National Institute for Health and Care Excellence

DIAGNOSTICS ASSESSMENT PROGRAMME

Evidence overview

Rapid tests for group A streptococcal infections in people with a sore throat

This overview summarises the key issues for the diagnostics advisory committee's consideration. This document should be read with NICE's final scope for the assessment and the diagnostics assessment report. A glossary of terms is in appendix B.

1 Background

1.1 Introduction

The purpose of this assessment is to evaluate the clinical and cost effectiveness of using rapid tests for detecting group A streptococcus (strep A) bacteria in people with a sore throat, to help inform appropriate prescribing of antibiotics. These tests are intended to be used together with clinical scoring tools, such as FeverPAIN and Centor.

Sore throat is usually a self-limiting condition which does not need treatment. It is usually caused by a viral infection, but some can be caused by a bacterial infection, usually group A streptococcus (strep A). Strep A throat infections are more common in children than adults and the incidence of strep A infections is highest in winter and spring. Most cases of strep A infection resolve without complications. However, in rare cases complications can develop, such as rheumatic fever (which affects the heart), post-streptococcal glomerulonephritis (which affects the kidneys), or necrotising fasciitis (a severe infection of soft tissue). Strep A can also cause invasive group A strep infections (when the bacteria move from the throat into other parts of the

body), leading to sepsis or streptococcal toxic shock syndrome and scarlet fever. Both are notifiable diseases, recognising that they may pose significant harm to human health, to allow for adequate monitoring and early warning of possible outbreaks.

The care pathway for assessing and treating a sore throat is in NICE's guideline on sore throat: antimicrobial prescribing. Healthcare professionals should advise people with a sore throat that the disease usually gets better without treatment, and explain measures of self-care. Antibiotic prescribing for sore throat should be guided by the FeverPAIN or Centor clinical risk scoring tools, unless the patient is systemically very unwell, has symptoms and signs of a more serious illness or condition, or is at high risk of complications. The clinical scoring tools can help identify people who are:

- more likely to benefit from antibiotic (FeverPAIN score of 2 or 3), or
- most likely to benefit from antibiotic (FeverPAIN score of 4 or 5, or a Centor score of 3 or 4).

The rapid tests' purpose is to increase diagnostic confidence of a suspected strep A infection and guide antimicrobial prescribing decisions. The tests have a faster turnaround time than laboratory culture of throat swabs. This may allow a prescribing decision to be made in the initial consultation (but some tests might need confirmation of negative test results by laboratory culture). This may contribute to improved antimicrobial stewardship. The tests could be suitable for all settings where patients present with an acute sore throat. This includes both primary and secondary care, and community pharmacies.

Provisional recommendations on these technologies will be made by the diagnostics advisory committee at the committee meeting on 17 June 2019.

1.2 Scope of the assessment

Table 1 Scope of the assessment

Decision question	Does using rapid tests for group A streptococcal infection as an adjunct to clinical scoring tools to guide antibiotic

	prescribing in people aged 5 and over with sore throats represent a clinical- and cost-effective use of NHS resources?
Populations	People aged 5 and over presenting with symptoms of an acute sore throat who are more or most likely to benefit from an antibiotic by a clinical scoring tool. Potential subgroups include: • Children aged 5 to 14* • Adults aged 15 to 75 • Adults aged over 75** * Children aged 5 to 14 are thought to be at greatest risk of developing scarlet fever. ** Adults aged over 75 are thought to have the greatest case mortality rate for invasive group A strep.
Interventions	• Clearview exact Strep A cassette (Abbott) • Clearview exact Strep A dipstick (Abbott) • BD Veritor plus system group A Strep (Beckton Dickinson) • Strep A rapid test cassette (Biopanda Reagents) • Strep A rapid test dipstick (Biopanda Reagents) • NADAL Strep A test strip (Nal von Minden) • NADAL Strep A cassette (Nal von Minden) • NADAL Strep A plus cassette (Nal von Minden) • NADAL Strep A plus test strip (Nal von Minden) • NADAL Strep A scan test (Nal von Minden) • OSOM Strep A test (Sekisui diagnostics) • QuikRead Go Strep A test kit (Orion Diagnostica) • Alere TestPack Plus Strep A (Abbott) • Bionexia Strep A plus cassette (Biomerieux) • Bionexia Strep A dipstick (Biomerieux) • Biosynex Strep A (Biosynex) • Sofia Strep A FIA (Quidel) • Alere i Strep A (discontinued – replaced by ID NOW Strep A 2 test; Abbott) • Alere i Strep A 2 (rebranded to ID NOW Strep A 2; Abbott) • Cobas Strep A assay on Liat system (Roche) • Xpert Xpress Strep A (Cepheid) All rapid tests would be used in conjunction with clinical

	judgement and a clinical scoring tool such as FeverPAIN or Centor.
Comparator	Antibiotic prescribing decisions using clinical judgement and a clinical scoring tool such as FeverPAIN or Centor. The reference standard for assessing the accuracy of the rapid strep A tests is microbiological culture of throat swabs.
Healthcare setting	Primary care: • medical services • pharmacy services • urgent care/walk-in services. Secondary care: • urgent care/walk-in services • emergency departments.
Outcomes	Intermediate measures for consideration may include: • diagnostic accuracy • 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.
	Clinical outcomes for consideration may include: • morbidity, including post-strep A infection complications such as rheumatic fever and side-effects from antibiotic therapy • mortality • contribution to antimicrobial stewardship and onward transmission of infection.
	Patient-reported outcomes for consideration may include: • health-related quality of life • patient or carer 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 perspective. Costs for consideration may include: • cost of equipment, reagents and consumables for

	rapid 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 from testing and care such as appointments in primary care or attendance at an urgent care centre • medical costs from adverse events, including those associated with false negative results and missed treatment, and false positive test results and inappropriate treatment.
	The cost effectiveness of interventions should be expressed in terms of incremental cost per quality-adjusted life year.
Time horizon	The time horizon for estimating clinical and cost effectiveness should be long enough to reflect any differences in costs or outcomes between the compared technologies.

Further details including descriptions of the interventions, comparator, care pathway and outcomes can be found in the final scope.

2 The evidence

This section summarises data from the diagnostics assessment report compiled by the external assessment group (EAG).

2.1 Clinical effectiveness

The EAG did a systematic review to identify evidence on the clinical effectiveness of rapid tests for detecting suspected strep A infection in people with sore throats, including:

- diagnostic performance
- impact on prescribing behaviours and clinical outcomes
- contribution to antimicrobial stewardship and onward transmission of infection.

Full details of the inclusion and exclusion criteria start on page 40 of the diagnostics assessment report.

The EAG found 38 studies that met the inclusion criteria, described in detail in table 6, starting on page 53 of the diagnostic assessment report:

- Of these studies, 35 studies reported test accuracy data and 12 reported antibiotic prescribing behaviours (of which 9 studies reported both outcomes). There were no studies reporting on clinical outcomes such as morbidity, mortality, contribution to antimicrobial stewardship or onward transmission rate.
- There were 26 studies reported in peer-reviewed journals (full-text articles), 3 in conference abstracts, 4 in the FDA documents, and 5 in unpublished manufacturers' data.
- There were 31 studies reporting on rapid antigen detection tests, and 9 on rapid molecular tests, including 2 studies that compared rapid antigen detection tests and molecular tests.

The included studies reported data for either children or adults, or for mixed age groups. However, age group definitions varied between studies. Only 2 studies met the age criterion for children (ages 5 to 14 years) and further 2 studies met the age criterion for adults (age 15 years or more) defined in the topic scope. There were no studies reporting data for the elderly population.

Sore throat clinical scoring tools such as Centor, modified Centor (McIsaac) or FeverPAIN were reported in 16 studies. Only 2 studies included people with a Centor score of 3 or more, or FeverPAIN score of 4 or more; the people who would have a rapid test in current practice. Both studies reported antibiotic prescribing behaviours only. There were 2 test accuracy studies that reported outcomes separately by Centor score. All other studies enrolled people with lower clinical scores than those in the scope, or did not use clinical scores as an inclusion criterion.

Across studies, the prevalence of strep A ranged from 15% to 49%, with no clear demographic or clinical patterns accounting for this variation, and no identified differences between primary and secondary care settings.

Quality assessment of included studies

The QUADAS-2 quality assessment of the test accuracy studies is described starting on page 63 of the diagnostic assessment report. The methodological and reporting quality of the 26 studies was poor. All studies were considered at high risk of bias in at least 1 domain, and 13 studies were considered at high risk of bias in 2 or more domains. There were also concerns about generalisability of findings to the NHS because rapid tests would only be offered to people with Centor scores of 3 or more, or FeverPAIN scores of 2 or more (see above). However, all but 3 studies either did not use any clinical scoring tool, or used lower cut-offs than recommended in the UK (1 of these 3 studies was later excluded because of the incomplete accuracy data). There were 17 studies that also enrolled children under the age of 5 (less than 10% of the total enrolled population). In the UK, these children would follow a different care pathway to adults and children above 5 and so were excluded from the scope of this assessment.

The risk of bias assessment of studies reporting antibiotic prescribing behaviours is described starting on page 68 of the diagnostic assessment report. The methodological quality of the 3 randomised controlled trials (RCTs) was fair, as assessed by the Cochrane risk of bias tool. No domains were considered at high risk of bias but 1 to 3 domains per study had unclear risk of bias. Of 9 cohort studies, 3 assessed hypothetical prescribing behaviours according to the prescribing guidelines and were not quality appraised. The remaining 6 cohort studies were assessed using the Joanna Briggs Institute Critical Appraisal Checklist for analytical cross-sectional studies. There was 1 study with unclear risk of bias in 1 domain, and 5 studies were at high risk of bias in 1 or more domains.

Evidence on the diagnostic performance of rapid tests for strep A infection

Diagnostic accuracy of rapid tests in people more and most likely to benefit from antibiotics

Only 2 studies reported the diagnostic accuracy of the rapid tests in people who are more (FeverPAIN score of 2 or 3), or most (Centor score of 3 or 4, or a FeverPAIN score of 3 or 4) likely to benefit from antibiotics. A full description of these starts on page 92 of the diagnostic assessment report.

Humair et al. (2006) investigated the accuracy of the Alere TestPack Plus Strep A test in adults with a Centor score of 2 or more, in a primary care setting in Switzerland. In patients with a Centor score of 3 or more (n=224), the sensitivity of the rapid test was 95% (95% confidence interval [CI], 89% to 98%), and the specificity was 94% (95% CI, 88% to 98%). In comparison, in patients with a Centor score of 2 (n=148), the sensitivity was lower, estimated as 80% (95% CI, 63% to 92%), but the specificity was similar, estimated as 96% (95% CI, 91% to 99%).

Llor et al. (2011) investigated the accuracy of the OSOM Strep A test in adults with a Centor score of 1 or more, in a primary care setting in Spain. In patients with a Centor score of 3 or more (n=160), the test had a sensitivity of 92% (95% CI, 76% to 98%) and a specificity of 96% (95% CI, 89% to 99%). In comparison, in patients with a Centor score of 1 or 2 (n=116), the test had a sensitivity of 85% (95% CI, 55% to 98%) and a specificity of 93% (95%CI, 87% to 96%).

Diagnostic accuracy of rapid tests in unselected populations with acute sore throat

Most studies recruited either all patients with acute sore throat, without using the clinical scoring tools, or used these tools at a lower threshold than in the scope. Across studies (n=33), there was a wide variation in sensitivity (67.9% to 100%), and specificity (73.3% to 100%) of the rapid tests. There were 2

studies with inconsistent results, preventing the construction of a reliable 2×2 table. These were excluded during the data extraction. Accuracy data for all individual tests are summarised in table 11, figure 7 and figure 8, starting on page 81 of the diagnostic assessment report.

Accuracy estimates for 9 tests (Strep A rapid test cassette and dipstick [Biopanda], 5 NADAL Strep A tests, Alere i Strep A 2 tests and Xpert Xpress Strep A test) were only available from unpublished manufacturer data or Food and Drug Administration (FDA) reports. The EAG noted that estimates of test accuracy from studies in FDA documents or unpublished company data seem systematically higher than estimates from the peer-reviewed published studies. Also, quality assessment of unpublished studies was not possible because of lack of information. Therefore, comparisons between tests with different levels of evidence (unpublished manufacturer data, single peer-reviewed study and multiple peer-reviewed studies) should be made with caution.

Meta-analysis was only possible for 5 tests (see figure 9 on page 91 of the diagnostic assessment report for details).

Head-to-head comparison of the diagnostic accuracy of different tests

Only 4 studies directly compared tests, details start on page 90 of the diagnostic assessment report. These studies suggest there may be some variation in accuracy between tests (Table 2). Because of the large degree of inter-study variability, it is not possible to compare the relative accuracy of different tests across different studies.

Table 2. Head-to-head comparison of accuracy of different rapid tests

Study	Setting	Age group	Clinical scoring tool criteria	Number of patients	Strep A prev, %	Rapid strep A test	Sensitivity (95% CI), %	Specificity (95% CI), %
Azrad et al. 2019	Secondary care	Not reported	None	100	25.0	BD Veritor System[1]	80 (59 to 92)	79 (67 to 87)
						QuikRead Go Strep A kit	80 (59 to 92)	73 (62 to 83)
Berry et al. 2018	Secondary care	Children	None	215	19.5	BD Veritor System[1]	76 (60 to 87)	94 (89 to 97)
						Alere i Strep A	100 (90 to 100)	91 (86 to 95)
Lacroix et al. 2018	Secondary care	Children	McIsaac ≥ 2	1002	35.7	Alere TestPack Plus Strep A	76 (71 to 80)	97 (95 to 98)
						Sofia Strep A FIA	85 (81 to 89)	95 (93 to 97)
Weinzierl et al. 2018	Secondary care	Children	None	160	38.1	Alere i Strep A	98 (90 to 100)	100 (95 to 100)
						OSOM Strep A test	89 (77 to 95)	91 (83 to 96)

[1] BD Veritor plus system group A strep

Diagnostic accuracy by age group

A summary of the diagnostic accuracy of rapid tests for different age groups starts on page 97 of the diagnostic assessment report. There were 7 studies that enrolled adults only and 10 studies that enrolled children only. There were 3 other studies that enrolled both adults and children, with separate accuracy data for each age group, allowing for a within-study comparison (Table 3). These studies showed there were no clear trends in the diagnostic accuracy of the rapid tests between different age groups. All other studies enrolled a mixed population of adults and children, or did not report the age group.

Table 3. Comparison of accuracy of rapid strep A tests by age group

Citation	Test	Setting	Clinical scoring tool criteria	Number of patients	Strep A prev, %	Age group	Sensitivity (95% CI), %	Specificity (95% CI), %
Cohen et al. 2015	Alere i Strep A	Secondary	McIsaac, all scores	481	30.3	Children	96 (91 to 99)	93 (89 to 96)
						Adults	95 (74 to 100)	97 (92 to 99)
McIsaac et al. 2004	Alere TestPack Plus Strep A	Primary	McIsaac 2 or above	787	29	Children	86 (79 to 91)	99 (97 to 100)
						Adults	77 (65 to 86)	99 (97 to 100)
Stefaniuk et al. 2017	QuikRead Go Strep A test kit	Primary	McIsaac/ Centor, all scores	96	22.4	Children	80 (56 to 94)	91 (72 to 99)
						Adults	100 (86 to 95)	79 (60 to 92)

Diagnostic accuracy by healthcare setting

Diagnostic accuracy data for the rapid tests by healthcare setting is summarised starting on page 105 of the diagnostic assessment report. A total of 10 studies were done in primary care and 14 in secondary care; healthcare setting was not reported in the remaining studies. No studies compared the diagnostic accuracy of the rapid tests in different healthcare settings. Because of the large degree of variability between studies, it is not possible to make any conclusions about the relative accuracy of rapid tests in the primary setting compared with the secondary care setting.

Diagnostic accuracy of the rapid strep A tests using polymerase chain reaction (PCR) to resolve discordant cases

Discordant results between the rapid tests and microbiological culture of throat swabs were resolved using PCR in 4 studies (Table 4). A large proportion of false positive results (that is, results that were positive by the rapid tests and negative microbiological culture of throat swabs) were confirmed positive for strep A by PCR. A large proportion of false negative results (that is, results that were negative by the rapid tests and positive by microbiological culture of throat swabs) were also confirmed positive for strep A by PCR. This shows that the reference standard used in this assessment is not 100% accurate. Therefore, the accuracy of rapid strep A tests could be

under or overestimated. However, as PCR can detect indolent strep A ('strep A carriers'), the clinical significance of this is unclear.

Table 4. Accuracy of the rapid tests using PCR to resolve discordant cases

Citation	Rapid test	False positive results[a]	PCR positive	False negative results[b]	PCR positive
Wang et al. 2017	Cobas Strep A assay on Liat system	20	20/20	3	3/3
Berry et al. 2018	BD Veritor plus system group A Strep	11	6/11	10	10/10
	Alere i Strep A	15	14/15	0	n/a
Cohen et al. 2015	Alere i Strep A	18	13/18	6	2/6
Lacroix et al. 2018	Sofia Strep A FIA	31[c]	11/20[c]	53	NR
	Alere TestPack Plus Strep A	21	9/21	87	NR

[a] False positive result: results that were positive by the rapid strep A test and negative by the microbiological culture of throat swab.
[b] False negative result: results that were negative by the rapid strep A test and positive by the microbiological culture of throat swab.
[c] There were 11 samples missing, for which PCR assays could not be performed.

Diagnostic accuracy of rapid tests compared with clinical scoring tools

The diagnostic accuracy of rapid tests and clinical scoring tools was directly compared in 6 studies, of which 4 studies used Centor and 2 used McIsaac tools (Table 5). At a score of 3 or more, the estimates of sensitivity for the clinical scoring tools ranged from 73.5% to 97.2%, but the specificity estimates were low, ranging from 17.2% to 64.8%. Rapid tests showed higher specificity in all studies (range, 84.9% to 99.1%), and also higher sensitivity in 4 of 6 studies (range, 82.9% to 94.6%), than the clinical scoring tools.

There were 2 studies comparing the accuracy of clinical scoring tools in different age groups, reporting higher sensitivity and lower specificity in children compared with adults. In the study by McIsaac et al. (2004), a McIsaac score of 3 or more produced sensitivity estimates of 88.4% (95% CI 82.0% to 92.8%) in children and 76.7% (95% CI 65.1% to 85.8%) in adults, and specificity estimates of 23.4% (95% CI 18.8% to 28.7%) and 43.9% (95% CI 37.8% to 50.1%), respectively. In the study by Stefaniuk et al. (2017),

Centor or McIsaac score of 3 or more produced sensitivity estimates of 100% (95% CI 80.0% to 100.0%) in children and 73.9% (95% CI 51.3% to 88.9%) in adults, and specificity estimates of 8.3% (95% CI 1.5% to 28.5%) and 41.4% (95% CI 24.1% to 60.9%), respectively.

All but 1 study were done in primary care. The single study in secondary care reported higher sensitivity and lower specificity of the McIsaac scoring tool compared with most studies done in primary care. However, it is unclear if this difference is related to the healthcare setting, age group (the study was done in children), or because of other differences between the studies.

Table 5. Accuracy of clinical scoring tools compared with rapid strep A tests

Citation	Rapid test	Setting	Age group	Population	Number of patients	Strep A prevalence, %	Centor/McIsaac score 3 or higher		Rapid strep A test	
							Sensitivity (95% CI), %	Specificity (95% CI), %	Sensitivity (95% CI), %	Specificity (95% CI), %
Humair et al. 2006	Alere TestPack Plus Strep A	Primary care	Adults	Centor 2 or higher	372	46.9	75.0 (67.8 to 82.2)	48.7 (42.3 to 55.1)	91.4 (85.2 to 95.3)	95.3 (91.4 to 94.7)
Llor et al. 2009	OSOM Strep A test	Primary care	Adults	Centor 2 or higher	222	21.2	85.5 (76.1 to 94.8)	37.7 (30.4 to 45.1)	94.6 (83.9 to 98.6)	91.6 (86.1 to 95.2)
Llor et al. 2011	OSOM Strep A test	Primary care	Adults	Centor 1 or higher	276	16.7	73.5 (58.7 to 84.6)	64.8 (58.1 to 70.9)	89.8 (77.0 to 96.2)	93.8 (89.7 to 93.3)
Stefaniuk et al. 2017	QuikRead Go Strep A test kit	Primary care	Children and adults	Any Centor or McIsaac score	95	22.4	86.1 (71.4 to 94.2)	25.0 (14.5 to 39.2)	90.7 (77.0 to 97.0)	84.9 (71.9 to 92.8)
McIsaac et al. 2004	Alere TestPack Plus Strep A	Primary care	Children and adults	McIsaac 2 or higher	787	29	84.6 (80.0 to 89.3)	32.9 (29.0 to 36.8)	82.9 (77.2 to 87.4)	99.1 (97.8 to 99.7)
Pauchard et al. 2003	Strep A Rapid Test (Biopanda)	Secondary care	Children	Any McIsaac score	193	37	97.2 (89.3 to 99.5)	17.2 (11.2 to 25.3)	84.5 (73.5 to 91.4)	91.0 (84.1 to 95.2)

Evidence on test failure rates

Rapid test failure rates were generally low, as reported in 5 studies:

- Alere i Strep A: 0% and 2.8% (2 studies)
- Alere TestPack Plus Strep A: 0.3% and 1.3% (2 studies)
- Sofia Strep A FIA: 4.7% (1 study)

The EAG noted that these differences could be because of environmental factors such as staff training rather than issues with the tests.

Evidence on antibiotic prescribing behaviours

The 3 RCTs reporting on antibiotic prescribing, done in the UK, Spain and Canada, all showed a decrease in antibiotic prescribing with the rapid tests (see Table 6 for details). However, in the UK study by Little et al. (2013), although the rate of immediate or delayed prescriptions decreased with the use of rapid strep A test (Alere TestPack Plus Strep A), the reported use of antibiotics was comparable between the clinical scoring group and the clinical scoring group plus rapid strep A test group (37% versus 35%; Table 6).

The before-and-after study by Bird et al. (2018) assessed antibiotic prescribing rates before and after the introduction of the McIsaac clinical scoring tool and a rapid strep A test (Bionexia Strep A) in a UK paediatric emergency department. Following the introduction of this program, antibiotic prescribing rates decreased from 79% at baseline to 24% in the first year and 28% in the second year. However, random annual fluctuations and seasonality may have confounded the results (see Table 6 for details).

Information on single-arm cohort studies starts on page 131 in the diagnostic assessment report.

Table 6. Randomised clinical trials reporting antibiotic prescribing behaviours

Citation; country	Index test	Study details	Treatment decisions algorithms	Antibiotic prescribing behaviour
Little et al. 2013; UK	Alere TestPack Plus Strep A (IMI TestPack)	3-arm randomised trial: • Arm 1: delayed antibiotics • Arm 2: clinical scoring tool • Arm 3: clinical scoring tool plus rapid Strep A test Population: adults and children 3 years or older Setting: primary care	Arm 1: Treatment decisions based on clinical assessment without a tool. Depending on severity, either immediate antibiotic, no antibiotic, or delayed antibiotic (prescription for collection after 3 to 5 days if symptoms didn't improve or worsened). Arm 2: Patients with FeverPAIN scores of 0 to 1: no antibiotics; 2 to 3: delayed antibiotic; 4 or higher: immediate antibiotic. Arm 3: Patients with FeverPAIN score 0 to 1: no antibiotics or test; score 2: delayed antibiotics (no test); score 3 or higher: rapid strep A test (test positive: immediate antibiotic; test negative: no antibiotic).	Immediate or delayed prescribing: • Arm 1: 89% (185/207) patients • Arm 2: 59% (124/211) patients • Arm 3: 40% (86/213) patients Reported use of antibiotics: • Arm 1: 46% (75/164) patients • Arm 2: 37% (60/161) patients • Arm 3: 35% (58/164) patients
Llor et al. 2011; Spain	OSOM Strep A test	2-arm cluster randomised trial; healthcare centres randomised to: control arm (Centor) or intervention arm (rapid Strep A test + Centor) Population: adults ≥15 years Setting: primary care	No specific treatment algorithm. • control arm: patients assessed only using clinical criteria (Centor) • intervention arm: patients assessed with both a Centor score and a rapid strep A test.	Antibiotic prescribing: • Control arm: 64% (168/262) patients • Rapid Strep A test arm: 44% patients (123/281; 98% test-positive patients and 31% test-negative patients)
Worrall et al. 2007; Canada	Clearview Exact Strep A (not reported if cassette or dipstick)	4-arm cluster randomised trial (8-10 randomised doctors per arm): • Arm 1: control (usual practice) • Arm 2: sore throat decision rules (STDR; modified Centor) • Arm 3: rapid Strep A test • Arm 4: STDR plus rapid test Population: adults ≥19 years Setting: primary care	Arm 1: clinician's decisions as per usual practice Arm 2, STDR score 1 or lower: no need for antibiotics; score 2: decisions made by the clinician; score 3 to 4: antibiotics needed Arm 3: clinician's decisions informed by test results Arm 4, STDR score 1 or lower: no need for antibiotics; score 2: rapid strep A test; score 3 to 4: antibiotics needed Clinicians were recommended to follow the guidance but it was not enforced	Antibiotic prescribing: • Arm 1: 58% (82/141) patients • Arm 2: 55% (94/170) patients • Arm 3: 27% (32/120) patients • Arm 4: 38% (39/102) patients

2.2 Costs and cost effectiveness

The EAG did a search to identify existing studies investigating the cost effectiveness of the rapid strep A tests in people with a sore throat, and also developed 4 de novo economic models.

Systematic review of cost-effectiveness evidence

The EAG found 3 cost-effectiveness studies for the rapid strep A tests, described starting on page 139 of the diagnostics assessment report. However, 2 of these studies only reported cost per case and did not report sufficient information to allow full data extraction and critical appraisal of the models. The economic evaluation by Little et al. (2014) was considered high quality according to the consolidated health economic evaluation reporting standards (CHEERS) checklist.

Little et al. (2014) did an economic analysis alongside a RCT (reported in Little et al. 2013). The RCT was based in UK primary care clinics, and included both adults and children aged 3 years or more with acute sore throat (see Table 6 for details). Patients were randomised to targeted antibiotic use according to:

- delayed antibiotics
- FeverPAIN clinical scoring tool
- rapid strep A test (Alere TestPack Plus Strep A; used with FeverPAIN tool).

The economic analysis was from the NHS perspective and the time horizon was short (14 and 28 days), so long-term effects were not captured. The analysis included a cost-effectiveness analysis (cost per change in symptom severity) and a cost-utility analysis (cost per quality-adjusted life year [QALY]). QALYs were calculated using the mean EQ-5D scores from the 14-day diary records, and were adjusted for differences in baseline characteristics. Cost-effectiveness acceptability curves (CEACs) were generated using bootstrapping with 5,000 samples. Full details are in table 21, starting on page 142 of the diagnostic assessment report.

In the cost-utility analysis, the delayed prescribing group was dominated by the FeverPAIN group for both time frames. The incremental cost-effectiveness ratio (ICER) for testing strategy compared with FeverPAIN was £74,286 for the 14-day time frame and £24,528 for the 28-day time frame. At £30,000 per QALY, the probabilities of each strategy being cost effective were 28%, 38% and 35% for the delayed prescribing, FeverPAIN clinical score and the testing strategy, respectively, for the 28-day time frame.

Economic analysis methods

The study by Little et al. (2014) included only 1 of the 21 rapid tests relevant to this assessment. Also, it only considered a primary care setting, and did not assess adult and children populations separately. Therefore, the EAG constructed 4 de novo economic models to assess the cost effectiveness of all relevant rapid tests in people with acute sore throat:

- adults in primary care
- adults in secondary care
- children in primary care
- children in secondary care.

The model was created for adults in primary care and then adapted for children and secondary care. No economic model was developed for the elderly population or for the pharmacy setting because of the lack of evidence for the model.

Model structure

A decision tree was created to simulate the potential care pathways associated with the use of rapid tests in addition to clinical scoring tools compared with the use of clinical scoring tools only (current practice), in people with acute sore throat. The full model structure is in figures 12 to 14, starting on page 149 of the diagnostic assessment report.

The economic analysis was from the UK NHS and Personal Social Service (PSS) perspective. A 1-year time horizon was used to capture the impact of rare but serious complications of strep A infection on costs and outcomes (a shorter time frame of 14 days was analysed in sensitivity analyses). No discounting was applied to costs and benefits because of the 1-year time horizon.

Model inputs

Prevalence

A prevalence of 22.6% was used for adults, based on the study by Little et al. (2014). The study enrolled patients aged 5 years or older in the UK primary care. For children, an estimate of 30.2% was assumed, based on the median of 3 non-UK studies of children in primary care.

Diagnostic accuracy of clinical scoring tool

The accuracy estimates for the Centor clinical scoring tool were taken from the meta-analysis by Aalbers et al. (2011). It focused on Centor to predict strep A pharyngitis in adults (15 years or older) presenting in primary care. At the Centor threshold of 3 or more, the sensitivity was estimated as 49% (95% CI 38% to 60%), and specificity as 82% (95% CI 72% to 88%). Alternative Centor thresholds were looked at in sensitivity analyses. There were no studies reporting the accuracy of FeverPAIN clinical scoring tool so this tool could not be modelled.

Diagnostic accuracy of rapid tests

The accuracy estimates for the rapid strep A tests were from the systematic literature review done by the EAG.

The sensitivity of the rapid tests ranged from 68% to 100%, and the specificity from 79% to 100% (Table 7 and Table 8). The estimates of accuracy based on unpublished manufacturers' data or FDA reports (the only source of accuracy data for 9 rapid tests) were consistently higher than the estimates from the published peer-reviewed studies. Therefore, the economic models

based solely on manufacturers' test accuracy data should be interpreted with caution.

Table 7: Test accuracy data used in the economic model for adults in primary care

Test ID	Test Name	Manufacturer	Sensitivity (95%CI), %	Specificity (95%CI), %	Data source
1	Clearview Exact Strep A cassette	Abbott	68 (54 to 80)	95 (92 to 97)	1 abstract (Andersen 2003)
2	Clearview Exact Strep A dipstick	Abbott	68 (54 to 80)	95 (92 to 97)	1 abstract (Andersen 2003)
3	BD Veritor Plus system group A Strep cassette	Beckton Dickinson	78 (67 to 87)	90 (86 to 93)	2 studies (Berry 2018; Azrad 2019)
4	Strep A rapid test cassette	Biopanda Reagents	95 (90 to 98)	98 (96 to 99)	1 manufacturer response to NICE
5	Strep A rapid test dipstick	Biopanda Reagents	95 (90 to 98)	98 (96 to 99)	No data; assumed the same accuracy as the cassette version of the test
6	NADAL Strep A test strip	nal von minden GmbH	98 (92 to 100)	98 (94 to 99)	1 manufacturer response to NICE
7	NADAL Strep A cassette	nal von minden GmbH	98 (92 to 100)	98 (94 to 99)	1 manufacturer response to NICE
8	NADAL Strep A plus cassette	nal von minden GmbH	98 (92 to 100)	98 (94 to 99)	1 manufacturer response to NICE
9	NADAL Strep A plus test strip	nal von minden GmbH	98 (92 to 100)	98 (94 to 99)	1 manufacturer response to NICE
10	NADAL Strep A scan test cassette	nal von minden GmbH	98 (92 to 100)	98 (94 to 99)	1 manufacturer response to NICE
11	OSOM Strep A test test strip	Sekisui Diagnostics	92 (76 to 98)	96 (89 to 99)	3 studies (Llor 2011; Llor 2009; Bura 2017)
12	QuikRead Go Strep A test kit	Orion Diagnostica	100 (85 to 100)	79 (60 to 92)	1 study (Stefaniuk 2017)
13	Alere TestPack Plus Strep A cassette	Abbott	95 (89 to 98)	94 (88 to 98)	1 study (Humair 2006)
14	Bionexia Strep A plus cassette	Biomerieux			No data
15	Bionexia Strep A dipstick dipstick	Biomerieux	85 (74 to 92)	91 (84 to 95)	1 abstract (Pauchard 2003)
16	Biosynex Strep A cassette	Biosynex			No data
17	Sofia Strep A FIA	Quidel	85 (81 to 89)	95 (93 to 97)	1 study (Lacroix 2018)
18	Alere i Strep A (discontinued)	Abbott	95 (74 to 100)	97 (92 to 99)	1 study (Cohen 2015)
19	Alere i Strep A 2 (ID NOW Strep A 2)	Abbott	98 (96 to 100)	93 (91 to 95)	1 FDA Report
20	Cobas Strep A Assay on Liat system	Roche Diagnostics	98 (93 to 100)	93 (90 to 96)	1 study (Wang 2017)
21	Xpert Xpress Strep A	Cepheid	100 (99 to 100)	94 (92 to 96)	1 manufacturer response to NICE and 1 FDA report

Table 8: Test accuracy data used in economic model for children in primary care

Test ID	Test Name	Manufacturer	Sensitivity (95%CI), %	Specificity (95%CI), %	Data source
1	Clearview Exact Strep A cassette	Abbott	68 (54 to 80)	95 (92 to 97)	1 study (Andersen 2003)
2	Clearview Exact Strep A dipstick	Abbott	68 (54 to 80)	95 (92 to 97)	1 study (Andersen 2003)
3	BD Veritor Plus system group A Strep cassette	Beckton Dickinson	76 (61 to 88)	94 (89 to 97)	1 study (Berry 2018)
4	Strep A rapid test cassette	Biopanda Reagents	95 (90 to 98)	98 (96 to 99)	1 manufacturer response to NICE
5	Strep A rapid test dipstick	Biopanda Reagents	95 (90 to 98)	98 (96 to 99)	No data; assumed the same accuracy as the cassette version of the test
6	NADAL Strep A test strip	nal von minden GmbH	98 (92 to 100)	98 (94 to 99)	1 manufacturer response to NICE
7	NADAL Strep A cassette	nal von minden GmbH	98 (92 to 100)	98 (94 to 99)	1 manufacturer response to NICE
8	NADAL Strep A plus cassette	nal von minden GmbH	98 (92 to 100)	98 (94 to 99)	1 manufacturer response to NICE
9	NADAL Strep A plus test strip	nal von minden GmbH	98 (92 to 100)	98 (94 to 99)	1 manufacturer response to NICE
10	NADAL Strep A scan test cassette	nal von minden GmbH	98 (92 to 100)	98 (94 to 99)	1 manufacturer response to NICE
11	OSOM Strep A test test strip	Sekisui Diagnostics	94 (89 to 98)	95 (91 to 98)	1 study (Llor 2011)
12	QuikRead Go Strep A test kit	Orion Diagnostica	80 (56 to 94)	91 (72 to 99)	1 study (Stefaniuk 2017)
13	Alere TestPack Plus Strep A cassette	Abbott	86 (79 to 91)	99 (97 to 100)	1 study (McIsaac 2004)
14	Bionexia Strep A plus cassette	Biomerieux			No data
15	Bionexia Strep A dipstick	Biomerieux	85 (74 to 92)	91 (84 to 95)	1 abstract (Pauchard 2013)
16	Biosynex Strep A cassette	Biosynex			No data
17	Sofia Strep A FIA	Quidel	85 (81 to 89)	95 (93 to 97)	1 study (Lacroix 2018)
18	Alere i Strep A (discontinued)	Abbott	98 (95 to 100)	96 (89 to 100)	3 studies (Berry 2018; Cohen 2015; Weinzierl 2018)
19	Alere i Strep A 2 (ID NOW Strep A 2)	Abbott	98 (96 to 100)	93 (91 to 95)	1 FDA Report
20	Cobas Strep A Assay on Liat system	Roche Diagnostics	98 (93 to 100)	93 (90 to 96)	1 study (Wang 2017)
21	Xpert Xpress Strep A	Cepheid	100 (99 to 100)	94 (92 to 96)	1 manufacturer response to NICE and 1 FDA report

Treatment-related probabilities and complication rates

Treatment-related probabilities and complication rates used in the model are in Table 9.

Table 9 Treatment-related probabilities and complication rates

Description of parameter	Mean	SE[a]
GP practice		
Proportion attending repeat GP consultation following GAS infection	0.142	0.007
Antibiotic prescribing probabilities		
Probability immediate prescription if Centor score is 3 or higher, or positive test	1.00	
Probability delayed prescription if Centor score is below 3 (current practice arm)	0.51	0.026
Probability delayed prescription if negative test (intervention arm)	0.267	0.014
Probability antibiotics use given delayed prescription	0.46	0.023
Probability antibiotics use given immediate prescription	1.0	
Complication rates following GAS infection		
Probability of complication given antibiotics (treated infection)	0.013	0.0005
Probability of complications given no antibiotics (untreated infection)	0.015	0.0007
Proportion of complications that are non-suppurative (i.e. rheumatic fever)	0.0001	
Adverse effects of penicillin		
Penicillin-induced rash	0.02	
Penicillin-induced anaphylaxis	0.0001	

[a] Standard error (SE) derived assuming upper and lower bound equal to 10% of the mean estimate.

Health-related quality of life and QALY decrements

The health impact of each pathway was expressed in QALYs, calculated by subtracting the disutilities associated with treated and untreated strep A infection, complications of strep A infection and adverse effects of penicillin (Table 10) over 1 year from the mean baseline utilities. Mean disutilities were based on published literature (Neuner et al. 2003; reported as quality-adjusted life days [QALD]), by converting QALDs to utility decrements.

The mean baseline utilities in the model were based on a general UK population: 0.863 for adults and 0.94 for people under 25 years (Kind et al. 1998). The latter is the closest age group to children and therefore was used as a baseline utility in the paediatric models.

Table 10 Disutilities associated with strep A infection and complications

	Mean quality-adjusted life days lost	Mean utility decrement used in the model[1]	Standard error[2]
Utility decrement associated with strep A infections			
Untreated infection	0.25	0.000685	0.00005
Treated infection	0.15	0.000411	0.00003
Utility decrement associated with strep A infection complications			
Peritonsillar abscess	5	0.0137	0.0007
Rheumatic fever	76.5	0.209	0.011
Utility decrement associated with adverse effects of penicillin			
Penicillin-induced anaphylaxis	9	0.025	0.0013
Penicillin-induced rash	0.65	0.0017	0.0001

[1] Calculated by converting quality adjusted life days to utilities;

[2] Standard error (SE) derived assuming upper and lower bound equal to 10% of the mean estimate.

Costs

Costs were calculated using 2017/2018 prices. The total costs for each strategy (current practice and rapid tests) include GP consultations, antimicrobial therapy, and managing strep A infection-related complications and adverse effects of penicillin.

Cost data were available for 14 of the 21 rapid tests in this assessment (Table 11). The cost of testing also accounted for additional GP time needed to process the test, which ranged from 5 to 12 minutes depending on the test. The cost of testing also accounted for hardware costs. The annual equivalent costs of hardware were estimated using a discount rate of 3.5% and its appropriate lifespan (as reported by manufacturers or assumed an average 2-years lifespan as per expert advice). This cost was then added to the total cost of testing, assuming that 2 people with a sore throat would be seen every day in a medium sized GP practice. Some rapid tests also need confirmation of the negative results by the microbiological culture of throat swabs (£8 per sample), as specified in the information for use documents and indicated in Table 11.

Treatment costs of strep A infection, its complications, and adverse events of penicillin are listed in Table 12.

Table 11 Test costs

Test ID	Test Name	Cost	Test process time	Throat culture[1]
1	Clearview Exact Strep A cassette (Abbott)	£2.72	5	Yes
2	Clearview Exact Strep A dipstick (Abbott)	£1.92	5	Yes
3	BD Veritor Plus system group A Strep Assay cassette (Beckton Dickinson)			
4	Strep A rapid test cassette (Biopanda Reagents)	£0.82	5	Yes
5	Strep A rapid test dipstick (Biopanda Reagents)	£0.64	5	Yes
6	NADAL Strep A test strip (nal von minden GmbH)	£1.20	5	No
7	NADAL Strep A cassette (nal von minden GmbH)	£1.40	5	No
8	NADAL Strep A plus cassette (nal von minden GmbH)	£1.50	5	No
9	NADAL Strep A plus test strip (nal von minden GmbH)	£1.30	5	No
10	NADAL Strep A scan test cassette (nal von minden GmbH)	£1.96	5	No
11	OSOM Strep A test strip (Sekisui Diagnostics)			
12	QuikRead Go Strep A test kit (Orion Diagnostica)	£4.34	5	Assumed yes[2]
13	Alere TestPack Plus Strep A cassette (Abbott)	£2.70	5	Assumed no[3]
14	Bionexia Strep A plus - cassette (Biomerieux)			
15	Bionexia Strep A dipstick – test strip (Biomerieux)			
16	Biosynex Strep A cassette (Biosynex)			
17	Sofia Strep A FIA (Quidel)			
18	ALERE i Strep A (Abbott)[4]			
19	ALERE i Strep A 2 (Abbott)[5]	£22.94	5	No
20	Cobas Strep A assay on Liat system (Roche Diagnostics)	£64.63	6	No
21	Xpert Xpress Strep A (Cepheid)	£4.25	12	Assumed yes[2]

[1] Confirmatory microbiological culture of throat swabs for negative results of rapid tests is needed, as specified in the information for use documents.

[2] Not known if confirmatory test is needed, assumed that it is

[3] Confirmatory testing warranted only if symptoms persist

[4] This test has been replaced by ID NOW Strep A 2 test

[5] Rebranded to ID NOW Strep A 2

Table 12 Treatment costs (2017/18 price year)

Treatment costs	Mean	SE	Source
Antibiotic (phenoxymethylpenicillin 250 mg, 28-tablets pack)	£0.91	£0.046	BNF 72 (2017)
Pain relief (paracetamol 500 mg, 32-tablets pack)	£0.74	£0.037	BNF 72 (2017)
GP consultation (9.22 minutes)	£37.4	£1.91	PSSRU Unit costs 2017
Treatment costs, penicillin induced rash (switch to erythromycin 500 mg)	£10.00	£0.51	BNF 72 (2017)
Treatment costs, sepsis	£1,744.64	£89.01	Derived from Hex et al. 2017
Treatment costs, abscess (tonsillectomy)	£1,571.28	£80	2017 NHS reference costs
Treatment costs, acute rheumatic fever	£1,772.44	£90.43	2017 NHS reference costs

Base-case assumptions

Adult primary care model

The model was created for adults in primary care, which was then adapted for children and secondary care. Key assumptions (see Table 9 for corresponding probabilities used in the base case):

- In current practice, antibiotic prescribing (immediate, delayed or no prescribing) is based on the Centor score.
- In the rapid test cohort, people with Centor score of 3 or more are offered the rapid test. Antibiotic prescribing decisions (immediate, delayed or no prescribing) are based on the test results.
- Of people offered delayed prescription, 46% use their prescription.
- There are 1.3% to 1.5% of people with strep A infection who develop complications, depending whether or not they received antibiotics.
- People who take antibiotics are at risk of penicillin-related adverse effects.

Adult secondary care model

The model for adults in secondary care was adapted from the adult primary care model:

- The cost of the initial GP consultation was excluded.

- It was assumed that all rapid tests can be done within the standard time allocated for secondary care appointments.
- The accuracy of rapid tests was assumed to be the same as in primary care (because of the lack of specific data in secondary care) except for 3 tests for which the sensitivity estimates were adjusted: OSOM Strep A test (94% instead of 92% in the primary care), QuikRead Go Strep A test kit (87% instead of 100% in the primary care) and the Alere TestPack Plus Strep A (90% instead of 95% in the primary care). All other assumptions and inputs are the same as in the primary care model.

Children primary care model

The model for children in primary care was adapted from the corresponding adult model by adjusting the prevalence of strep A infections from 22.6% to 30.2%, and using the accuracy estimates from studies in children whenever these were available (Table 8). In addition, the costs of treating peritonsillar abscess and related complications in children were assumed to be lower than in adults (£1,420.50 compared with £1,571.28), based on the NHS reference costs for both age groups.

Children secondary care model

The test accuracy data for children in primary and secondary care were assumed to be the same in both models (because of the lack of specific data in secondary care), except for 3 tests for which the following accuracy data was used:

- OSOM Strep A test (test strip), sensitivity: 94%, specificity: 97%
- QuikRead Go Strep A test kit; sensitivity: 87%, specificity: 78%
- Alere TestPack Plus Strep A; sensitivity: 77%, specificity: 97%.

Economic analysis results

Adult primary care model

The base-case results for adults in primary care with sore throats start on page 166 of the diagnostic assessment report. The mean simulated costs and QALYs for current practice and the different rapid tests are in Table 13. The EAG multiplied both by 1,000 because of the very small incremental QALYs. The Clearview Exact Strep A cassette and Clearview Exact Strep A dipstick were dominated by current practice (that is, current practice was more effective and cheaper than the rapid tests). The ICERs for the remaining 12 tests ranged from £1,353,677 per QALY gained for NADAL Strep A test strip (nal von minden GmbH) to £6,059,081 per QALY gained for the Cobas Strep A assay on Liat system, compared with current practice.

Table 13 Adult primary care model: Base-case cost-effectiveness results

Test Name	Mean costs[1]	Mean QALYs[1]	Incremental costs[1]	Incremental QALYs[1]	ICER versus current practice
Current practice (Clinical scoring based on Centor 3 or higher plus clinical assessment)	£49,147	859.82458955	£0	0.0000000	–
Clearview Exact Strep A cassette (Abbott)[2]	£56,180	859.82063008	£7,033	−0.0039595	Dominated
Clearview Exact Strep A dipstick (Abbott)[2]	£55,980	859.82063008	£6,833	−0.0039595	Dominated
Strep A rapid test cassette (Biopanda Reagents)[3]	£55,442	859.82769587	£6,295	0.0031063	£2,026,496
Strep A rapid test dipstick (Biopanda Reagents)[3,4]	£55,397	859.82769587	£6,250	0.0031063	£2,012,006
NADAL Strep A test strip (nal von minden GmbH)[3]	£54,394	859.82846603	£5,248	0.0038765	£1,353,677
NADAL Strep A cassette (nal von minden GmbH)[3]	£54,444	859.82846603	£5,298	0.0038765	£1,366,577
NADAL Strep A plus cassette (nal von minden GmbH)[3]	£54,469	859.82846603	£5,323	0.0038765	£1,373,029
NADAL Strep A plus test strip (nal von minden GmbH)[3]	£54,419	859.82846603	£5,273	0.0038765	£1,360,126
NADAL Strep A scan test cassette (nal von minden GmbH)[3]	£54,584	859.82846603	£5,438	0.0038765	£1,402,700
QuikRead Go Strep A test kit (Orion Diagnostica)	£56,083	859.82810269	£6,936	0.0035131	£1,974,319
Alere TestPack Plus Strep A cassette (Abbott)	£54,781	859.82751669	£5,634	0.0029271	£1,924,717
ALERE i Strep A 2 (rebranded to ID NOW Strep A 2; Abbott)[3]	£59,837	862.82824206	£10,691	0.00365250	£2,926,915
Cobas Strep A assay on Liat system (Roche Diagnostics)	£71,277	859.82824206	£22,131	0.0036525	£6,059,081
Xpert Xpress Strep A (Cepheid)[3]	£63,323	859.82854357	£14,177	0.0039540	£3,585,436

Note: Cost-effectiveness analyses were not done for 7 tests that had no cost data (Bionexia Strep A plus cassette and Biosynex Strep A cassette had neither costs nor accuracy data available)

[1] Per 1,000 individuals

[2] Based on the accuracy data presented in a conference abstract only

[3] Based on the accuracy data from the FDA or manufacturer's data

[4] Assumed equal accuracy to the cassette version of this test

The results of the probabilistic sensitivity analysis mirrored the results of the deterministic base-case analysis. The probability of a rapid test being cost-effective was 0, regardless of the rapid test used.

A range of sensitivity analyses were done. However, none produced ICERs that were around or below £30,000 per QALY gained.

In addition, some scenario analyses favoured rapid testing. The Clearview Exact Strep A cassette and Clearview Exact Strep A dipstick were no longer dominated by current practice but produced ICERs above £100,000 per QALY gained. Changes to the ICERs for all other rapid tests did not change conclusions:

- changing the Centor threshold for starting antibiotics and testing to 1 or more (from 3 or more in base case)
- lowering the prevalence of strep A infection to 10% (from 22.6%)
- doubling the complication rates for the treated strep A infection to 2.6%
- changing the rate of penicillin-induced anaphylaxis from 0.01% (Neuner et al. 2003; base-case) to 0.64% (Van Howe and Kusnier 2006)
- doubling the rate of penicillin-related rash to 4%
- halving the utility decrement of untreated strep A infection
- doubling the utility decrement of treated strep A infection
- doubling the utility decrement of penicillin-induced rash.

Doubling the utility decrement associated with untreated strep A infection favoured current practice. Under that assumption, 3 additional tests were also dominated by current practice: Strep A rapid test cassette (Biopanda), Strep A rapid test dipstick (Biopanda), and Alere TestPack Plus Strep A.

Adult secondary care model

The cost-effectiveness results for adults in secondary care (Table 14) were aligned with the adult primary care model. The ICERs for the remaining 12 tests ranged from £44,184 per QALY gained for NADAL Strep A test strip (nal

von minden GmbH) to £12,700,432 per QALY gained for the QuikRead Go Strep A test kit, compared with current practice.

Table 14 Adult secondary care model: Base-case cost-effectiveness results

Test Name	Mean costs[1]	Mean QALYs[1]	Incremental costs[1]	Incremental QALYs[1]	ICER versus current practice
Current practice (Clinical scoring based on Centor 3 or higher plus clinical assessment)	£49,147	859.82458955	£0	0.0000000	–
Clearview Exact Strep A cassette (Abbott)[2]	£51,103	859.82063008	£1,957	−0.0039595	Dominated
Clearview Exact Strep A dipstick (Abbott)[2]	£50,903	859.82063008	£1,757	−0.0039595	Dominated
Strep A rapid test cassette (Biopanda Reagents)[3]	£50,365	859.82769587	£1,219	0.0031063	£392,342
Strep A rapid test dipstick (Biopanda Reagents)[3,4]	£50,320	859.82769587	£1,174	0.0031063	£377,852
NADAL Strep A test strip (nal von minden GmbH)[3]	£49,318	859.82846603	£171	0.0038765	£44,184
NADAL Strep A cassette (nal von minden GmbH)[3]	£49,368	859.82846603	£221	0.0038765	£57,085
NADAL Strep A plus cassette (nal von minden GmbH)[3]	£49,393	859.82846603	£246	0.0038765	£63,537
NADAL Strep A plus test strip (nal von minden GmbH)[3]	£49,343	859.82846603	£196	0.0038765	£50,636
NADAL Strep A scan test cassette (nal von minden GmbH)[3]	£49,508	859.82846603	£361	0.0038765	£93,211
QuikRead Go Strep A test kit (Orion Diagnostica)	£51,136	859.82474622	£1,990	0.0001567	£12,700,432
Alere TestPack Plus Strep A cassette (Abbott)	£49,713	859.82627789	£566	0.0016883	£335,358
ALERE i Strep A 2 (rebranded to ID NOW Strep A 2; Abbott)[3]	£54,761	859.82824206	£5,614	0.00365250	£1,537,126
Cobas Strep A assay on Liat system (Roche Diagnostics)	£65,186	859.82824206	£16,039	0.0036525	£4,391,332
Xpert Xpress Strep A (Cepheid)[3]	£51,141	859.82854357	£1,994	0.0039540	£504,287

Notes: Broader secondary care costs such as cost of A&E attendance and treatment were assumed to be the same for current practice and rapid testing strategies and therefore not included in analysis. Cost-effectiveness analyses were not done for 7 tests that had no cost data (Bionexia Strep A plus cassette and Biosynex Strep A cassette had neither costs nor accuracy data)

[1] Per 1,000 individuals

[2] Based on the accuracy data presented in a conference abstract only

[3] Based on the accuracy data from the FDA or manufacturer's data

[4] Assumed equal accuracy to the cassette version of this test

The results of the probabilistic sensitivity analysis were aligned with the results of the deterministic base-case analysis. The probability of rapid testing being cost-effective was 0, regardless of the rapid test used.

The sensitivity analyses largely mirrored the results for the adult primary care model. All scenario analyses that were more favourable to rapid testing in primary care were also more favourable to rapid testing in secondary care. However, the effect of these sensitivity analyses was more pronounced in secondary care. When the rate of penicillin-induced anaphylaxis was changed from 0.01% (Neuner et al. 2003) to 0.64% (Van Howe and Kusnier 2006), the 5 NADAL tests and Alere TestPack Plus Strep A dominated standard care (that is, testing was cheaper and more effective than standard care). The ICERs for additional 4 tests (2 Clearview Exact Strep A tests and 2 Strep A rapid tests from Biopanda) decreased to around or below £30,000 per QALY gained, compared with standard practice. In addition, the ICERs for the 5 NADAL tests decreased to around or below £30,000 per QALY gained, compared with current care for the following assumptions:

- changing the Centor threshold for starting antibiotics and testing to 2 or more (ICERs: £30,230 to £69,690 per QALY gained)
- changing the Centor threshold for starting antibiotics and testing to 1 or more (ICERs: £22,220 to £56,190 per QALY gained)
- lowering the prevalence of strep A infection to 10% (ICERs: £20,628 to £53,506 per QALY gained)
- doubling the rate of penicillin-related rash to 4% (ICERs: £8,913 to £32,557 per QALY gained)
- doubling the utility decrement of penicillin-induced rash (ICERs: £21,309 to £44,953)

Compared with the adult primary care model, there were more scenario analyses that favoured current practice, with additional tests being dominated by current practice under the following assumptions:

- increasing the prevalence rate to 35.9%
- halving the rate of complications of treated strep A infection to 0.65%
- doubling the rate of complications of untreated strep A infection to 3%
- halving the rate of penicillin-related rash to 1%
- doubling the utility decrement of untreated strep A infection
- halving the utility decrement of treated strep A infection
- halving the utility decrement of penicillin-induced rash
- doubling the utility decrement of an abscess.

Children primary care model

The base-case cost-effectiveness results for children in primary care with sore throats start on page 186 of the diagnostic assessment report.

The mean simulated costs and QALYs for current practice and the different rapid tests are presented in Table 15 (the costs and QALYs were multiplied by 1,000). Current practice dominated (that is, current practice was more effective and cheaper than testing strategy) 4 of 14 tests for which cost-effectiveness analysis was possible. The ICERs for the remaining 10 tests ranged from £1,762,306 to £7,893,857per QALY gained, compared with current practice.

Table 15 Children primary care model: Base-case cost-effectiveness results

Test Name	Mean costs[1]	Mean QALYs[1]	Incremental costs[1]	Incremental QALYs[1]	ICER versus current practice
Current practice (Clinical scoring based on Centor 3 or higher plus clinical assessment)	£50,185	939.77019917	£0	0.0000000	−
Clearview Exact Strep A cassette (Abbott)[2]	£57,773	939.76305927	£7,588	−0.0071399	Dominated
Clearview Exact Strep A dipstick (Abbott)[2]	£57,554	939.76305927	£7,369	−0.0071399	Dominated
Strep A rapid test cassette (Biopanda Reagents)[3]	£56,899	939.77244279	£6,715	0.0022436	£2,992,743
Strep A rapid test dipstick (Biopanda Reagents)[3,4]	£56,850	939.77244279	£6,665	0.0022436	£2,970,792
NADAL Strep A test strip (nal von minden GmbH)[3]	£55,952	939.77347194	£5,768	0.0032728	£1,762,306
NADAL Strep A cassette (nal von minden GmbH)[3]	£56,007	939.77347194	£5,822	0.0032728	£1,779,026
NADAL Strep A plus cassette (nal von minden GmbH)[3]	£56,035	939.77347194	£5,850	0.0032728	£1,787,386
NADAL Strep A plus test strip (nal von minden GmbH)[3]	£55,980	939.77347194	£5,795	0.0032728	£1,770,666
NADAL Strep A scan test cassette (nal von minden GmbH)[3]	£56,160	939.77347194	£5,976	0.0032728	£1,825,846
QuikRead Go Strep A test kit (Orion Diagnostica)	£58,012	939.76701428	£7,827	−0.0031849	Dominated
Alere TestPack Plus Strep A cassette (Abbott)	£56,389	939.76939575	£6,204	−0.0008034	Dominated
ALERE i Strep A 2 (rebranded to ID NOW Strep A 2; Abbott)[3]	£61,907	939.77326996	£11,722	0.003070785	£3,817,336
Cobas Strep A assay on Liat system (Roche Diagnostics)	£74,425	939.77326996	£24,240	0.0030708	£7,893,857
Xpert Xpress Strep A (Cepheid)[3]	£65,521	939.77368771	£15,336	0.0034885	£4,396,205

Note: Cost-effectiveness analyses were not done for 7 tests that had no cost data (Bionexia Strep A plus cassette and Biosynex Strep A cassette had neither costs nor accuracy data)

[1] Per 1,000 individuals

[2] Based on the accuracy data presented in a conference abstract only

[3] Based on the accuracy data from the FDA or manufacturer's data

[4] Assumed equal accuracy to the cassette version of this test

The results of the probabilistic sensitivity analysis mirrored the results of the deterministic base-case analysis. The probability of rapid testing being cost-effective was 0, regardless of the rapid test used.

A range of scenario sensitivity analyses were done to test the robustness of the base-case model. However, none of the alternative assumptions produced ICERs that were below £30,000 per QALY gained compared with current practice. The following alternative assumptions were more favourable to rapid testing, and all or some of the 4 tests that were dominated by current practice in base-case analyses were no longer dominated (ICERs above £100,000):

- lowering the Centor threshold for starting antibiotics and testing (2 or more, or 1 or more; from 3 or more in the base-case)
- lowering the prevalence rate of strep A infection to 10% (from 30.2%)
- doubling the complications rates of treated strep A infection to 2.6%
- halving the complication rates of untreated strep A infection to 0.75%
- changing the rate of penicillin-induced anaphylaxis from 0.01% (Neuner et al. 2003; base-case) to 0.64% (Van Howe and Kusnier 2006)
- doubling the rate of penicillin-induced rash to 4%
- halving the utility decrement of untreated strep A infection
- doubling the utility decrement of treated strep A infection
- doubling the utility decrement of penicillin-induced rash
- changing the accuracy estimates to the lower confidence limits for both the rapid test and Centor clinical scoring tool.

In contrast, doubling the utility decrement associated with untreated strep A infection favoured current practice. There were 2 additional tests (Strep A rapid test cassette and dipstick from Biopanda) dominated by current practice compared with base-case scenario.

Children secondary care model

The mean simulated costs and QALYs for current practice and the different rapid tests are presented in Table 16 (the costs and QALYs were multiplied by

1,000). As with the model for children in primary care, 4 of 14 rapid tests were dominated by current practice (that is, current practice was more effective and cheaper than rapid testing). The ICERs for the remaining tests ranged from £65,122 to £5,723,279 per QALY gained, compared with current practice.

Table 16 Children secondary care model: Base-case cost-effectiveness results

Test Name	Mean costs[1]	Mean QALYs[1]	Incremental costs[1]	Incremental QALYs[1]	ICER versus current practice
Current practice (Clinical scoring based on Centor 3 or higher plus clinical assessment)	£50,185	939.77019917	£0	0.0000000	−
Clearview Exact Strep A cassette (Abbott)[2]	£52,219	939.76305927	£2,034	−0.0071399	Dominated
Clearview Exact Strep A dipstick (Abbott)[2]	£52,000	939.76305927	£1,815	−0.0071399	Dominated
Strep A rapid test cassette (Biopanda Reagents)[3]	£51,345	939.77244279	£1,160	0.0022436	£517,066
Strep A rapid test dipstick (Biopanda Reagents)[3,4]	£51,296	939.77244279	£1,111	0.0022436	£495,115
NADAL Strep A test strip (nal von minden GmbH)[3]	£50,398	939.77347194	£213	0.0032728	£65,122
NADAL Strep A cassette (nal von minden GmbH)[3]	£50,453	939.77347194	£268	0.0032728	£81,845
NADAL Strep A plus cassette (nal von minden GmbH)[3]	£50,480	939.77347194	£295	0.0032728	£90,205
NADAL Strep A plus test strip (nal von minden GmbH)[3]	£50,425	939.77347194	£240	0.0032728	£73,482
NADAL Strep A scan test cassette (nal von minden GmbH)[3]	£50,606	939.77347194	£421	0.0032728	£128,662
QuikRead Go Strep A test kit (Orion Diagnostica)	£52,457	939.76701428	£2,273	−0.0031849	Dominated
Alere TestPack Plus Strep A cassette (Abbott)	£50,834	939.76939575	£649	−0.0008034	Dominated
ALERE i Strep A 2 (rebranded to ID NOW Strep A 2; Abbott)[3,5]	£56,353	939.77326996	£6,168	0.003070785	£2,008,522
Cobas Strep A assay on Liat system (Roche Diagnostics)	£67,760	939.77326996	£17,575	0.0030708	£5,723,279
Xpert Xpress Strep A (Cepheid)[3]	£52,190	939.77368771	£2,006	0.0034885	£574,900

Notes: Broader secondary care costs such as cost of emergency department attendance and treatment were assumed to be the same for current practice and rapid testing strategies and therefore not included in analysis. Cost-effectiveness analyses were not done for 7 tests that had no cost data (Bionexia Strep A plus cassette and Biosynex Strep A cassette had neither costs nor accuracy data)

[1] Per 1,000 individuals

[2] Based on the accuracy data presented in a conference abstract only

[3] Based on the accuracy data from the FDA or manufacturer's data

[4] Assumed equal accuracy to the cassette version of this test

The results of the probabilistic sensitivity analysis mirrored the results of the deterministic base-case analysis. The probability of rapid testing being cost-effective was 0, regardless of the rapid test used.

The sensitivity analyses largely mirrored the results for the children primary care model. All scenario analyses that were more favourable to rapid testing in primary care were also more favourable to rapid testing in secondary care. When the rate of penicillin-induced anaphylaxis was changed from 0.01% to 0.64%, all 5 NADAL tests and the Alere TestPack Plus Strep A test and the ICERs for additional 3 tests (2 Strep A rapid tests from Biopanda and Clearview Exact Strep A test strip) decreased to around or below £30,000 per QALY gained, compared with standard care. In addition, the ICER for Strep A rapid test strip decreased to £29,702 per QALY gained when the cost of confirmatory microbiological culture of throat swabs following a negative test result was excluded. The ICERs for the 5 NADAL tests decreased to around or below £30,000 per QALY gained, compared with current care for the following assumptions:

- changing the Centor threshold for starting antibiotics and testing to 1 or more (ICERs: £29,604 to £68,697 per QALY gained)
- lowering the prevalence of strep A infection to 10% (ICERs: £20,575 to £53,453 per QALY gained)
- doubling the rate of penicillin-related rash to 4% (ICERs: £17,378 to £46,855 per QALY gained)
- doubling the utility decrement of penicillin-induced rash (ICERs: £30,212 to £59,689 per QALY gained)

As in the model for children in primary care, doubling the utility decrement associated with untreated strep A infection favoured current practice. There were 2 additional tests (Strep A rapid test cassette and dipstick from Biopanda) dominated by current practice compared with base-case scenario.

3 Issues for consideration

Clinical effectiveness

There was limited evidence on the clinical impact of the rapid tests. In particular, there were no data on clinical outcomes such as morbidity, mortality, contribution to antimicrobial stewardship or onward transmission rate.

There were no studies found in the elderly population or in a pharmacy setting. The elderly population could benefit more from testing because of the higher risk of serious complications, such as invasive strep A, and higher risk of associated mortality. However, it was not possible to model the use of the rapid tests in this population.

There were no recent UK studies on the antimicrobial prescribing behaviours found. Non-UK studies and UK studies done before the introduction of the antimicrobial prescribing guidelines might not be representative of the current NHS practice.

Only 2 studies reported the diagnostic accuracy of the rapid tests in people who are more or most likely to benefit from antibiotics (Centor or modified Centor [McIsaac] score of 3 or more), as defined in the scope. All other studies enrolled patients with lower clinical scores than those defined in the scope, or did not use clinical scores as an inclusion criterion. These studies might not be generalisable to the current NHS practice, in which only people who are more or most likely to benefit from antibiotics would potentially be offered the rapid test. Prevalence of strep A is expected to be higher in this population compared with the unselected population of people with sore throats.

Only 2 studies met the age criterion for children (ages 5 to 14 years) and only 2 studies met the age criterion for adults (age 15 years or more) as defined in the scope. Other studies used different definitions of children and adult

populations, included mixed age groups, or did not report the age group. It is unclear how age would impact the accuracy of the rapid tests.

It was not possible to determine the relative accuracy of different tests because of limited head-to-head comparative studies. Large heterogeneity between studies prevented any meaningful comparisons across different studies, but it is expected that different test may have different accuracy.

The large heterogeneity across studies (even among studies for the same test) suggests that the accuracy estimates based on a single study are unlikely to be accurate. However, multiple published studies were available for 5 tests only. Meta-analysis was possible for those tests.

The reference standard (microbiological culture of throat swabs) is unlikely to be 100% accurate and could vary with different culture media. This may either under or overestimate the accuracy of rapid tests. False positive results could be true positive results if the reference standard failed to detect the presence of strep A infection. However, both rapid tests and the reference standard can detect strep A carriage (presence of strep A without signs of infection), so the clinical significance of the imperfect reference standard is unclear.

The quality of the sample collection is important for the accuracy of both the rapid tests and the reference standard, and may depend on the training and experience of the healthcare personnel collecting the samples. Studies done in a controlled setting might not represent routine clinical practice.

Cost effectiveness

The accuracy data for the rapid tests were generally limited and reported for a population not matching the scope (in particular for the FeverPAIN or Centor score). These estimates may not be generalisable to the current NHS practice, in which testing would be offered only to people who are more or most likely to benefit from antibiotics.

- The accuracy estimates for several tests were from unpublished manufacturers' data and should be interpreted with caution. These estimates were consistently higher than the accuracy estimates from the published peer-reviewed studies. They might reflect the 'best case scenario' rather than the accuracy achievable in the routine clinical practice.
- For most tests there was a lack of data specific for children compared with adults, and primary care compared with secondary care. This could affect the results of the modelling.

In the models, the accuracy estimates for Centor clinical scoring tool at a score of 3 or more were taken from the meta-analysis by Aalbers et al. (2011). It focused on Centor to predict strep A pharyngitis in adults (15 years or more) in primary care, so the estimate might not be generalisable for children or for the secondary care setting. The 2 studies found by the EAG that reported the accuracy of clinical scoring tools in both children and adults showed higher sensitivity and lower specificity in children compared with adults. All 6 studies identified by the EAG that reported accuracy data for clinical scoring tools (Table 5) reported higher sensitivity but lower specificity than estimates from Aalbers et al. (2011).

The prevalence estimate for strep A infection in adults was based on the study by Little et al. (2014). The study enrolled patients aged 3 years or older in UK primary care, and might not be generalisable to an adult population or secondary care. The prevalence estimate for strep A in children was based on non-UK studies. In addition, strep A prevalence has a strong seasonal variation and the prevalence estimates from 1 time period might not be generalisable to another period. However, sensitivity analyses exploring lower and higher prevalence rates could approximate seasonality effect.

The rate of penicillin-induced anaphylaxis in the base-case analyses was based on Neuner et al. (2003). Using an alternative data source (Van Howe and Kusnier 2006) had considerable impact on the secondary care model

results, with 6 tests dominating standard care, and the ICERs for additional 3-4 tests decreasing to around or below £30,000 per QALY gained, compared with current practice. This was related to reduction in the use of antibiotics predicted in the model. The secondary care models were also sensitive to changes in several other model assumptions, which either favoured standard care (additional tests dominated by standard care), or rapid tests (the ICERs for several NADAL tests decreasing to around or below £30,000 per QALY gained).

The 1-year time horizon might not capture all consequences of strep A complications. However, such complications are very rare and associated with a low mortality rate. Also, it is unclear if the use of antibiotics reduces the risk of long-term consequences.

The potential wider public health benefits of the rapid tests, such as contribution to the antimicrobial stewardship or impact on the onward transmission of infection, were not captured in the model.

4 Summary

Clinical effectiveness

The EAG found 38 eligible studies; 35 reported test accuracy data, and 12 reported antibiotic prescribing behaviours (9 reported both outcomes). No studies were found reporting clinical outcomes such as morbidity, mortality, contribution to antimicrobial stewardship or onward transmission rate.

Only 2 studies reported accuracy data for people with Centor or McIsaac (modified Centor) score of 3 or more (population defined in the scope). In these 2 studies, sensitivity of rapid tests was reported as 82.9% and 94.6%, and specificity as 84.9% and 99.1%, respectively.

Across all accuracy studies (that is, studies not restricted by Centor score, age group and healthcare setting), there was a wide variation in the estimates of sensitivity (67.9% to 100%) and specificity (73.3% to 100%) of different

rapid tests. Accuracy estimates for 9 tests (Strep A rapid test cassette and dipstick [Biopanda], 5 NADAL Strep A tests, 2 Alere i Strep A tests and Xpert Xpress Strep A test) were available from unpublished manufacturer data or FDA reports only. These estimates were consistently higher than the accuracy estimates from published peer-reviewed studies.

Evidence from 3 RCTs reporting antibiotics prescribing behaviours suggested that rapid tests could help reduce antibiotic prescribing rates, compared with the use of the clinical scoring tools only.

Cost effectiveness

The EAG constructed 4 de novo models for adults and children with sore throats in primary or secondary care. There was no economic model for the elderly population or for the pharmacy setting because of a lack of evidence to populate the model.

Only 14 of 21 rapid tests had relevant data on test accuracy and costs, to be included in the economic modelling. For 9 of these 14 rapid tests, the estimates of accuracy data were only available from unpublished manufacturer's data or FDA documents.

There was considerable uncertainty about the cost effectiveness of the different rapid tests:

- In the base-case analyses, current practice dominated (was more effective and cheaper) 2 tests in adult models (both in primary and secondary care) and 4 tests in children models (both in primary and secondary care). The ICERs for all other tests in the primary care models (both children and adults models) were above 1 million (range, £1,353,677 to £7,893,857) per QALY gained, compared with current practice. In secondary care models, the ICERs ranged from £44,184 to £12,700,432 per QALY gained, compared with current practice.
- The model was most sensitive to changing the assumption about the rate of penicillin-induced anaphylaxis. 6 tests dominated standard care, and the

ICERs for additional tests decreased to around or below £30,000 per QALY gained, compared with current practice, when the alternative data input was used. The secondary care models were also sensitive to changes in several other model assumptions, which either favoured standard care (additional tests dominated by standard care), or rapid tests (the ICERs for some NADAL tests decreasing to around or below £30,000 per QALY gained).

5 Equality considerations

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

The incidence of strep A, and associated infections such as scarlet fever are most common in children. The mortality rate associated with invasive group A strep is greatest in people aged over 75. Healthcare professionals may be more concerned about onward transmission of strep A where a person is in close contact with someone who is pregnant or someone who is immunocompromised.

People with cognitive impairment may be less able to communicate their symptoms to a carer or healthcare professional. Injecting drug users are thought to be at a greater risk of developing invasive group A strep.

6 Implementation

Potential adoption levers identified by the NICE Adoption and Impact team include:

- the potential for the tests to support a diagnosis and a clinical decision to not prescribe antibiotics and encourage patients to self-care

- the potential to reduce visits to primary care if the tests are done in alternative settings, such as a community pharmacy.

Potential adoption barriers identified by the NICE Adoption and Impact team include:

- the cost of the tests
- the time needed to process the test and interpret the result which may disrupt an appointment in primary care
- concerns about the reliability of the tests and missing an alternative diagnosis when the tests are used in community pharmacies
- a belief that the tests may encourage over-medicalisation of sore throats and discourage people to self-care.

During the scoping workshop it was also highlighted that additional training might be needed in community pharmacies about using clinical scoring tools such as FeverPAIN and Centor.

7 Authors

Ewa Rupniewska
Topic lead

Rebecca Albrow
Technical adviser

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Appendix A: Sources of evidence considered in the preparation of the overview

A. The diagnostics assessment report for this assessment was prepared by Warwick Evidence:

Rapid Tests for Group A Streptococcal infections in people with sore throat. Diagnostic Assessment Report commissioned by the NIHR HTA Programme on behalf of the National Institute for Health and Care Excellence.

B. The following organisations accepted the invitation to participate in this assessment as stakeholders. They were invited to attend the scoping workshop and to comment on the diagnostics assessment report.

Manufacturer(s) of technologies included in the final scope:

- Biopanda Reagents
- Roche Diagnostics Ltd
- nal von minden GmBH
- Biomerieux
- Cepheid UK Ltd
- Orion Diagnostica Oy
- Abbott

Manufacturers of related technologies (not included in scope):

- Saw Diagnostics

Other commercial organisations:

- None

Professional groups and patient/carer groups:

- Royal College of Physicians
- Institute of Biomedical Science
- British Infection Association

- British Society for Antimicrobial Chemotherapy

Research groups:

- None

Associated guideline groups:

- None

Others:

- Department of Health and Social Care
- Healthcare Improvement Scotland
- Leeds Teaching Hospitals NHS Trust
- Medicines and Healthcare products Regulatory Agency
- Medicines Management Partnership
- NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC)
- NHS England
- Welsh Government

Appendix B: Glossary of terms

Glomerulonephritis
Damage to the glomeruli (filters in the kidneys), which is often caused by the immune system.

Group A streptococcus (strep A)
A bacterium which commonly colonises the skin and throat. It can cause a range of infections including tonsillitis and pharyngitis.

Necrotising fasciitis
A rare infection caused by strep A that affects the tissue beneath the skin, including the muscles.

Pharyngitis
Inflammation of the pharynx, which is at the back of the throat. It is commonly described as a sore throat. It is usually caused by a viral infection.

Phenoxymethylpenicillin
Antibiotic used to treat group A streptococcus throat infections. It is also known as penicillin V.

Quinsy (peritonsillar abscess)
A complication of tonsillitis where an abscess forms between a tonsil and the wall of the throat.

Rheumatic fever
A complication that can happen after a strep A throat infection. It is caused by the immune system's reaction to strep A and is characterised by inflammation in the joints and heart problems (rheumatic heart disease), and can reoccur. People who have had rheumatic fever are therefore a high risk of a recurrence if they have strep A throat infection in the future.

Streptococcal toxic shock syndrome
A severe illness caused by an invasive strep A infection which results in shock and multiorgan failure.

Suppurative
Causing, or characterised by, production of pus.

Tonsillitis
Inflammation of the tonsils, usually caused by a viral infection.