	The Results report "No studies were identified for objectives 2 and 4", being the objective #2 "Diagnosis of ADHD in people referred with suspected ADHD for whom current assessment cannot reach a diagnosis" and objective #4 "Evaluating treatment effectiveness during long-term treatment monitoring for people with ADHD". **Comments #4 and #5 respectively report on published studies with Nesplora Aquarium and Nesplora AULA that fit into these two objectives. These studies below have been ignored in the systematic review:** Areces, D., García, T., Cueli, M., & Rodríguez, C. (2019). Is a Virtual Reality Test Able to Predict Current and Retrospective ADHD Symptoms in Adulthood and Adolescence?. *Brain sciences*, *9*(10), 274. https://doi.org/10.3390/brainsci9100274	Both of these studies were identified by our searches and were screened for inclusion in the review. We have clearly documented reasons for exclusion in Appendix 2 as follows: **Areces, D., García, T., Cueli, M., & Rodríguez, C. (2019). Is a Virtual Reality Test Able to Predict Current and Retrospective ADHD Symptoms in Adulthood and Adolescence?. *Brain sciences*, *9*(10), 274. https://doi.org/10.3390/brainsci9100274**

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				Diaz-Orueta, U., Fernandez-Fernandez, M. A., Morillo-Rojas, M. D., & Climent, G. (2016). Eficacia de la lisdexanfetamina en la mejora sintomatica conductual y cognitiva del trastorno por deficit de atencion/ hiperactividad: tratamiento monitorizado mediante el test AULA Nesplora de realidad virtual [Efficacy of lisdexamphetamine to improve the behavioural and cognitive symptoms of attention deficit hyperactivity disorder: treatment monitored by means of the AULA Nesplora virtual reality test]. *Revista de Neurologia, 63*(1), 19–27. https://neurologia.com/articulo/2015488 and https://pubmed.ncbi.nlm.nih.gov/27345276/	Exclusion reason: Does not report on one of the outcomes of interest (Table 35) **Diaz-Orueta, U., Fernandez-Fernandez, M. A., Morillo-Rojas, M. D., & Climent, G. (2016). Eficacia de la lisdexanfetamina en la mejora sintomatica conductual y cognitiva del trastorno por deficit de atencion/ hiperactividad: tratamiento monitorizado mediante el test AULA Nesplora de realidad virtual [Efficacy of lisdexamphetamine to improve the behavioural and cognitive symptoms of attention deficit hyperactivity disorder: treatment monitored by means of the AULA Nesplora virtual reality test]. *Revista de Neurologia, 63*(1), 19–27. https://neurologia.com/articulo/2015488 and https://pubmed.ncbi.nlm.nih.gov/27345276/** Exclusion reason: Not an evaluation of the test (Table 35)
11.	Nesplora	6-9	Results	With Objective #1 being “What is the diagnostic accuracy and clinical- and cost-effectiveness of sensor CPT for the diagnosis of ADHD in people referred with suspected ADHD?”, **this systematic review totally ignores up to 6 studies in relation to the ability of AULA test to accurately diagnose ADHD and differentiate between ADHD and controls, and 1 study on Nesplora Aquarium that also is relevant to this Objective**:	All of these studies were identified by our searches and were screened for inclusion in the review. We have clearly documented reasons for exclusion in Appendix 2 as follows: **Díaz-Orueta, U., Garcia-López, C., Crespo-Eguílaz, N., Sánchez-Carpintero, R., Climent, G., & Narbona, J. (2014). AULA virtual reality test as an attention measure: convergent validity with Conners' Continuous**

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				1. Díaz-Orueta, U., Garcia-López, C., Crespo-Eguílaz, N., Sánchez-Carpintero, R., Climent, G., & Narbona, J. (2014). AULA virtual reality test as an attention measure: convergent validity with Conners' Continuous Performance Test. *Child Neuropsychology*, *20*(3), 328–342. https://doi.org/10.1080/09297049.2013.792332 This study shows how AULA (but not Conners' CPT) was able to differentiate between ADHD children with and without pharmacological treatment for a wide range of measures related to inattention, impulsivity, processing speed, motor activity, and quality of attention focus. 2. Areces, D., Dockrell, J., García, T., González-Castro, P., & Rodríguez, C. (2018). Analysis of cognitive and attentional profiles in children with and without ADHD using an innovative virtual reality tool. *PloS One*, *13*(8), e0201039. https://doi.org/10.1371/journal.pone.0201039 This study developed different classification models to discriminate between individuals with ADHD and controls based on tasks and testing conditions included in AULA. Considering the first model (with Aula Nesplora general measures), only omissions and age were statistically significant predictors of group membership. Omissions showed the highest standardized coefficient, being the most relevant variable identifying subjects with and without ADHD. The statistics indicated that the older the student and the higher the score in omissions, the higher the probability to present ADHD. This model classified	**Performance Test. *Child Neuropsychology*, *20*(3), 328–342. https://doi.org/10.1080/09297049.2013.792332** Exclusion reason: Did not report on one of the outcomes of interest (Table 35) **Areces, D., Dockrell, J., García, T., González-Castro, P., & Rodríguez, C. (2018). Analysis of cognitive and attentional profiles in children with and without ADHD using an innovative virtual reality tool. *PloS One*, *13*(8), e0201039. https://doi.org/10.1371/journal.pone.0201039** Exclusion reason: Not an evaluation of the test (Table 35) **Areces, D., Rodríguez, C., García, T., Cueli, M., & González-Castro, P. (2018). Efficacy of a Continuous Performance Test Based on Virtual Reality in the Diagnosis of ADHD and Its Clinical Presentations. *Journal of Attention Disorders*, *22*(11), 1081–1091. https://doi.org/10.1177/1087054716629711** Exclusion reason: Did not report on one of the outcomes of interest (Table 35) **Rodríguez, C., Areces, D., García, T., Cueli, M., & González-Castro, P. (2018). Comparison between two continuous performance tests for identifying ADHD: Traditional vs. virtual**

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				76.1% of the sample correctly (66% from the control group, and 89.5% from the ADHD group). Another model, X vs. X-no task classified correctly 75% of the sample (64% of the controls, and 89.5% of the students with ADHD, respectively). A third model classified better the controls (Distractors vs. No distractors condition, where 76.1% of the students were correctly classified (70% from the control group, and 84.2% from the ADHD group)). The current results demonstrated the important roles of omissions, age, and working memory deficit in predicting the probability of a child receiving a diagnosis of ADHD. 3. Areces, D., Rodríguez, C., García, T., Cueli, M., & González-Castro, P. (2018). Efficacy of a Continuous Performance Test Based on Virtual Reality in the Diagnosis of ADHD and Its Clinical Presentations. *Journal of Attention Disorders*, *22*(11), 1081–1091. https://doi.org/10.1177/1087054716629711 This study enhanced the advantages of differentiating between visual and auditory performance in AULA. Each of the test conditions allowed the discrimination between the Impulsive/Hyperactive and combined presentations with respect to the control group, and between the Impulsive/Hyperactive and inattentive presentations. However, differences among ADHD presentations were only evident when the results were separately analysed for the visual and auditory modalities. This study showed that the indicators offered by the AULA Nesplora	**reality. *International Journal of Clinical and Health Psychology: IJCHP*, *18*(3), 254–263. https://doi.org/10.1016/j.ijchp.2018.06.003** Exclusion reason: Did not report on one of the outcomes of interest (Table 35) **Zulueta, A., Díaz-Orueta, U., Crespo-Eguilaz, N., & Torrano, F. (2019). Virtual reality-based assessment and rating scales in ADHD diagnosis. *Psicología Educativa, 25*(1), 13–22. https://doi.org/10.5093/psed2018a18** This study is included in the review (table 33) **Fernández-Martín, P., Rodríguez-Herrera, R., Cánovas, R., Díaz-Orueta, U., Martínez de Salazar, A., & Flores, P. (2024). Data-driven profiles of attention-deficit/hyperactivity disorder using objective and ecological measures of attention, distractibility, and hyperactivity. *European Child & Adolescent Psychiatry*, *33*(5), 1451–1463. https://doi.org/10.1007/s00787-023-02250-4** Exclusion reason: Not an evaluation of the test (Table 35) **Camacho-Conde, J. A., & Climent, G. (2022). Attentional profile of adolescents with ADHD in virtual-reality dual execution tasks: A pilot study. *Applied Neuropsychology, Child, 11*(1), 81–90.**

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				test (omissions, commissions, response times, and motor activity) make it possible to establish a differential diagnosis of ADHD presentations when analysed under different contextual conditions. 4. Rodríguez, C., Areces, D., García, T., Cueli, M., & González-Castro, P. (2018). Comparison between two continuous performance tests for identifying ADHD: Traditional vs. virtual reality. *International Journal of Clinical and Health Psychology: IJCHP*, *18*(3), 254–263. https://doi.org/10.1016/j.ijchp.2018.06.003 This study compared the discriminant value of attentional variables provided by a traditional CPT test (TOVA) with those from a virtual reality test (Aula Nesplora) to identify the ADHD presentations along with the presence or absence of ADHD symptomatology. According to the analysis, the Aula Nesplora test showed better sensitivity and specificity than the TOVA test. The percentages of correctly identified children with the combined presentation of ADHD and children without ADHD were similar for both tests. However, the percentage of identification of inattentive and impulsive-hyperactive presentations was significantly higher using Aula Nesplora. 5. Zulueta, A., Díaz-Orueta, U., Crespo-Eguilaz, N., & Torrano, F. (2019). Virtual reality-based assessment and rating scales in ADHD diagnosis. *Psicología Educativa, 25*(1), 13–22. https://doi.org/10.5093/psed2018a18	**https://doi.org/10.1080/21622965.2020.1760103** Exclusion reason: Not an evaluation of the test (Table 35)

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				The current study presents findings from analysing the external validity of AULA and its contribution to the diagnosis of ADHD. Four hundred and seven children (272 girls and 135 boys) from 6 to 16 years old (213 with ADHD diagnosis, 105 inattentive children, 108 combined-type, and 194 controls) were evaluated. First, a factor analysis of AULA variables was conducted in order to reduce data to factor and five factors or components that account for 82.37% of the total variance were obtained from 407 subjects, namely, sustained attention, impulsivity control, processing speed, response variability, and control of motor activity. Second, a discriminant analysis was then performed on data obtained by participants from whom the five factors were obtained, showing that AULA presents moderate levels of both specificity and sensitivity. Finally, in order to study whether AULA adds relevant information in the diagnosis of ADHD, a cluster analysis was conducted, showing four clusters in the analysis of conglomerates with the control group and six groups of clusters in the ADHD group. In summary, AULA test shows adequate external validity, allows correct classification of children with and without attentional problems, and confirms and provides additional ADHD diagnostic information that it is essential for the design of interventions. 6. Fernández-Martín, P., Rodríguez-Herrera, R., Cánovas, R., Díaz-Orueta, U., Martínez de Salazar, A., & Flores, P. (2024). Data-driven profiles of attention-deficit/hyperactivity disorder using objective and ecological measures of attention, distractibility, and	

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				hyperactivity. *European Child & Adolescent Psychiatry*, *33*(5), 1451–1463. https://doi.org/10.1007/s00787-023-02250-4 **This research was initially published on the 30th of June 2023, which means it was available for inclusion in the systematic review**. In his study, one hundred and ten Spanish-speaking participants (6–16 years) with ADHD (medication-naïve, n = 57) and typically developing participants (n = 53) completed AULA. They performed hybrid hierarchical k-means clustering methods over the whole sample on the normalized t-scores of AULA main indices. A five-cluster structure was the most optimal solution. Instead of replicating ADHD subtypes, the authors identified two clusters sharing clinical scores on attention indices, susceptibility to distraction, and head motor activity, but with opposing scores on mean reaction time and commission errors; two clusters with good performance; and one cluster with average scores but increased response variability and slow RT. DSM-5 subtypes cut across cluster profiles. These results suggest that latency of response and response inhibition in AULA could serve to distinguish among ADHD subpopulations and guide neuropsychological interventions. Motor activity, in contrast, seems to be a common feature among ADHD subgroups. This study highlights the poor feasibility of categorical systems to parse ADHD heterogeneity and the added value of data-driven approaches and VR-based assessments to obtain an accurate characterization of cognitive functioning in individuals with and without ADHD.	

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				7. Camacho-Conde, J. A., & Climent, G. (2022). Attentional profile of adolescents with ADHD in virtual-reality dual execution tasks: A pilot study. *Applied Neuropsychology, Child, 11*(1), 81–90. https://doi.org/10.1080/21622965.2020.1760103 This paper aims to study the cognitive-executive performance of adolescents between the ages of 17 and 23 with an ADHD diagnosis, relative to a control group. The total sample consisted of 120 male participants who were given the Nesplora Aquarium test. Dual execution tasks assessed attention, response speed, and inhibition capability. When comparing the experimental and control groups, statistically significant differences were detected in processing speed, selective attention, and cognitive inhibition [general execution (T_correct_n) (p = 0.008), attention arousal (T_omission_n) (p = 0.008), and processing speed (T_correctreactime_mean) (p = 0.008)]. This study demonstrates that Nesplora Aquarium, designed to measure attention in people over the age of 16 years, is effective at measuring attention and working memory. In addition, item difficulty and discrimination values were also acceptable.	
12.	Nesplora	9	Results	For Objective #2, there was a study on Nesplora Aquarium which is an example of non-diagnosed individuals that could be retrospectively diagnosed using this VR test. The present study aimed to explore whether Nesplora Aquarium is able to predict ADHD symptoms in adults and adolescents, based on both current and retrospective self-reports. A non-clinical sample of 156 adults and adolescents (70 women and 86 men) between 16 and 54 years of age (M = 21.23, SD = 8.04) took part in the study. Virtual reality (VR) variables such as the number of correct answers, omission, and commission errors, among others,	This study was identified by our searches and was screened for inclusion in the review. It was excluded as it did not report on one of the outcomes of interest (see Table 35).

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				were used to predict current and retrospective self-reported symptoms of ADHD using multiple regression models. Correct answers and omission errors in the VR test significantly predicted both current and retrospective ADHD symptoms. However, only the number of perseveration errors and gender were able to significantly predict retrospective ADHD symptoms. These findings suggest that inattention problems tend to remain after adolescence, while perseveration errors (which have been related to impulsive behaviour) and gender differences tend to diminish. Areces, D., García, T., Cueli, M., & Rodríguez, C. (2019). Is a Virtual Reality Test Able to Predict Current and Retrospective ADHD Symptoms in Adulthood and Adolescence?. *Brain sciences*, *9*(10), 274. https://doi.org/10.3390/brainsci9100274	
13.	Nesplora	9	Results	For Objective #4, despite the limitations it may have, the study by Diaz-Orueta et al. (2016) fits precisely into Objective #4, as it measures the outcome of long-term pharmacological treatment, with one administration of AULA test before the first administration of Lisdexamphetamine to 85 children with ADHD between 6 and 16 years-old, and a re-test after an average of 7.5 months of pharmacological treatment, with results showing "*highly significant improvements in selective and sustained attention, quality of attention focus and hyperactivity; moderate improvements in impulsivity; and an incidence close to zero in processing speed*". The reference is linked below: Diaz-Orueta, U., Fernandez-Fernandez, M. A., Morillo-Rojas, M. D., & Climent, G. (2016). Eficacia de la lisdexanfetamina en la mejora sintomatica conductual y	This study was identified by our searches and was screened for inclusion in the review. It was excluded as it was not an evaluation of a test of interest (see Table 35).

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				cognitiva del trastorno por deficit de atencion/ hiperactividad: tratamiento monitorizado mediante el test AULA Nesplora de realidad virtual [Efficacy of lisdexamphetamine to improve the behavioural and cognitive symptoms of attention deficit hyperactivity disorder: treatment monitored by means of the AULA Nesplora virtual reality test]. *Revista de Neurologia, 63*(1), 19–27. https://neurologia.com/articulo/2015488 and https://pubmed.ncbi.nlm.nih.gov/27345276/	
14.	Nesplora	28	1.3.1	There is no description of the theoretical model of attention underlying the construction and development of the QBTest. The theoretical model behind AULA is clearly described in the "Measure" section of the normative study of this tool (Iriarte, Y., Diaz-Orueta, U., Cueto, E., Irazustabarrena, P., Banterla, F., & Climent, G. (2016). AULA-Advanced Virtual Reality Tool for the Assessment of Attention: Normative Study in Spain. Journal of Attention Disorders, 20(6), 542–568. https://doi.org/10.1177/1087054712465335).	This section is intended as a brief overview of the tests included in scope.
15.	Nesplora	28-30	1.3.1. to 1.3.5.	There is no balance in the presentation of the different sensor CPTs presented in this report. There is a clear overrepresentation of the QBTest, including information of its current representation in the NHS (i.e. "*implemented across 69 NHS trusts between 2020 and 2023 as part of an Academic Health Science Network (AHSN) initiative known as "Focus ADHD" which aimed to improve the diagnosis of ADHD in children and young people*"). They even highlight the existence of a recent NICE Medical Innovation Briefing that highlighted that "*the QbTest should be used as an addition to routine clinical assessment, not as a standalone test*" (https://www.nice.org.uk/advice/mib318/chapter/summary). There is no such level of detail for the rest of Sensor CPTs	QbTest is "over-represented" as we found more studies of this test that fulfilled our inclusion criteria. Searches focused equally on all tests, and screening and inclusion assessment was conducted independently by two reviewers. Our inclusion criteria were pre-specified in the protocol. We have been transparent in reporting reasons for exclusion of all studies at full text review and for all studies submitted by the manufacturers in appendix 2.

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				included in the report (when, at least for Nesplora tests, information of its wide international implementation can be easily obtained from the company website - www.nesplora.com-), which may, we believe, constitute a bias towards a more favourable consideration of the QBTest versus the other tests.	
16.	Nesplora	58	Accuracy of Nesplora Attention Kids Aula	The systematic review is ignoring several studies about AULA and totally ignoring the research on Aquarium, as already stated through comments 1 to 7 above.	See response above.
17.	Nesplora	186 to 189	Appendix 1	The data search parameters state that Data parameters that the studies were searched from 1946 to November 16, 2023. The search was conducted on November 17, 2023. The study on AULA by Fernandez-Martin et al. (2024) was initially published and available through database search since the 30th June 2023 (https://doi.org/10.1007/s00787-023-02250-4), which poses great concern on the accuracy and quality of this systematic review. In addition, the search terms (Nesplora* or "Giunti psychometrics") are not exhaustive enough for tests that appear on the literature with clearly defined names such as AULA and AQUARIUM, both of which terms were not included in any of the searches conducted in this systematic review.	This study was identified by our searches and was screened for inclusion in the review. It was excluded as it was not an evaluation of a test of interest but we have since reviewed this and have changed the exclusion reason to “does not report outcomes of interest” (see Table 35), .
18.	Nesplora	214 and beyond	Table 14	We consider the systematic review has ignored relevant research related to AULA published in the search time frame (i.e. up to November 2023) and the whole research related to Aquarium. From the revision of the study report, a substantial bias in favour of the QBTest and an inefficient search strategy (excluding words such as “AULA” or “Aquarium”) is evidenced, lowering the quality of what should be expected from a systematic review of the literature.	See responses above. Had qualitative evaluations of Nesplora been available then we would have included these. All literature was assessed in an unbiased systematic way. Note that two studies of the EF Sim test were also included in this section and so it does not just focus on QbTest.

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				Appendix 4 from page 298 and a focus on what clinicians say about the QBTest is an additional example of this bias towards a more favourable consideration of the QBTest against the alternatives. This type of information would not be accepted if coming from a manufacturer like Nesplora, which could be seen like "cherry-picking" the most favourable opinions about the test.	
19.	Nesplora	120-122	5.3.8 Resource use and costs	"Costs related to using the technologies". We sent the "DAP75 Request for information Nesplora_Dec2023" file with the information about the costs of Nesplora. Nesplora has available at www.nesplora.com/plans information on pricing and hardware requirements. To administer the Nesplora tests, a computer, a virtual reality device, headphones and internet access are required. The Nesplora tests do not require a specific room, as virtual reality and the headphones introduce the examinee to an immersive experience without external distractions to obtain objective measures. The scenario you've considered with "the test cost of £10.32 (based on 22 uses per quarter)" is aimed at professionals with few people to assess. We have estimated that an unlimited licence costs £1345.85 per year, and we consider 40 assessments per month (this is our internal rate for medium-sized clinics and hospitals) with an outcome of £2.8 per test.	Please note that our remit and our model is to evaluate cost-effectiveness. It is not a cost-comparison. This means that we need data on the implications of the Nesplora tests for diagnostic performance (diagnostic accuracy, number of appointments, length of appointments, etc.) to include the Nesplora tests in the model. We did not identify any such data in our reviews, and so could not include the Nesplora tests in our cost-effectiveness model. We have now added a scenario 4(e) where we use the test cost based on the annual "Professional plan" with 40 assessments per month, giving a per test cost of £2.80 plus nurse time to administer the cost. However, we stress that these results should not be interpreted as the cost-effectiveness of the Nesplora AULA test.

Section B Economic model - Comments

Comment no	Stakeholder	Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)	EAG response
1	[redacted]	The economic model used in the report aimed to assess the cost-effectiveness of sensor-based continuous performance tests (sensor CPTs), particularly the QbTest, for diagnosing and managing ADHD. While the model provides valuable insights, several limitations and areas for improvement can be identified. **1. Scope and Generalisability** • **Children Focus**: The model primarily focuses on children and adolescents, with limited applicability to adult populations. Given the differences in ADHD presentation and management between children and adults, the model's findings may not be generalizable across all age groups. • **Other Sensor CPTs**: The economic evaluation was primarily based on data			We respond to each point in turn. 1. We are clear in the report that the scope and generalisability of the cost-effectiveness analysis is limited to children and QbTest. This is because we only identified evidence to populate the model for these groups, and so any model built for older patients and for other tests would have been largely based on assumptions which we could not verify. 2. The risk of bias rating for AQUA was based on the way that censoring was handled in the model. The way we have used the data from AQUA (by having a proportion who do not get a diagnosis, and then modelling time to diagnosis for those who do get a diagnosis) aims to avoid the potential bias in the AQUA study. As well as the AQUA study, the implementation studies also found that number of appointments were reduced with QbTest, supporting this

		for the QbTest, with insufficient consideration of other sensor CPTs like EF Sim and Nesplora Kids. This narrow focus limits the model's applicability to other potentially effective technologies. **2. Data Quality and Assumptions** • **High Risk of Bias**: Many of the included studies, particularly the AQUA trial, were judged to be at high risk of bias. This introduces uncertainty into the model's inputs and outputs. • **Heterogeneous Data**: The estimates of diagnostic accuracy were heterogeneous, leading to caution in interpreting the model's results. The wide range of sensitivity and specificity values reduces confidence in the robustness of the cost-effectiveness conclusions. • **Assumptions on Diagnostic Process**: The model assumes that integrating the QbTest reduces the number of appointments and			assumption in the model. Our model does however assume that there would be a corresponding reduction in waiting time for an appointment, and this was not measured in any of the studies, and so is based on assumption. We explored this in sensitivity analyses. We also agree that there is uncertainty in the diagnostic test accuracy of QbTest plus clinical assessment versus clinical assessment alone, for which AQUA was the only study to make this comparison. Our results are therefore reliant on a single study, and heterogeneity found for the other DTA data could also apply for the compbination of QbTest with clinical assessment vs clinical assessment alone. Replication of the findings in AQUA would be valuable to assess this. We have conducted sensitivity analyses to the diagnostic accuracy of QbTest. 3. It is correct that we did not include staff training costs in the model, as this is a start-up cost that isn't allocated per patient treated. We do however indicate the approximate cost of staff training and highlight that this is not included. We do not include

		consultation time required for a diagnosis. However, these assumptions are based on limited and potentially biased data. **3. Cost Components** • **Healthcare Costs**: While the model includes healthcare costs such as reduced appointment times and fewer consultations, it may not comprehensively account for all associated costs. For example, it might overlook costs related to training staff, technology maintenance, and potential repeat tests. • **Broader Economic Impact**: The model primarily considers direct healthcare costs and savings. It could be improved by incorporating indirect costs, such as productivity losses for parents and caregivers, educational support services, and long-term societal impacts of untreated ADHD. **4. Utility Estimates** • **Quality of Life (QALYs)**: The model uses quality-adjusted life years			repeat tests, but we do assume in scenarios that a proportion of patients do not complete the test and so would incur the test cost but not the benefits of the test results. The device equipment is all provided as part of QbTest, as well as clinical advisor support, and training material, and this is included in the cost. Because the equipment is loaned in this way, the EAG understands that the cost of maintenance and replacement is covered by the company. Our remit was to provide an NHS perspective, but we acknowledge that that there would be wider societal impacts, that have not been captured by the model. We highlight this in the EAG report. 4. We agree that there is limited data on utilities. We have made assumptions that are in line with previous models of treatment for ADHD. We have added an additional sensitivity analysis 17(a)-(c) using the 3 sets of utilities unsed as sensitivity analyses in the Zimovetz study, which covers the range of assumed utility values used in previous models. We acknowledge that our model of treatment for ADHD is not a

		(QALYs) to measure the benefits. The utility estimates for QALYs are derived from limited data, particularly for non-responders to treatment. The robustness of these utility values can significantly impact the model's outcomes. • **Adverse Effects**: The impact of adverse effects from medication is included, but the model may not fully capture the long-term quality of life impacts and adherence challenges associated with ADHD medications. **5. Sensitivity Analyses** • **Limited Scenarios**: Although sensitivity analyses were performed, they were limited in scope. More comprehensive sensitivity analyses could explore a wider range of scenarios, including varying prevalence rates of ADHD, different healthcare settings, and alternative assumptions on diagnostic accuracy and costs. • **Threshold Analyses**: The model includes threshold			detailed long-term model of treatment. However, we do include treatment discontinuation, adverse events, response to treatment, and treatment switching. All the models we identified of ADHD treatment are limited by lack of long-term data on the consequences on utilities and adherence to treatment. 5. We conducted 16 different scenario/sensitivity analyses, including those for assumptions on diagnostic test accuracy, prevalence in those without a diagnosis within 6 appointments, test costs, and health-state costs. We did not conduct a sensitivity analysis by health-care setting because the AQUA study did not report results based on setting, and included a mix of community child and adolescent mental health services (CAMHS) (48%) or community paediatric clinics (52%). It is a limitation of our analysis that we could not report results by setting. We have reported results for different WTP thresholds to aide the committee with their decision making. It is the committee who make the recommendation and decide on an appropriate threshold.

		analyses for willingness-to-pay (WTP) thresholds. However, the assumptions underlying these thresholds could be further scrutinized to ensure they reflect realistic decision-making contexts. **6. Long-Term Follow-Up** • **Short-Term Focus**: The model's focus is primarily short-term, concentrating on immediate diagnostic and initial treatment phases. Long-term follow-up data are necessary to understand the sustained impact of sensor CPTs on ADHD management and cost-effectiveness. • **Chronic Nature of ADHD**: Given that ADHD is a chronic condition, the economic model should incorporate longer time horizons to capture the ongoing costs and benefits of using sensor CPTs in both diagnosis and long-term management.			6. Our model has a 10 year time-horizon which was in line with the longest previous treatment models, and we felt was a balance between capturing long-term benefits/costs without extrapolating short-term data too far into the long-term. We did run scenarios with longer (15 and 20 year) time horizons, but these are not based on long-term data and so are very uncertain. We acknowledge this limitation clearly in the report.
2	Peili Vision Oy (ARVO)	Only QB test was evaluated for the economic analysis.	We would like for the additional technologies including EFSim to be evaluated alongside the QB	By ensuring that the cost model clearly differentiates between web-based/screen only interventions, and those which	Our remit and our model is to evaluate cost-effectiveness. It is not a cost-comparison. This means that we need data on the

	Section 7.2.3, page 164		test as the technologies all require different hardware, infrastructure/resource costs, and training time which will affect the costs. We had submitted our costs breakdown in our executive summary.	require extra kit and/or a specific room set up, you will enable proper cost comparison. Importantly, this differentiation within the guidance will ensure that any purchasing decisions made due to it will be properly informed as to which version they should be purchasing.	implications of EFSim for diagnostic performance (diagnostic accuracy, number of appointments, length of appointments, etc.) to include EFSim in the model. We did not identify any such data in our reviews, and so could not include EFSim in our cost-effectiveness model. We have now added an additional scenario 4(f), which uses the costs as estimated by the company, assuming 15 test per monthly practise session day, giving a per-test cost of £13.14. However, we stress that these results should not be interpreted as the cost-effectiveness of EFSim.