

US Cost-effectiveness and Budget Impact of Point-of-Care NAAT for Streptococcus

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Group A streptococcus (GAS) pharyngitis is common in the United States. Each year, approximately 12 million individuals seek medical care for pharyngitis, accounting for about 2% of ambulatory care visits.¹ The economic burden associated with GAS pharyngitis is substantial. A retrospective study in children diagnosed with GAS pharyngitis between 2005 and 2006 in the United States estimated total costs to range between \$224 million and \$539 million per year,² mostly attributable to outpatient visits, antibiotic treatment, and diagnostic testing.² In treating GAS pharyngitis, the use of a recommended antibiotic regimen shortens the duration of symptoms; reduces the likelihood of transmission to family members, classmates, and other close contacts; and prevents complications such as acute rheumatic fever (ARF) and peritonsillar abscess.³ Although antibiotics are recommended to treat GAS, they are not appropriate for viral pharyngitis. Yet a review of prescribing practices for pharyngitis found that in 2010, doctors prescribed antibiotics in almost 60% of cases,⁴ far exceeding GAS prevalence of approximately 37% in children⁵ and 10% in adults.⁶ Therefore, diagnostic strategies that quickly and accurately identify GAS would be valuable to support appropriate treatment decisions.

The current gold-standard testing method for GAS is throat culture⁷; however, culture typically takes at least 2 days to return results and is therefore not commonly used as a first-line diagnostic test in the United States to aid clinical decisions. Per the Infectious Diseases Society of America, rapid antigen detection tests (RADT), either alone or with culture confirmation, are the recommended approach to diagnose GAS.⁸ With RADT, results are available without delay, yet test sensitivity is low,⁹ and therefore it is recommended that negative results be followed up by culture confirmation to ensure that the negative result reported by RADT is a true negative. In comparison, the cobas Liat system is a highly sensitive and specific compact system designed for on-demand point-of-care (POC) nucleic acid amplification tests (NAAT) with a turnaround time of approximately 15 minutes.¹⁰ Accurate POC testing has the potential to improve GAS diagnosis, guide timely treatment decisions, and advance antibiotic stewardship goals.

ABSTRACT

OBJECTIVES: In the United States, approximately 12 million individuals seek medical care for pharyngitis each year, accounting for about 2% of ambulatory care visits. Although the gold standard for diagnosing group A streptococcus (GAS) is culture, it is time intensive. Rapid antigen detection tests (RADT) with or without culture confirmation are commonly used instead. Although RADT provide results quickly, they generally have lower test sensitivity. Recently, point-of-care nucleic acid amplification tests (POC NAAT) have emerged. This study evaluates the cost-effectiveness and budget impact to the US payer of adopting POC NAAT.

STUDY DESIGN: This study was a cost-effectiveness analysis, with costs and outcomes calculated via a decision tree.

METHODS: A decision-tree model quantified costs and outcomes associated with a GAS diagnostic strategy using POC NAAT compared with RADT + culture confirmation. Model inputs were derived from the published literature. Model outputs included costs and clinical effects: quality-adjusted life-days lost, GAS and antibiotic complications, number of patients appropriately treated, and antibiotic utilization. Sensitivity and scenario analyses were performed.

RESULTS: Base-case analysis projected that a POC NAAT strategy would cost \$44 per patient compared with \$78 for RADT + culture. Compared with RADT + culture, POC NAAT would increase the number of appropriately treated patients and avert unnecessary use of antibiotics. The budget impact of POC NAAT was -0.4% relative to current budget over 5 years. Findings were robust in sensitivity analyses.

CONCLUSIONS: Our results suggest that POC NAAT would be less costly and more effective than RADT + culture; POC NAAT adoption may yield cost savings to US third-party payers. Access to POC NAAT is important to optimize GAS diagnosis and treatment decisions in the United States.

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TAKEAWAY POINTS

- ▶ Point-of-care nucleic acid amplification tests (POC NAAT) have emerged as new test options for group A streptococcus (GAS) that may provide more accuracy than rapid antigen detection tests (RADT), with faster turnaround than culture.
- ▶ Through decision-modeling methods, costs and outcomes associated with GAS diagnostic strategies in the United States were quantified, finding that a POC NAAT strategy is slightly less costly than RADT + culture confirmation while also increasing the number of appropriately treated patients and averting unnecessary antibiotics.
- ▶ Access to POC NAAT is important to optimize GAS diagnosis and treatment decisions in the United States.

As US health care expenditures compose one-fifth of the national economy,¹¹ it is particularly important to ensure that adopting novel technologies improve clinical outcomes without exacerbating costs. Given the burden of GAS pharyngitis in the United States combined with the challenge of accurate diagnosis and appropriate treatment, considering cost-effectiveness as well as overall budget impact can be valuable when deciding whether to adopt new products. There is limited evidence on the economic value of GAS diagnostics in the US population. Previous cost-effectiveness studies have shown increased value of tests with higher diagnostic accuracy in terms of quality-adjusted life-days (QALDs) but with limited comparability between studies given the assessment of varying diagnostic strategies and subpopulations (pediatric or adult). This is the first study to evaluate the cost-effectiveness and overall budget impact of GAS diagnosis strategies, including POC NAAT. The specific aim of this analysis was to assess the economic value, from a third-party payer perspective, of a GAS diagnostic strategy with POC NAAT compared with an approach using RADT with culture confirmation of negative results (RADT + culture).

METHODS

Model Overview

An economic model with a decision-tree structure (**eAppendix Figure 1** [eAppendix available at ajmc.com]) was developed in Microsoft Excel 2016 to provide insight into the economic value of GAS diagnostic testing strategies for patients presenting with pharyngitis. The cost-effectiveness model compares a diagnostic strategy with POC NAAT against a strategy of RADT + culture confirmation of negative results, as this strategy is generally recommended in children and adolescents by clinical guidelines⁸ and for all ages by laboratory-based guidelines.¹² In the cost-effectiveness analysis, modeled costs and clinical effects (measured in QALDs lost due to GAS, GAS complications, and antibiotic complications) and the incremental cost-effectiveness ratio were calculated to demonstrate the comparative value of a POC NAAT diagnostic approach over a 1-year period. The budget impact analysis integrated the entire range of diagnostic techniques available in the United States, including rapid testing options, culture, or clinical diagnosis (“Clinician Scoring Method”) to

estimate the budget impact to a third-party payer of adopting POC NAAT for GAS diagnosis over the course of 5 years.

Given the acute nature of the disease, the model assumed that all disease-specific events resolve within the year disease occurs. Direct medical costs presented in 2018 US\$ were included from the payer perspective in the base-case analysis. An alternate scenario analysis also incorporated indirect costs associated with lost productivity. Other key scenarios, as well as one-way sensitivity analysis (OWSA) and

probabilistic sensitivity analysis (PSA), were performed.

Model Inputs

Key model inputs are available in **Table 1**.^{5,6,12-31} The population under consideration included patients presenting with pharyngitis with sore throat who are tested for GAS in the United States. Patients were assumed to reflect the population distribution of the United States according to data from the US Census Bureau,¹³ with a mean age of 38 years, 22.6% younger than 18 years, and 77.4% 18 years and older. Prevalence of GAS was 37% among children⁵ and 10% among adults⁶ based on published estimates. The prevalence reflects estimates in the population with sore throat and tested for GAS, hence those estimates may be higher than GAS pharyngitis prevalence among the general population.

Clinical inputs included test performance, GAS treatment and related adverse events, and risk of complications from progressive disease. Test sensitivity and specificity for POC NAAT, RADT, culture, and the Clinician Scoring Method were extracted from the literature and are reported in Table 1.^{5,6,12-31} Two clinician scoring methods are currently recommended: the FeverPAIN and the Centor criteria.⁶ Performance of the Centor criteria was used to represent the Clinician Scoring Method, as it is the most widely used clinical scoring method in the United States¹⁴ and detailed quantitative performance data of this method as a stand-alone diagnostic approach are available, whereas this is not true for FeverPAIN.¹⁵ Test performance values were used in the model to identify the proportion of patients correctly identified as having GAS and subsequent treatment effects. The antibiotic regimens for adults and children determined to have GAS pharyngitis were based on US guidelines.^{6,8} The recommended regimen is oral penicillin V^{6,8} for 10 days, at the dose of 250 mg twice daily for children and 500 mg twice daily for adults.³ In the model, all patients with a positive GAS test result were assumed to be treated with penicillin. In the base case, it was assumed that patients do not have penicillin allergy, but this assumption was tested in a scenario analysis where 10%¹⁶ of patients were assumed to be allergic and treated with cephalexin.¹⁴ For patients with “true positive” results, antibiotics were assumed to reduce downstream GAS complications, whereas for patients without GAS but with a positive result (false positive), antibiotics were

TABLE 1. Key Model Inputs^{5,6,12-31}

Input name	Value		References/comments				
	Population						
	Children (< 18 years)	Adult (≥ 18 years)					
Mean age in the pharyngitis population	38 years		12				
Age distribution in the pharyngitis population	22.6%	77.4%					
Proportion of pharyngitis with GAS	37%	10%	5,6				
Test performance							
	Sensitivity	Specificity					
POC NAAT	95.5%	99.3%	29				
RADT only	85.5%	93.7%					
Culture	71.8%	100%					
Clinician Scoring Method	49%	82%	Centor score 3+ ³⁰				
Downstream complications of GAS and effectiveness of antibiotics							
Acute rheumatic fever	0.05%		13				
Complicated ARF	10%						
Death from ARF	1%						
Peritonsillar abscess	1.5%		31				
Effectiveness of antibiotics in reducing GAS complications	70%		14				
Adverse effects of antibiotics							
Mild antibiotic reaction	9.499%		15,16 Note: death from antibiotic reaction is conditional on having a severe antibiotic reaction.				
Severe antibiotic reaction	0.5%						
Death from antibiotic reaction	0.001%						
Utilities and disutilities							
Healthy utility	0.95		13				
Death (utility)	0		Assumption				
Disutility of pharyngitis	0.05		13				
Disutility of GAS complications	0.5		26				
Disutilities of mild antibiotic reactions (eg, rash)	0.05		27				
Disutilities of severe antibiotic reactions (eg, anaphylaxis)	0.5		26				
Test costs							
POC test cost	\$25.65		CPT: 87651 ¹⁷				
RADT	\$16.53		CPT: 87880 ¹⁷				
Culture screen and pathogen identification	\$20.17		CPT: 87081 (test), CPT: 87077 (identification) ¹⁷				
GAS complication costs							
	Children	Adult					
ARF	\$4820		13,17,21,22,25				
Complicated ARF	\$32,682						
Peritonsillar abscess	\$17,285	\$10,062	23,24				
Treatment costs							
	Children	Adult					
Antibiotics (oral penicillin V)	\$5.67	\$7.56	19				
Antibiotics (oral cephalexin)	\$14.52		14				
Mild antibiotic complications (eg, rash)	\$74.16		CPT: 99213 ¹⁸				
Severe antibiotic complications (eg, anaphylaxis)	\$8759		20				
Budget impact: tests' market share							
	Current	Year 1	Year 2	Year 3	Year 4	Year 5	
POC NAAT	0.0%	1.2%	1.9%	2.8%	3.8%	4.7%	Roche Diagnostics
RADT	49.0%	48.2%	47.7%	47.1%	46.4%	45.7%	
RADT + culture	21.7%	21.3%	21.1%	20.8%	20.5%	20.3%	Calculated from Luo et al ²⁸
Clinician Scoring Method	29.3%	29.3%	29.3%	29.3%	29.3%	29.3%	

ARF, acute rheumatic fever; CPT, Current Procedural Terminology; GAS, group A streptococcus; NAAT, nucleic acid amplification tests; POC, point-of-care; RADT, rapid antigen detection tests.

TABLE 2. Budget Impact Model Population Cascade, Each Year

Diseases	Pediatrics (0-17 years)	Adults (≥ 18 years)	Total
GAS	919,820	851,400	1,771,220
No GAS	2,085,704	7,143,076	9,228,780
Total	3,005,524	7,994,476	11,000,000

GAS, group A streptococcus.

considered inappropriate. Patients with GAS and a negative result (false negative) were assumed to receive over-the-counter (OTC) medication. In the model, the proportion of patients with GAS who develop ARF and peritonsillar abscess was based on a previously published model.³² Appropriate treatment via antibiotics was given to all patients with a positive test and was associated with a 70% decrease in ARF and peritonsillar abscess compared with patients with GAS not receiving appropriate antibiotics (false negative result) (Table 1^{5,6,12-31}). Effectiveness of treatment in preventing complications reflected the lowest prevalence of complications used in prior cost-effectiveness studies.¹⁷ Rates of reaction to antibiotics (mild and severe) and death from severe reaction were also integrated in the analysis, based on values used in previous economic analyses.^{18,19}

Consistent with US cost-effectiveness guidelines,²⁰ direct medical costs from a third-party payer perspective included costs of tests, treatments, antibiotic-related adverse events, and managing complications from GAS. OTC medication costs were not included. Test costs were identified using the CMS Clinical Laboratory Fee Schedule.²¹ Medication unit costs for GAS treatment were taken from the Medi-Span Price Rx database.²² Costs due to mild and severe adverse events from antibiotic intake were included. Antibiotic rash was assumed to require 1 follow-up appointment and treatment with OTC medications.^{3,8} Cost of antibiotic anaphylaxis was based on a proxy of the cost to treat food-induced anaphylaxis.²³ For management of GAS complications, costs directly reflected the literature or current fee schedule costs applied to appropriate resource utilization.^{21,24} For ARF, resource utilization from a prior modeling study was used³² and was verified for continued relevance with a clinician. Severe ARF was assumed to require hospitalization, and its cost was derived from the Healthcare Cost and Utilization Project.²⁵ Finally, costs associated with peritonsillar abscess for children and adults were taken from 2 database analyses using the Kids' Inpatient Database and the National Inpatient Sample, respectively.^{26,33} Where necessary, costs were inflated to 2018 US\$.²⁷

Productivity loss was considered in a scenario analysis as recommended by the Institute for Clinical and Economic Review guidelines.²⁰ The number of working adults, derived from the Bureau of Labor Statistics,³⁴ was applied to the general population extracted from the Census Bureau¹³ to calculate the proportion of working adults. Productivity loss was based on the median wage in the United States for the third quarter of 2018.³⁴ The model

assumed that a working adult would need to stay home with a sick child and, therefore, productivity loss was considered the same for children as for adults. Productivity loss was calculated separately for immediately treated GAS, delayed treatment of GAS (due to culture confirmation), and untreated GAS. For each group, total productivity loss was calculated by multiplying the proportion of the working population by the duration of illness and wage. **eAppendix Table 1** shows productivity loss calculations in more detail.

Health-related quality of life inputs are presented in Table 1.^{5,6,12-31} Disease-specific disutilities were derived from previous GAS models for the same conditions in US populations. These include pharyngitis,³² GAS complications,²⁸ severe antibiotic complications,²⁸ and mild antibiotic complications.³⁵

The budget impact analysis calculated the difference in costs between a current scenario without POC NAAT and projected scenario with POC NAAT from the payer perspective over 5 years. Although the budget impact analysis reflects clinical inputs and cost calculations from the larger model, it required consideration of additional epidemiological and market distribution information to scale results to the US population level. According to a description of the epidemiology of GAS in the United States, 11 million patients are diagnosed with GAS each year and therefore this value was used as the hypothetical "total market" of GAS tests conducted each year.²⁹ Epidemiology data, including prevalence and age distribution as described in the population section, were used to calculate a population cascade (**Table 2**). The model applied expected market share distributions for POC NAAT and alternative testing strategies. The market share for the scenario without POC NAAT was extracted from a retrospective study.³⁰ Projected POC NAAT market shares and assumptions were applied to estimate the total costs in the scenario with POC NAAT. It was assumed that POC NAAT would pull market share equiproportionally from the RADT market. The assumed market share distribution over 5 years is reported in Table 1.^{5,6,12-31}

Analyses

In the base-case cost-effectiveness analysis, incremental 1-year costs and GAS-related QALDs lost were estimated for POC NAAT vs RADT + culture from the US payer perspective. The base-case budget impact analysis estimated the total costs and net budget impact for the US population based on the distribution of testing approaches and associated consequences over 5 years.

Uncertainty was explored through 5 scenario analyses, as well as OWSA and PSA. The scenario analyses included incorporation of productivity loss into the model; evaluation of results by age group with scenarios for children only and for adults only; modeling an outbreak scenario with a GAS prevalence of 60%; and including cephalexin to treat GAS for 10%¹⁶ of patients assumed to be allergic to penicillin. OWSA was performed to assess the impact of parameter uncertainty by varying each input by +/- 20% separately, and multivariate probabilistic analysis was run over 1000 simulations according to specified distributions.

RESULTS

Cost-effectiveness Results

Under the base-case assumptions, cost-effectiveness results showed that POC NAAT is a dominant diagnostic strategy compared with RADT + culture, leading to lower costs per patient and slightly fewer QALDs lost. Base-case results are presented in [Table 3](#).

Although the overall reduction of 0.0037 QALDs in lost quality-adjusted survival was small, when considering other outcomes, such as the proportion of patients appropriately treated and reductions in unnecessary antibiotic prescriptions, POC NAAT have potential to generate substantial benefits. As shown in [eAppendix Figure 2](#), a diagnostic strategy using POC NAAT would avert 54,229 unnecessary antibiotic prescriptions per 1,000,000 tests compared with RADT + culture. Under the POC NAAT diagnostic strategy, the number of patients appropriately treated would increase by 46,321 per 1,000,000 tests, therefore reducing overall inappropriate treatment by 5% compared with RADT + culture ([eAppendix Figure 3](#)). Mean costs per patient were \$44 for POC NAAT and \$78 for RADT + culture. The cost breakdown (Table 1^{5,6,12-31}) shows that the test cost was greater for POC NAAT, yet by increasing the proportion of patients accurately diagnosed, a POC NAAT approach yielded lower costs of treatment, GAS complications, and antibiotic complications. Relative to an RADT + culture approach, a POC NAAT strategy was associated with 11% and 27% reductions in GAS complication and antibiotic-related complication costs, respectively. A summary of costs per patient is displayed in [eAppendix Figure 4](#).

The tornado diagram comparing incremental costs is displayed in [eAppendix Figure 5](#), showing that POC NAAT remained cost-saving across all simulations. Results were most sensitive to POC NAAT and RADT specificity and sensitivity values. Overall results were robust, with per-patient cost savings from POC NAAT varying between \$25 and \$43. Thus, cost result variation was small across a +/-20% range in parameter values. The average probabilistic result was similar to the base case, with an incremental cost difference of \$34 and 0.0037 fewer QALDs lost associated with POC NAAT. POC NAAT were projected to be cost-saving in all 1000 simulations, with a cost decrease between \$25 and \$40 compared with RADT + culture. Incremental QALDs for POC NAAT vs RADT + culture varied between a gain of 0.030 QALDs and a loss of 0.023 QALDs. A scatterplot of PSA results is displayed in [eAppendix Figure 6](#). In all scenario analyses, POC NAAT remained dominant compared with a RADT + culture approach. When productivity loss was included, POC NAAT resulted in savings of \$53 ([eAppendix Table 2](#)). Lower productivity loss for POC NAAT was due to reduction in GAS complications. When considering different age groups, due to higher underlying risk of GAS-related morbidity, GAS-related QALD losses in children were greater than in the adult group for both strategies, with 0.0419 and 0.0456 QALDs lost among children under the POC NAAT and RADT + culture strategies, respectively, vs 0.0410 and 0.0448 QALDs lost

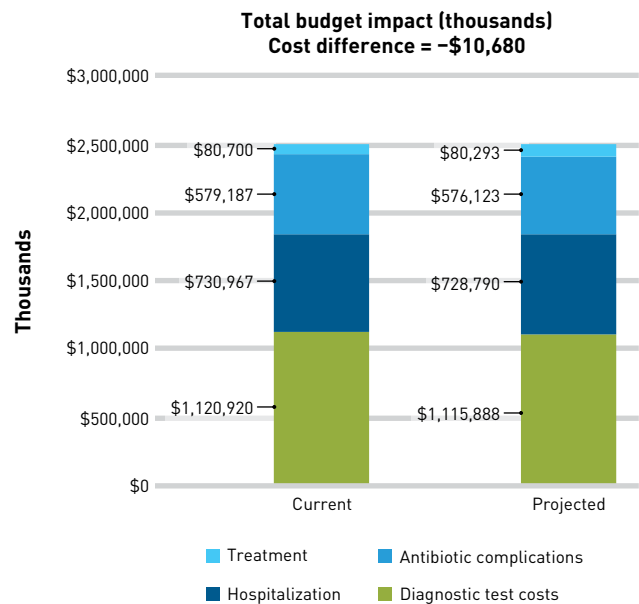
TABLE 3. Cost-effectiveness Results: Base Case

Test Name	Cost, mean per patient		QALDs lost		ICER per QALD gained
	Total	Incremental ^a	Total	Incremental ^a	
POC NAAT	\$44	–	0.0413	–	DOMINANT
RADT + culture	\$78	\$34	0.0451	0.0037	DOMINATED

ICER, incremental cost-effectiveness ratio; NAAT, nucleic acid amplification tests; POC, point-of-care; QALD, quality-adjusted life-day; RADT, rapid antigen detection tests.

^aAll incremental results are compared with POC NAAT.

FIGURE. Budget Impact Results: Years 1-5



in the adult population. Incremental results in the 2 populations remained consistent with the base case ([eAppendix Tables 3 and 4](#)). In an outbreak scenario with a GAS prevalence of 60% for adults and children, incremental results between the 2 strategies were smaller but remained consistent with the base case ([eAppendix Table 5](#)). As shown in [eAppendix Table 6](#), modeling the use of cephalexin in patients allergic to penicillin had no impact on the results, due to the small difference between the 2 antibiotic costs and the relatively small weight of antibiotic costs among total costs (14% and 18% of total costs for POC NAAT and RADT + culture, respectively).

Budget Impact Results

As shown in the [Figure](#), based on 11 million expected GAS tests per year together with projected market uptake for POC NAAT of 1.2% in year 1 to 4.7% in year 5 (Table 1^{5,6,12-31} and [eAppendix Table 7](#)), adding POC NAAT to available testing for pharyngitis was calculated to be

cost-saving (\$10.68 million), which reflects a slight decrease of 0.4% relative to current budget for US payers. Although the uptake of POC NAAT was assumed to be proportional across diagnostic strategies, the increase in costs associated with a RADT + culture diagnostic approach specifically outweighed the cost of introducing POC NAAT. Detailed cost results are presented in [eAppendix Table 8](#).

DISCUSSION

This modeling analysis was undertaken to assess the cost-effectiveness and budget impact of POC NAAT for the diagnosis of GAS in the United States. Cost-effectiveness results indicate that POC NAAT were the dominant diagnostic approach over RADT + culture. The majority of the POC NAAT cost offsets were due to minimizing GAS complications, as well as test cost differences, compared with a RADT + culture approach. OWSA revealed that model results are relatively insensitive to 20% variation across parameters; the most sensitive parameters were test sensitivity and specificity of POC NAAT and RADT, yet the magnitudes of change observed in results were small and insufficient to affect conclusions. Explored scenarios likewise demonstrated robustness of the results, with consistent QALD gains and cost savings attributed to a diagnostic approach with POC NAAT. The model was not sensitive to variation in GAS prevalence, as shown in the outbreak scenario, which resulted in consistent costs and QALD compared with the base case. In addition to cost and QALD results, the analysis estimated that POC NAAT would increase the number of appropriate treatment decisions for more than 46,000 patients and prevent unnecessary antibiotic use for nearly 55,000 patients per 1 million GAS tests conducted relative to RADT + culture. In terms of overall budget impact, introduction of POC NAAT for US patients presenting with pharyngitis was cost-neutral, with a very slight decrease in payer costs of 0.4% relative to current budget.

GAS pharyngitis is a common infection. Correct and timely diagnosis has the potential to improve the quality of care and treatment outcomes, aid in antibiotic stewardship, and prevent secondary infections (eg, ARF, peritonsillar abscess). Given concerns with growing antibiotic resistance, reducing excessive or inappropriate antibiotic prescriptions and improving antibiotic stewardship is one approach to minimize the global health care threat.³¹

To our knowledge, this is the first study that compares GAS POC testing strategies including POC NAAT in children and adults in the United States. In the study conducted by Neuner et al,³² the authors considered observation without testing or treatment, empirical treatment with penicillin, treating based on throat culture, optical immunoassay (OIA) + culture confirmation, or OIA only. Although the specific strategies were not comparable with our analysis, a similar magnitude of QALD benefits and cost savings was observed from improving diagnostic accuracy and increasing appropriate treatment of GAS. Two other cost-effectiveness analyses using a decision tree model were conducted in pediatric populations, but with different strategies under comparison, and were

therefore not comparable to the current study. In 2006, Van Howe et al¹⁹ compared 6 management strategies to diagnose and treat GAS in the United States (eg, RADT vs alternate strategies including observation only, empirical treatment of all presenting patients, clinical diagnosis [scoring method], and culture) and showed that rapid antigen testing had the best cost-utility result from the payer perspective. Garcia et al¹⁸ compared 6 strategies to diagnose and manage pediatric pharyngitis from the Spanish National Health Services perspective. Culture was most effective and most costly of all compared strategies, whereas clinical scoring + rapid testing had the lowest cost-effectiveness ratio compared with treating all patients using clinical scoring, rapid tests, culture, or rapid test + culture strategies.

Limitations

Consistent with any economic model, this model is limited by assumptions. We assumed that clinicians treat based on test results and that patients receive treatment with no delay after positive results. Our analysis assumed penicillin as a proxy for antibiotic effectiveness; this was considered appropriate based on US treatment recommendations for GAS. In addition, OTC medication costs were not included in model calculations. However, given the higher sensitivity and specificity of POC NAAT, this omission minimizes any costs that would accrue to comparator strategies with larger numbers of misclassified patients. The effectiveness of antibiotic treatment in preventing complications was described in prior cost-effectiveness studies.¹⁷ Although rates were similar across published models, by selecting the lower estimate for antibiotic effectiveness, the model provides a conservative estimate of the value of timely diagnosis, as it leads to estimates of smaller potential benefit. Finally, the model did not consider the impact of reducing disease transmission due to timely treatment of patients with GAS. Although population dynamics may accurately depict potential effects of treatment, use of a decision tree model is consistent with the Neuner analysis³² and can be considered a conservative approach. Indeed, improved test performance could be expected to reduce transmission and thus lead to greater health benefits and cost offsets.

The comparator included in the cost-effectiveness analysis is RADT followed by reflex culture for negative results for both adults and children. Although reflex testing in adults is not required according to guidelines,^{6,8} it is often performed in clinical practice.³⁶ In addition, the main laboratories in the United States recommend that all negative RADT undergo culture confirmation.³⁷⁻³⁹ However, RADT alone remains an available option and has been reported by Luo et al to be performed in the majority of cases.³⁰ Supplemental analysis compared with RADT alone in the adult population led to similar QALDs and costs compared with POC NAAT (0.0049 incremental QALDs and -\$5 incremental costs). A threshold analysis showed that 87% of tests would need to be performed by RADT alone, and the remaining 13% by RADT with culture confirmation, to reach cost neutrality compared with POC NAAT.

CONCLUSIONS

Given the incidence of GAS each year, accurate and timely diagnosis may be an important way to limit costs and clinical consequences for a population. Correct and timely diagnosis of GAS at the point of care was projected to increase the proportion of patients receiving appropriate treatment, including minimizing unnecessary antibiotic use. Overall, use of POC NAAT is slightly more effective without incurring additional costs. At a population level, the diagnostic improvement associated with POC NAAT results in slight savings to overall budget. Therefore, POC NAAT for diagnosis of GAS may be considered of acceptable value compared with current standard of care in the United States. ■

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eAPPENDIX

eAppendix Table 1: Productivity Loss Inputs and Calculations

Productivity Loss Component	Input	Reference
Average weekly wage	\$893	27, 12
Proportion working adults	45%	
Duration of disease		
<i>Uncomplicated GAS</i>		
Untreated	5 days	13
Treated after Culture	4 days	13
Treated immediately	3 days	13
<i>GAS complications</i>		
ARF	103 days	28,36
Complicated ARF	166 days	
Peritonsillar abscess	10 days	13
Reaction to antibiotics		
Mild (i.e. rash)	5 days	13
Severe (i.e. anaphylaxis)	4 days	
Calculated variables		
Treat immediately	\$413.25	
Treat delay	\$540.83	
Untreated	\$733.28	

eAppendix Table 2: Cost-effectiveness Results, Payer + Productivity

Test	Costs		QALDs lost (Disc)		ICER per QALD gained
	Total	Incr.	Total	Incr.	
POC NAAT	\$110	--	0.0413	--	DOMINANT
RADT + Culture	\$163	\$53	0.0451	0.0037	DOMINATED

eAppendix Table 3: Cost-Effectiveness Results, Children Only Scenario

Test	Costs		QALDs lost (Disc)		ICER per QALD gained
	Total	Incr.	Total	Incr.	
POC NAAT	\$44	--	0.0419	--	DOMINANT
RADT + Culture	\$78	\$34	0.0456	0.0037	DOMINATED

eAppendix Table 4: Cost-Effectiveness Results, Adults Only Scenario

Test	Costs		QALDs lost (Disc)		ICER per QALD gained
	Total	Incr.	Total	Incr.	
POC NAAT	\$44	--	0.0410	--	DOMINANT
RADT + Culture	\$78	\$34	0.0448	0.0038	DOMINATED

eAppendix Table 5: Cost-Effectiveness Results, Outbreak Scenario (GAS prevalence 60%)

Test	Costs		QALDs lost (Disc)		ICER per QALD gained
	Total	Incr.	Total	Incr.	
POC NAAT	\$95	--	0.1524	--	DOMINANT
RADT + Culture	\$127	\$32	0.1536	0.0012	DOMINATED

eAppendix Table 6: Cost-Effectiveness Results, Allergy to Penicillin Scenario (10% of patients treated with cephalexin)

Test	Costs		QALDs lost (Disc)		ICER per QALD gained
	Total	Incr.	Total	Incr.	
POC NAAT	\$45	--	0.0413	--	DOMINANT
RADT + Culture	\$79	\$34	0.0451	0.0037	DOMINATED

eAppendix Table 7: Projected Number of Tests Per Year

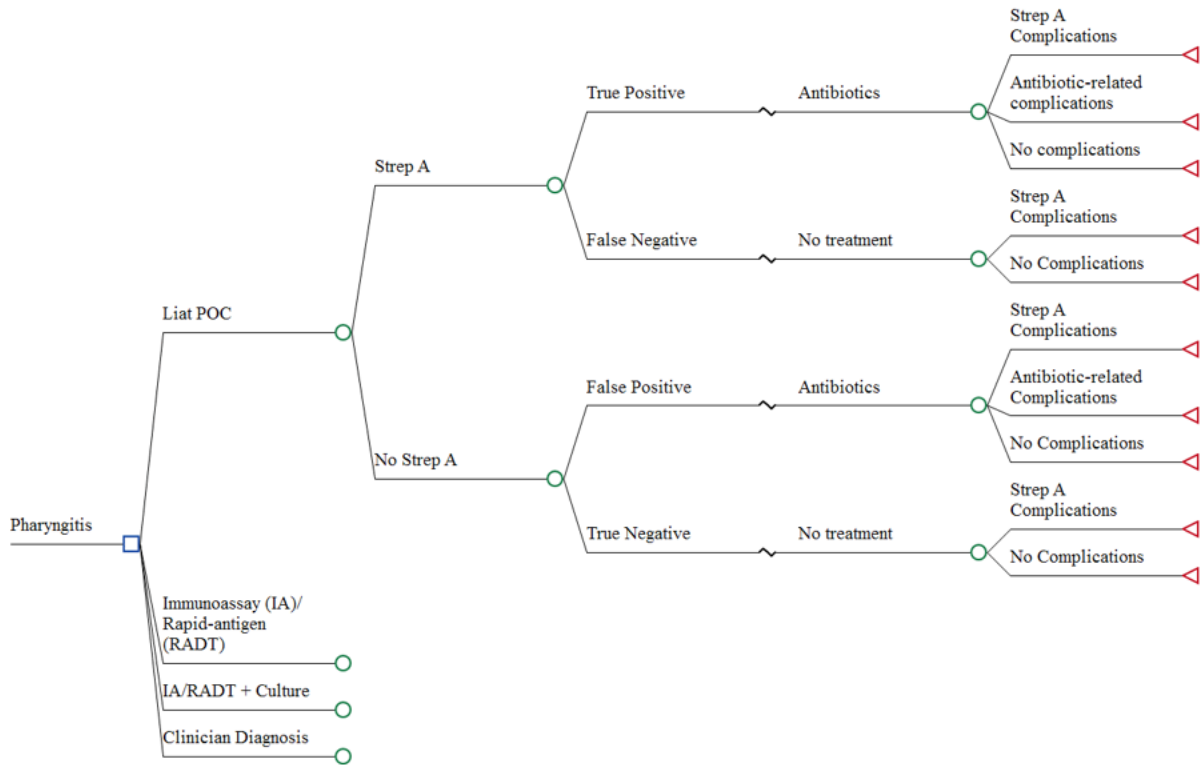
	Current scenario (5 years)	Projected scenario (Years 1-5)						Difference
		Year 1	Year 2	Year 3	Year 4	Year 5	Projected Total	
POC NAAT	-	132,000	209,000	308,000	418,000	517,000	1,584,000	1,584,000
IA / RADT only	26,950,000	5,298,515	5,245,149	5,176,535	5,100,297	5,031,683	25,852,178	-1,097,822 (-4.1%)
IA / RADT + culture confirmation	11,935,000	2,346,485	2,322,851	2,292,465	2,258,703	2,228,317	11,448,822	-486,178 (-4.1%)
Clinician Scoring Method	16,115,000	3,223,000	3,223,000	3,223,000	3,223,000	3,223,000	16,115,000	0
Total	55,000,000	11,000,000	11,000,000	11,000,000	11,000,000	11,000,000	55,000,000	0

eAppendix Table 8: Detailed Budget Impact Results (Thousands \$)

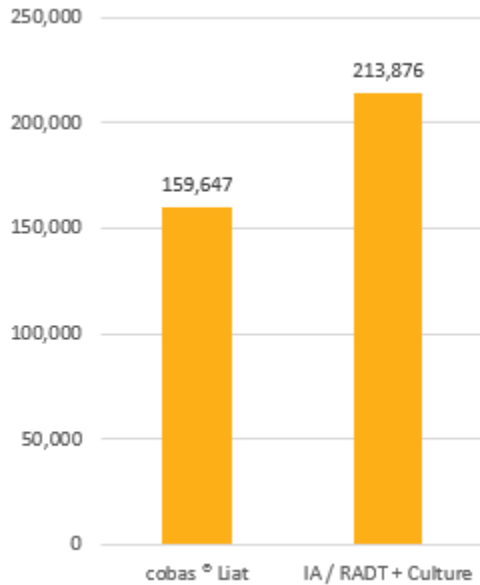
	Current years 1-5	Projected Years 1-5						Difference
		Year 1	Year 2	Year 3	Year 4	Year 5	Total	
Test Costs (Thousands)								
POC NAAT	\$0	\$3,386	\$5,361	\$7,900	\$10,722	\$13,261	\$40,630	
IA/ RADT	\$445,483	\$87,584	\$86,702	\$85,568	\$84,308	\$83,174	\$427,337	
IA/RADT + culture	\$675,436	\$132,794	\$131,457	\$129,737	\$127,827	\$126,107	\$647,922	
Clinician Scoring	\$0	\$0	\$0	\$0	\$0	\$0	\$0	
Total	\$1,120,919	\$223,765	\$223,520	\$223,206	\$222,856	\$222,542	\$1,115,888	-\$5,032
Treatment Costs (Thousands)								
POC NAAT	\$0	\$150	\$238	\$351	\$476	\$589	\$1,804	
IA/ RADT	\$36,625	\$7,201	\$7,128	\$7,035	\$6,931	\$6,838	\$35,133	
IA/RADT + culture	\$17,646	\$3,469	\$3,435	\$3,390	\$3,340	\$3,295	\$16,928	
Clinician Scoring	\$26,427	\$5,286	\$5,286	\$5,286	\$5,286	\$5,286	\$26,428	
Total	\$80,700	\$16,106	\$16,086	\$16,061	\$16,033	\$16,007	\$80,293	-\$407
Complications Costs (Thousands)								
POC NAAT	\$0	\$1,263	\$1,999	\$2,946	\$3,999	\$4,946	\$15,153	
IA/ RADT	\$312,251	\$61,390	\$60,772	\$59,977	\$59,094	\$58,299	\$299,532	
IA/RADT + culture	\$113,183	\$22,252	\$22,028	\$21,740	\$21,420	\$21,132	\$108,572	
Clinician Scoring	\$305,531	\$61,106	\$61,106	\$61,106	\$61,106	\$61,106	\$305,532	

Total	\$730,966	\$146,012	\$145,906	\$145,770	\$145,619	\$145,483	\$728,790	-\$2,177
Antibiotic Complications Costs (Thousands)								
POC NAAT	\$-	\$1,071	\$1,696	\$2,500	\$3,393	\$4,196	\$12,856	
IA/ RADT	\$261,047	\$51,323	\$50,806	\$50,142	\$49,403	\$48,739	\$250,414	
IA/RADT + culture	\$129,773	\$25,514	\$25,257	\$24,927	\$24,560	\$24,229	\$124,487	
Clinician Scoring	\$188,365	\$37,673	\$37,673	\$37,673	\$37,673	\$37,673	\$188,366	
Total	\$579,186	\$115,582	\$115,433	\$115,242	\$115,029	\$114,837	\$576,123	-\$3,064

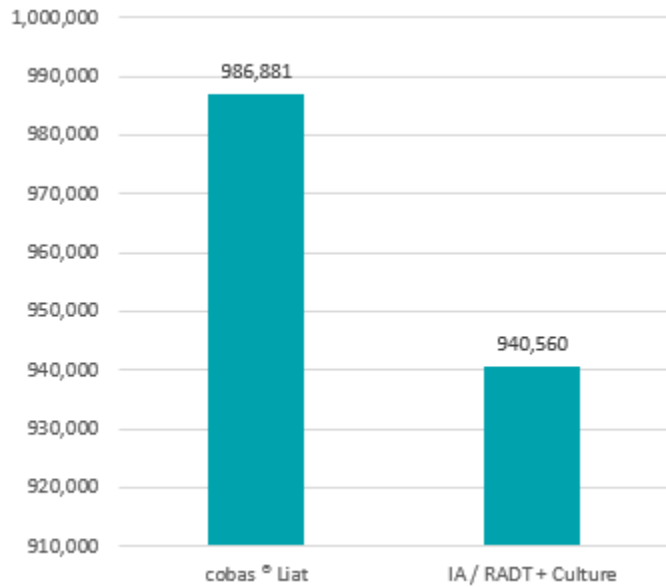
eAppendix Figure 1: Model Decision Tree



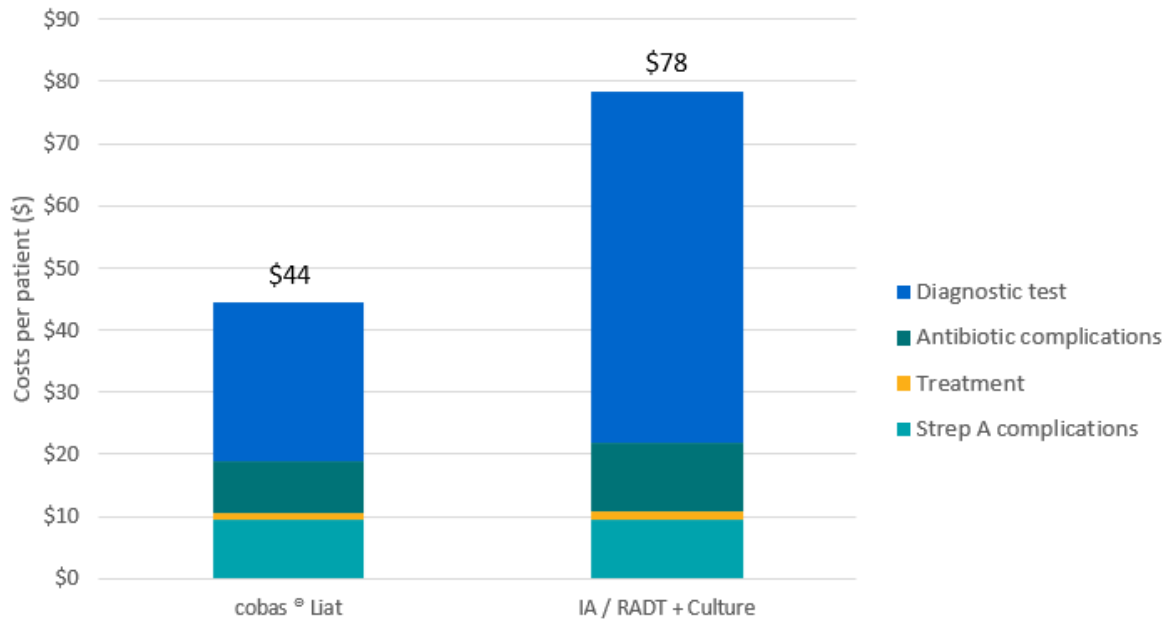
eAppendix Figure 2: Antibiotics Use Per 1 Million Tests



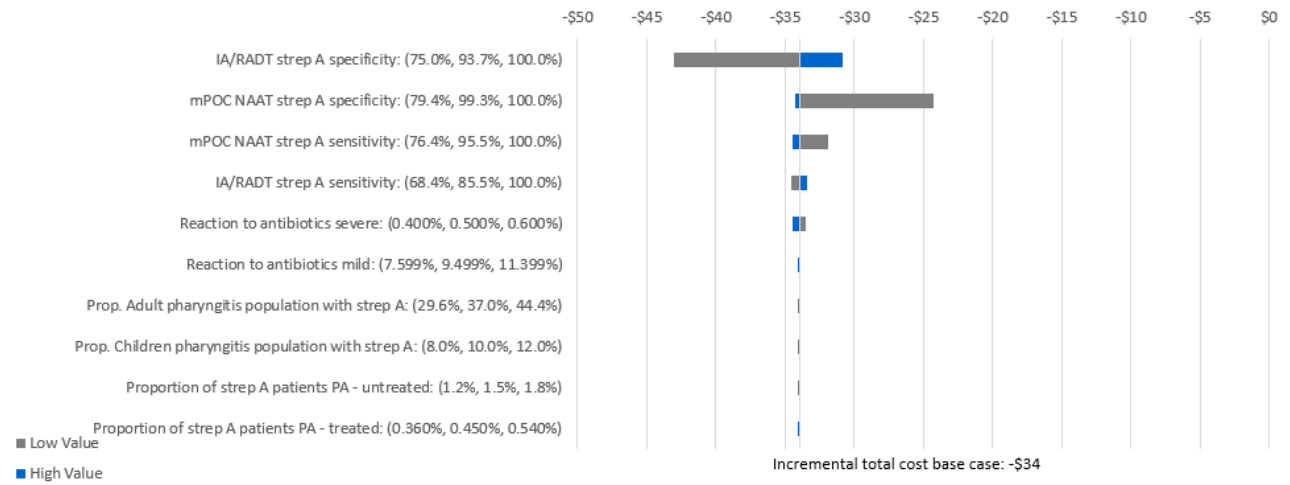
eAppendix Figure 3: Proportion of Patients Appropriately Treated



eAppendix Figure 4: Cost Results Per Patient



eAppendix Figure 5: One-way Sensitivity Analysis Tornado Diagram, Cost Difference of POC NAAT Versus IA/RADT + Culture



eAppendix Figure 6: Probabilistic Sensitivity Analysis Results

Calculated as results in total cost and QALDs for RADT + culture minus costs and QALDs for POC NAAT

