Evidence Assessment and Analysis Report commissioned by the NIHR HTA Programme on behalf of the National Institute for Health and Care Excellence – Final Protocol

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1. Title

Rapid Tests for Group A Streptococcal infections in people with a sore throat

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3. Plain English Summary

Sore throat is a common condition caused by an infection of the airway. Most cases are of a viral nature, however, a substantial number of these infections may be caused by the Group A Streptococcus (Strep A) bacteria. Most sore throats, including viral and bacterial sore throat infections, resolve spontaneously within a few weeks. To identify patients for whom antibiotic treatment is appropriate, National Institute for Health and Care Excellence (NICE) recommends the use of clinical scoring tools. In spite of this recommendation, there is a huge variation in antibiotic prescription for sore throat in practice; while some general practitioners (GPs) have a very low threshold for prescribing antibiotics for sore throat, others believe that prescribing antibiotics over-medicalises a condition that can largely be managed by self-care.[1]

Ideally, a throat swab culture should be undertaken to identify the organism causing the infection in cases where diagnosis is uncertain. However, this takes time, causing potential delays in administering the correct treatment.

For these reasons, the external assessment group (EAG) will determine the diagnostic accuracy and cost-effectiveness of 21 point-of-care tests for detecting Strep A bacteria. This assessment will inform the use of these tests within the NHS.

4. Decision problem

4.1 Purpose of the decision to be made

Sore throat is a very common condition[2] and the most common symptoms of a sore throat include pain in the throat, fever or a headache. Sore throat is defined as an infection in the upper respiratory airway affecting the mucosa.[3] Sore throats can be described as acute pharyngitis, inflammation of the pharynx; or as acute tonsillitis, inflammation of the tonsils. The highest incidence is in children and young adults, with 50% of cases occurring in people aged 5–24 years.[4] Although most cases of sore throat are viral, around 5%-17% are bacterial, typically Group A beta-haemolytic streptococcus (GABHS), also known as *Streptococcus pyogenes* or Strep A.[4, 5] Most cases of Strep A infection resolve without complications. Potential complications caused by Strep A include infections such as tonsillitis, pharyngitis, scarlet fever, impetigo, erysipelas (an infection in the upper layer of the skin), cellulitis and pneumonia.

According to UK guidelines, antibiotics are only recommended in patients with Strep A sore throat.[6] In order to appropriately identify patients who will likely benefit from antibiotic therapy, NICE recommends the use of the FeverPain or Centor criteria in combination with clinical assessment.[6] Despite this, most patients presenting with sore throat in the UK will be given antibiotics in primary care.[7, 8] Considering the emergence of multi-resistant pathogens,

'antimicrobial stewardship' has been a central strategy adopted by the Chief Medical Officer and NICE.[9, 10]

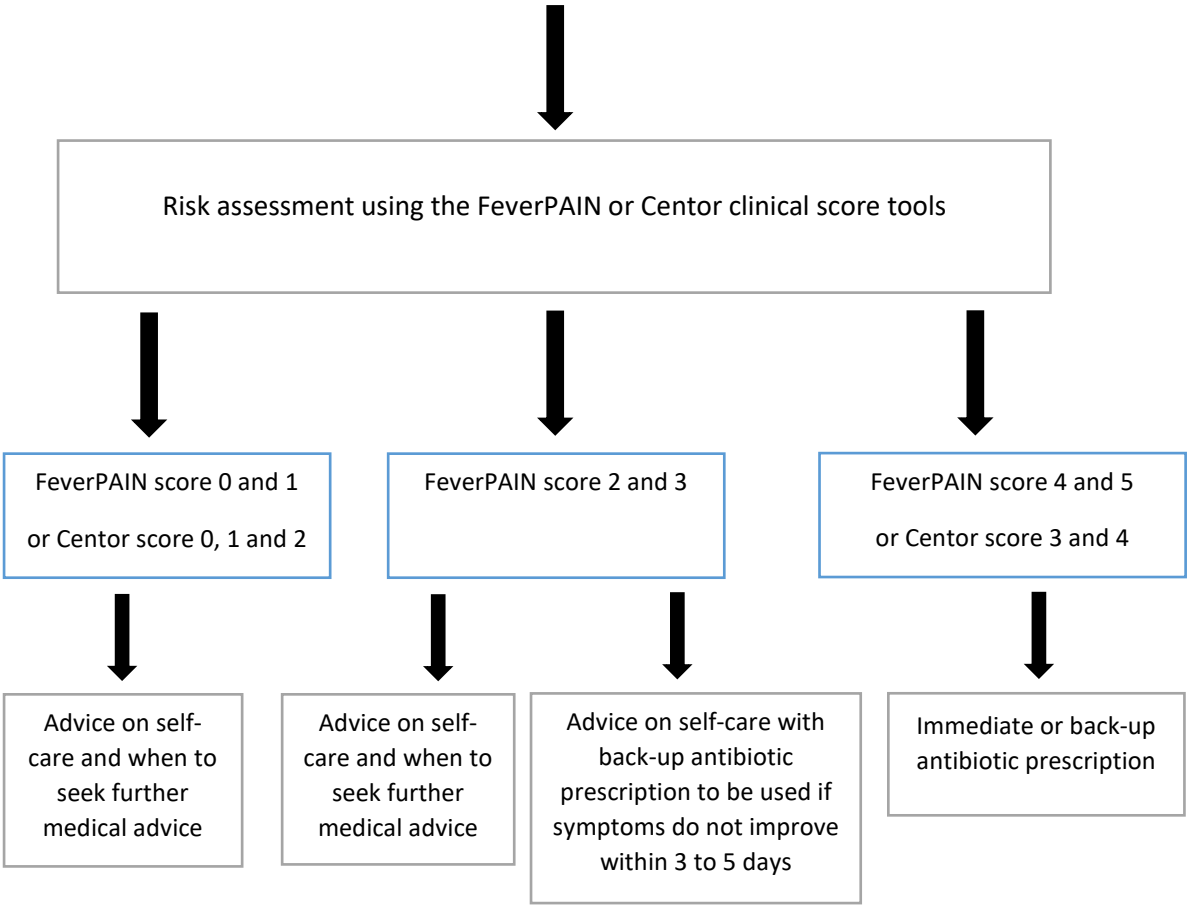
Point-of-care diagnostic testing in primary care has been recognised as an emerging technology for aiding targeted antibiotic prescribing in cases of sore throat.[11] Several technologies have been developed for point-of-care diagnostic testing in primary care for appropriate administration of antibiotics to those that would benefit and to prevent delay and associated complications.

The External Assessment Group (EAG) aims to assess the diagnostic accuracy and cost-effectiveness of point-of-care diagnostic tests for the detection of Strep A. This diagnostics assessment will inform the NICE Diagnostic Advisory Committee (DAC) guidance on the use of rapid GABHS tests for informing antimicrobial prescribing decisions within the NHS.

4.2. Diagnostic and care pathway

Figure 1 depicts the care pathway for assessing and treating a sore throat as outlined in the NICE's antimicrobial prescribing guidance on sore throat (NG84).[6] The majority of uncomplicated sore throats are managed without seeking medical advice and will tend to resolve within one week.[2] Suggested conservative measures include simple analgesia, maintaining hydration, salt gargling and throat lozenges. In selected cases where a GP or prescribing pharmacist feels that the patient may benefit from antibiotics, the prescriber should apply either the FeverPAIN or Centor scores to guide their decision-making. The NICE antimicrobial prescribing guideline on acute sore throat does not make any recommendations about using point-of-care tests or throat cultures to confirm strep A infection.[6]

Figure 1: Diagnostic and care pathway for managing acute sore throat in patients who are not at high-risk of complications



4.3. Clear description of interventions

Twenty-one tests are anticipated to be used in addition to clinical scoring tools and have been described in the NICE scope. These tests have a faster turnaround time than laboratory culture of throat swabs, and this may allow a prescribing decision to be made at the initial consultation. Tests may be used in a variety of clinical settings including GP surgeries, community pharmacies and in hospitals. Seventeen of the 21 tests are rapid antigen detection tests. Of these 17 rapid antigen tests, 16 tests used lateral flow (also known as immunochromatographic throat swabs), and one test uses turbidimetric immunoassays. The other four of the 21 tests are molecular tests which utilise nucleic acid amplification, via polymerase chain reaction (PCR) (two tests) or via isothermal nucleic acid amplification (two tests). Some companies recommend that negative test results are confirmed by microbiological culture of a throat swab.

The seventeen rapid-antigen technologies are summarised below:

1. *Clearview exact Strep A cassette (Abbott)*
   This technology utilises the principles of lateral flow via a two-site sandwich immunoassay technology for the detection of Group A Streptococcal antigen. Absence of a coloured line at the test line region indicates a negative result. The cassettes are supplied as 25 individually pouched test cassettes and time to test result is 5 minutes.

2. *Clearview exact Strep A dipstick – test strip (Abbott)*
   Similarly to its cassette variant, Abbott's Clearview exact strep A dipstick utilises the principles of lateral flow via a two-site sandwich immunoassay technology for the detection of Group A Streptococcal antigen. The dipstick is sold as a 25 test kits and it takes 5 minutes to generate a result.

3. *BD Veritor Plus system group A Strep assay - cassette (Beckton Dickinson)*
   This system utilises a lateral flow technology producing test results in 5 minutes. The test utilises strips then analysed by a BD Veritor system analyser module, and results are displayed digitally. Strips are supplied as 30 test kits for use with the BD Veritor system analyser module.

4. *Strep A rapid test - cassette (Biopanda Reagents)*
   Strep A rapid test uses a sandwich lateral flow immunoassay technology generating a positive or negative test result in 5 minutes. The presence of a coloured line in the test line region indicates a positive result. To serve as a procedural control, a coloured line will always appear in the control region to show that the test has been performed properly. The test is sold as 20 test cassettes.

5. *Strep A rapid test – test strip (Biopanda Reagents)*
   Strep A rapid test uses a sandwich lateral flow immunoassay technology generating a positive or negative test result in 5 minutes. The presence of a coloured line in the test line region indicates a positive result. To serve as a procedural control, a coloured line will always appear in the control region to show that the test has been performed properly. The test is sold as 20 test cassettes.

6. *NADAL Strep A - test strip (nal von minden GmbH)*
   This system utilises a lateral flow technology producing test results in 5 minutes. The test is sold as 40 test strips including controls, 50 test strips (tube) including controls, as well as positive and negative control vials.

7. *NADAL Strep A - cassette (nal von minden GmbH)*
   This system utilises a lateral flow technology producing test results in 5 minutes. The test is sold 20 test cassettes including controls as well as positive and negative control vials.

8. *NADAL Strep A plus - cassette (nal von minden GmbH)*
   Similarly to the NADAL strep A, the NADAL strep A plus uses a lateral flow technology producing test results in 5 minutes. This technology is sold as 20 pack cassettes including controls and 5 pack cassettes including controls.

9. *NADAL Strep A plus - test strip (nal von minden GmbH)*
   Similarly to the NADAL strep A, the NADAL strep A plus uses rapid antigen detection test and lateral flow technology producing test results in 5 minutes. This technology is sold as 40 test strips.

10. *NADAL Strep A scan test - cassette (nal von minden GmbH)*
    This technology utilises the principles of lateral flow via a two-site sandwich immunoassay technology for the detection of Group A Streptococcal antigen. It differs from the other NADAL strep A diagnostic tests as it is sold as a 20 pack cassettes including controls as well as a Colibri reader and Colibri USB and software. Time to test result is 5 minutes.

11. *OSOM Strep A test – test strip (Sekisui Diagnostics)*
    The OSOM system like many others uses a sandwich immunoassay lateral flow technology producing either a positive or negative test results in 5 minutes. It comes as a 50-test pack.

12. *QuikRead Go Strep A test kit (Orion Diagnostica)*
    Unlike the previous technologies, QuikRead uses Turbidimetric immunoassays. The test takes under 7 minutes to generate a positive or negative result. It is sold as 50 tests including controls alongside the QuikRead Go instrument.

13. *Alere TestPack Plus Strep A - cassette (Abbott)*

    This test detects the presence or absence of strep A antigens using lateral flow immunochromatographic assay. The test takes about 5 minutes to yield results and comes in a cassette format. However, its level of Strep A detection has not yet been provided by the manufacturer.

14. *Bionexa Strep A plus - cassette (Biomerieux)*

    This test detects the presence or absence of strep A antigens using lateral flow immunochromatographic assay. The test takes about 5 minutes to yield results and can detect a minimum of 10,000 organisms per swab.

15. *Bionexa Strep A dipstick – test strip (Biomerieux)*

    This test detects the presence or absence of strep A antigens using lateral flow immunochromatographic assay. The test takes about 5 minutes to yield results. However, its level of organism detection has not yet been provided by the manufacturer.

16. *Biosynex Strep A - cassette (Biosynex)*

    This test detects the presence or absence of strep A antigens using lateral flow immunochromatographic assay. The test takes about 5 minutes to yield results and detects about 100,000 organisms per swab.

17. Sofia Strep A FIA (Quidel)

    This tests uses immunofluorescence-based lateral-flow technology to detect Group A streptococcal antigens from throat swabs. The time to test result is about 5 to 6 minutes. It is sold as 25 cassettes, including positive and negative control vials.

The four molecular technologies are summarised below:

18. *ALERE i Strep A (Abbott)*
    ALERE i Strep A detects Strap A DNA using isothermal nucleic acid amplification to generate a test result, which becomes available within 8 minutes of test commencement. It is sold as 24 test kits for use in the ALEREi system.

19. *ALERE i Strep A 2 (Abbott)*
    ALERE i Strep A 2 detects strep A DNA using isothermal nucleic acid amplification. The results become available under 6 minutes. However, the level of organism detection has not yet been provided by the manufacturer.

20. *Cobas Strep A assay on Liat system (Roche Diagnostics)*
    The Cobas Liat Strep A assay by Roche Diagnostics utilises PCR to generate a test result in under 15 minutes. They are sold as Strep A assay box of 20 to accompany a Liat analyser that digitally displays test results.

21. *Xpert Xpress Strep A (Cepheid)*
    The Xpert Xpress Strep A assay by Cepheid utilises PCR, however, the time taken to generate a test result is just over 18 minutes.

4.4 Populations and relevant subgroups

The primary population is people aged over 5 presenting to healthcare providers in a primary (GP surgeries and community pharmacies) or secondary care (hospital) setting with symptoms of an acute sore throat. These patients are identified as being more (FeverPAIN score of 2 or 3) or most likely (FeverPAIN score of 4 or 5, or a Centor score of 3 or 4) to benefit from an antibiotic by a clinical

scoring tool. Relevant subgroups to be evaluated may include children (aged 5 to 14), adults (aged 15 to 75), and the elderly (adults over the age of 75 years). In elderly patients, the infection is more likely to be invasive and have a higher associated mortality rate. The incidence of Strep A infections is highest in winter and spring. We will incorporate any seasonality effects into the economic model if our review of the evidence identifies information to enable us do so. Strep A can also cause severe infections (invasive group A Strep) leading to sepsis or Streptococcal toxic shock syndrome and is also associated with necrotising fasciitis (a severe infection of soft tissue).

4.5 Relevant comparators

The comparator will be antibiotic prescribing on the basis of clinical judgment and clinical scoring tools alone. The clinical scoring tools which may be used in NHS practice are FeverPAIN and Centor/modified Centor (McIsaac).

4.5.1. FeverPAIN

The FeverPAIN clinical scoring tool includes the following variables:

- Clinical history
  - Sore throat (none; mild; moderate; severe)
  - Cough or cold symptoms (none; mild; moderate; severe)
  - Muscle aches (none; mild; moderate; severe)
  - Fever in last 24 hours (yes; no)
  - Onset of illness (0-3 days; 4-7 days; 7+ days)
- Clinical examination
  - Cervical glands (none; 1-2cm; >2cm)
  - Inflamed tonsils (none; mild; moderate; severe)
  - Pus on tonsils (yes; no)

The result of FeverPAIN is presented as a score ranging from 0 to 5.

4.5.2. Centor

The Centor clinical scoring tool includes the following variables:

- Cough (yes; no)
- Exudate or swelling on tonsils (no; yes)
- Tender/swollen anterior cervical lymph nodes (no; yes)
- Temperature >38°C (no; yes)

Expert advice suggests that the McIsaac (modified Centor) clinical scoring tool may also be used. The McIsaac score adjusts the Centor score to account for the higher incidence of Strep A in children and reduced incidence in older adults. This adds age criteria (3-14 years; 15-44 years; ≥45 years), and adds one point for those aged under 15 and subtracts one point for those aged 45 and over.[12] The result of Centor/modified Centor is presented as a score ranging from 0 to 4.

Microbiological culture of throat swabs is the reference standard for assessing the diagnostic accuracy of point-of-care Strep A tests.

4.5 Outcomes

Where possible subject to the systematic review, this appraisal will consider the following outcomes:

A. Intermediate outcomes:

- Diagnostic accuracy i.e. negative predictive value (NPV), positive predictive value (PPV), sensitivity, specificity
- Discordant results with standard microbiology tests
- Time to test results
- Test failure rate
- Time to antimicrobial prescribing decision
- Changes to antimicrobial prescribing decision
- Number of appointments required per episode
- Number of delayed or immediate antibiotic prescriptions issued

B. Clinical outcomes:

- Morbidity, including post-strep A infection complications such as rheumatic fever and side-effects from antibiotic therapy
- Mortality
- Contribution to antimicrobial stewardship

C. Patient reported outcomes

- Health-related quality of life
- Patient satisfaction with test and antimicrobial prescribing decision
- Healthcare professional satisfaction with test and antimicrobial prescribing decision

Costs will be considered from an NHS and Personal Social Services (PSS) perspective. Costs for consideration may include:

- Cost of equipment, reagents and consumables for tests
- Costs of throat swabs and microbiological culture
- Cost of staff and associated training
- Costs associated with treatment
- Costs associated with onward transmission
- Costs associated with antimicrobial resistance
- Medical costs arising from testing and care such as appointments in primary care or attendance at an urgent care centre
- Medical costs arising from adverse events, including those associated with false negative results and missed treatment; and false positive test results and inappropriate treatment.

5. Methods for assessing clinical effectiveness

5.1. Identification and selection of studies

5.1.1. Search strategy

Scoping searches have been undertaken to inform the development of the search strategies. Additional searches will be carried out where necessary. Searches for studies for cost and quality of life will be developed separately. An iterative procedure will be used, building on the scoping searches undertaken by NICE for this assessment and the searches underpinning the related

Medtech innovation briefing published by NICE in 2018.[11] A copy of the main draft search strategy that is likely to be used in the major databases is provided in Appendix 1. This strategy may be further refined. The search strategy developed for Medline will be adapted as appropriate for other databases. All retrieved full text articles will be screened for potential inclusion.

The search strategy will comprise the following main elements:

- Searching of electronic bibliographic databases
- Contact with experts in the field
- Scrutiny of references of included studies
- Screening of manufacturer's and other relevant organisations' websites for relevant publications

Bibliographic databases will include:

MEDLINE; MEDLINE In-Process & Other Non-Indexed Citations; EMBASE; Cochrane Library (including Cochrane Systematic Reviews, DARE (n.b. ceased adding new records in 2015), CENTRAL, and Health Technology Assessment (HTA) databases); Science Citation Index and Conference Proceedings (Web of Science); and PROSPERO (International Prospective Register of Systematic Reviews).

The following trial databases will also be searched: ClinicalTrials.gov; WHO International Clinical Trials Registry Platform. Specific conference proceedings, to be selected with input from clinical advisors, will be checked for the last five years.

The online resources of various health services research agencies, regulatory bodies, professional societies and manufacturers will be consulted via the Internet. These are likely to include:

- International Network of Agencies for Health Technology Assessment (INAHTA) Publication http://www.inahta.org/
- FDA medical devices: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Databases/default.htm
- European Commission medical devices http://ec.europa.eu/health/medical-devices/
- Professional societies (including British Society for Antimicrobial Chemotherapy, British Infection Association and Public Health England)
- Manufacturers (to be specified – see final scope)

This will be supplemented by targeted web searching using Google advanced search. The reference lists of included studies and relevant review articles will be checked. Identified references will be downloaded to Endnote software.

5.1.2. Inclusion criteria

Studies will be included that meet the criteria for population, interventions, comparator and/or reference standard, outcomes and setting. Inclusion will be restricted to primary studies of any design and year of publication. Full text articles and conference abstracts will be retrieved.

5.1.3. Exclusion criteria

Systematic reviews will not be included in the analysis, unless to identify relevant primary studies from the reference lists. Biological studies, case reports, narrative reviews and editorials will be excluded. Conference abstracts without relevant outcomes data will also be ineligible for evidence synthesis. The EAG will provide details of excluded studies.

5.2. Quality assessment strategy

Two independent reviewers will assess the methodological quality of the included studies, and any disagreements will be resolved by consensus. The methodological quality of the included studies will be assessed using a quality assessment tool for primary diagnostic accuracy studies (QUADAS-2).[13] The methodological quality of studies that report clinical outcomes other than diagnostic accuracy will be assessed using the appropriate quality assessment tools.

5.3. Data extraction strategy

Selection of studies and extraction of study findings will be conducted independently by two reviewers using a piloted data extraction form. Disagreements between reviewers will be resolved by consensus or a third person. The form will collect information on study design, methods, participants, testing procedures and test accuracy. Two reviewers will enter extracted data from selected studies independently into separate Excel spreadsheets. Reviewers will not be blinded to the names of study authors, institutions or publications. Where raw outcome data cannot be extracted directly, authors will be contacted.

5.4. Evidence synthesis strategy

The EAG will describe the tests and outcome characteristics in tables and texts.

If traditional measures of test accuracy can be determined then we will use Review Manager, using its section for diagnostic reviews, to generate coupled forest plots and ROC curves. We will also use MedCalc for producing figures. RevMan may not provide all the statistical analysis required, if so Stata will be used for more complex analysis.

Pooling the results by pairwise or network meta-analysis will be considered using R-Studio and Stata.

Where possible, studies comparing one or more tests with one another will be pooled. The EAG assumes that older versions of tests will have no more implications for practice than current versions, and will only be considered in the analyses if there is no information on the diagnostic accuracy of the newer versions of the tests. However, where meta-analysis is deemed unsuitable for some or all of the data identified (e.g. due to heterogeneity in study characteristics), the EAG may employ a narrative synthesis of the findings or perform meta-regression analyses to identify possible sources of heterogeneity.

If evidence allows, the EAG will stratify meta-analyses according to: children aged 5 to 14 years, adults aged 15 to 75 years, and the elderly, aged over 75 years.

6. Methods for synthesising evidence of cost effectiveness

6.1 Identifying and systematically reviewing published cost-effectiveness studies

Published cost-effectiveness studies will be reviewed. All papers which present findings on the costs and outcomes of the different rapid antigen or molecular tests for detecting Strep A will be reviewed in detail.

6.1.1 Search strategy and data extraction

A comprehensive search of the literature for published economic evaluations (including any existing models), cost studies and quality of life (utility) studies will be performed. The search strategy used will be based on the population element of the strategy developed for the clinical effectiveness review (see Appendix 1), with the addition of appropriate search terms for study types in the large medical databases. Searches will be developed iteratively.

Databases will include:

- MEDLINE (Ovid)
- MEDLINE In-Process Citations and Daily Update (Ovid)
- EMBASE (Ovid)
- NHS Economic Evaluation Database (NHS EED) (Cochrane Library) – N.b. ceased adding new records in 2015
- Science Citation Index (Web of Knowledge)
- Cost-effectiveness analysis (CEA) registry
- Research Papers in Economics (RePAC)
- ScHARRHUD

Additional targeted searches will be performed where necessary to identify other relevant information to support the development of an economic model for this project, these may be directed towards costs, utilities and probabilities as required.

All papers which present findings on the costs and outcomes of the different rapid antigen or molecular tests for detecting Strep A will be reviewed in detail. Data will be extracted by one reviewer and checked by a second, using a standardised data extraction form for the economic studies; this will be developed to summarise the main characteristics of the studies and to capture useful data that can inform the economic model. Any discrepancies will be resolved by discussion. If this is not feasible, a third reviewer will be consulted.

We will review all models identified, examining the scope to refine and update them. The structure of economic models, use of evidence and assumptions, and findings together with deterministic and probabilistic sensitivity analysis, will be critically appraised. The quality of any full economic evaluation studies will be assessed using the CHEERS checklist.[14] Any studies containing an economic model will be further assessed using the framework for the quality assessment of decision analytic modelling.[15]

6.2 Development of a health economic model

In developing the economic model we will consult the previous Health Technology Assessment report assessing rapid antigen detection tests for acute sore throats conducted by Little and colleagues.[16] The main aim of this HTA report was to assess the cost-effectiveness of rapid antigen detection tests for acute sore throats in a GP setting. The authors conducted an economic evaluation alongside the randomised trial; resource use was obtained from GP case notes and from study clinicians and quality-adjusted life years (QALYs) were estimated from EQ-5D scores obtained from a 14-day diary.[16]

We will assess the cost-effectiveness of the alternative rapid antigen detection and molecular tests in conjunction with clinical judgement and the clinical scoring tools in various health-care settings (GP practice, community pharmacy and hospital) from the perspective of UK NHS and PSS. If evidence permits, we will evaluate various subgroups which may include: children (aged 5 to 14), adults (aged 15 to 75), and the elderly (adults over the age of 75 years). We will use a decision-type model and model development will follow NICE reference case recommendations where possible.[17] A final decision on the modelling approach will be made in the light of the clinical effectiveness findings. The time horizon of the model for the majority of patients will be 14 days from presentation at a GP practice/community pharmacy/hospital. If data permits, for the few patients who experience complications, the model time horizon will be extended to 6 months. The EAG may draw on a range of modelling techniques and will finalise its methods when the evidence review is complete. Models will reflect net changes in intermediate, clinical and patient outcomes and costs as data evidence allows.

Information on resource use and costs associated with the different patient pathways will be collected from systematic reviews of the literature, discussions with individual manufacturers (through NICE), and GPs/pharmacists/hospitals and if need be, by eliciting expert clinical advice. Any

remaining gaps for resource use parameters will be filled by assumptions made by the research team. Unit costs data will be based on national data were possible such as the NHS reference costs.[18] For the different rapid antigen or molecular tests, costs will be from published list prices from the NHS supply chain or the manufacturers (through NICE) may be approached to refine understanding and estimation of acquisition, maintenance, service configuration, training and running costs of interventions and the comparator. Costs of consultations with secondary care staff will be drawn from Unit Costs of Health and Social Care[19] and drug costs will be obtained from the British National Formulary.[20]

Health outcomes and utility data will be derived from the literature review including the previous HTA report and other sources, if available. If necessary, to characterise and value the consequences of the tests, published evidence will be augmented with elicitation of expert opinion from specialist advisors and/or the assessment sub-group (ASG) or by assumptions made by the research team.

Models will be constructed in Excel and the statistical programming language R. Results will be expressed as cost per QALY. Using this approach we will summarise the net costs of intervention and comparator approaches, exploring a range of parameters such as test performance, timed saved, scale of use, laboratory configuration, using deterministic and probabilistic sensitivity analyses and sub-group analyses as evidence allows.

7. Handling information from the companies

All data submitted by stakeholders will be considered if received by the EAG no later than 25th February 2019. Data arriving after this date will not be considered. If the data meet the inclusion criteria for the review they will be extracted and quality assessed in accordance with the procedures outlined in this protocol.

Commercial in confidence data provided and specified as such will be highlighted in blue and underlined in the assessment report, followed by an indication of the relevant company name in brackets.

8. Competing interests of authors

The project team have no competing interests in connection with this assessment.

9. Timetable/milestones

Milestone	Date to be completed
Final protocol to NICE	23 November 2018
Progress report to NICE and NETSCC	25 February 2019
Draft assessment report to NICE	22 April 2019
Final assessment report to NICE	20 May 2019
1st Diagnostics Advisory Committee meeting:	17 or 18 June 2019
2nd Diagnostics Advisory Committee meeting:	20 August 2019

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Appendix 1: Draft Medline search strategy for clinical effectiveness review

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) <1946 to November 19, 2018>

Search Strategy:

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1 exp Pharyngitis/ (15044)

2 pharyngit*.ti,ab,kf. (5454)

3 (nasophyryngit* or rhinopharyngit* or epipharyngit*).ti,ab,kf. (177)

4 (tonsillit* or tonsilit*).ti,ab,kf. (5594)

5 ((sore or pain* or ache* or aching or inflam* or infect*) adj3 (pharyn* or throat* or tonsil* or nasopharyn* or rhinopharyn* or epipharyn*)).ti,ab,kf. (9903)

6 or/1-5 (25140)

7 Streptococcal Infections/di, mi (13341)

8 Streptococcus pyogenes/im, ip (5443)

9 7 or 8 (16603)

10 ((strep or streptococcal or group) adj2 A).ti,ab,kf. (559061)

11 9 and 10 (4830)

12 (strep* adj5 (throat* or pharyn* or tonsil*)).ti,ab,kf. (3396)

13 streptoco* A.ti,ab,kf. (475)

14 (group A adj5 streptoco*).ti,ab,kf. (9478)

15 ((streptococcus or strep or staphylococcus) adj1 (pyogenes or pyogenic)).ti,ab,kf. (7684)

16 ((streptococcus or strep) adj1 (epidemicus or erysipelatis or erysipelatos or hemolyticus or haemolyticus or scarlatinae or lancefield)).ti,ab,kf. (237)

17 (s pyogenes or pyogenes s or micrococcus scarlatinae).ti,ab,kf. (2486)

18 lancefield group.ti,ab,kf. (475)

19 gabhs.ti,ab,kf. (392)

20 or/11-19 (18794)

21 Point-of-Care Systems/ (11107)

22 exp Reagent Kits, Diagnostic/ (19322)

23 Antigens, Bacterial/an (7616)

24 (point-of-care or poc or poct or pocts).ti,ab,kf. (17683)

25 ((rapid* or bedside*1 or bed-side*1 or near-patient or nearpatient or extra-laboratory or extralaboratory or office*1) adj6 (test or tests or testing or tested or detect* or diagnos* or screen* or kit or kits or assay* or immunoassay* or determin* or identif* or antigen*1)).ti,ab,kf. (136654)

26 (radt or radts or rdt or rdts).ti,ab,kf. (1812)

27 (antigen*1 adj6 (test or tests or testing or tested or detect* or diagnos* or screen* or kit or kits or assay* or immunoassay* or determin* or identif*)).ti,ab,kf. (100730)

28 (clearview exact* or BD veritor* or strep A rapid test* or quikread go* or alere i* or cobas liat* or genexpert* or ((alere* or testpack* or test-pack* or bionexia* or bio-nexia* or biosynex* or veritor* or cobas* or quikread* or quik-read* or NADAL* or OSOM* or sofia* or xpert*) and (strep A or point of care or point-of-care or POC))).ti,ab,kf. (804)

29 ((abbott or "beckton dickinson" or biopanda or "nal von minden" or sekisui or "orion diagnostica" or roche or cepheid or biomerieux or quidel) and ("strep A" or "point of care" or POC or "rapid test*" or "rapid antigen" or "antigen test*")).ti,ab,kf,in. (621)

30 or/21-29 (269736)

31 (6 or 20) and 30 (1758)

32 exp animals/ not humans/ (4516350)

33 31 not 32 (1645)

34 31 use medp,prem,mesx (115) [medp,prem,mesx are codes for Ovid Medline segments Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily]

35 33 or 34 (1645)