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Participatory Medicine: A Home Score for Streptococcal Pharyngitis Enabled by Real-Time Biosurveillance:

A Cohort Study

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Abstract

Background—Consensus guidelines recommend that adults at low risk for group A streptococcal (GAS) pharyngitis be neither tested nor treated

Objective—To help patients decide when to visit a clinician for the evaluation of sore throat.

Design—Retrospective cohort study.

Setting—A national chain of retail health clinics.

Patients—71 776 patients aged 15 years or older with pharyngitis who visited a clinic from September 2006 to December 2008.

Measurements—The authors created a score using information from patient-reported clinical variables plus the incidence of local disease and compared it with the Centor score and other traditional scores that require clinician-elicited signs.

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Note: Dr. Fine had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Results—If patients aged 15 years or older with sore throat did not visit a clinician when the new score estimated the likelihood of GAS pharyngitis to be less than 10% instead of having clinicians manage their symptoms following guidelines that use the Centor score, 230 000 visits would be avoided in the United States each year and 8500 patients with GAS pharyngitis who would have received antibiotics would not be treated with them.

Limitation—Real-time information about the local incidence of GAS pharyngitis, which is necessary to calculate the new score, is not currently available.

Conclusion—A patient-driven approach to pharyngitis diagnosis that uses this new score could save hundreds of thousands of visits annually by identifying patients at home who are unlikely to require testing or treatment.

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Globally, group A streptococcal (GAS) pharyngitis affects hundreds of millions of persons each year (1, 2). In the United States, more than 12 million persons make outpatient visits for pharyngitis; however, clinicians cannot differentiate GAS pharyngitis from other causes of acute pharyngitis (for example, viral) on the basis of a physical examination of the oropharynx (3).

The American College of Physicians and Centers for Disease Control and Prevention recommend that health care providers apply clinical scores to classify risk for GAS pharyngitis and direct management of adults with acute pharyngitis (Table 1) (4–6). When the clinical score indicates a low risk, consensus guidelines recommend that adult patients should be neither tested nor treated for GAS pharyngitis. The updated 2012 guidelines from the Infectious Diseases Society of America concur that clinical scoring systems may help identify patients with pharyngitis at sufficiently low risk for GAS pharyngitis that testing may not be necessary (7).

We recently showed that the contemporaneous local incidence of GAS pharyngitis is an important predictor of this condition among patients presenting with a sore throat to CVS MinuteClinics, a large chain of retail health clinics where data are captured uniformly in a single electronic health record (8). Building on this framework, we derived a disease prediction model that we call the “home score” because it was designed for use at home by the patient without input from a clinician and relies on the patient to provide historical features but not physical examination findings (Table 1). The model also includes a local incidence variable for streptococcus, bringing biosurveillance data into the clinical process. We seek to evaluate whether this participatory medicine approach could reduce unnecessary outpatient and emergency department visits for pharyngitis not requiring antibiotic treatment.

Methods

Study Design

We retrospectively analyzed a cohort of patients tested for GAS pharyngitis when they presented with a sore throat from 1 September 2006 to 1 December 2008 to CVS

MinuteClinics, which has about 600 sites in 25 states and the District of Columbia (9–13). MinuteClinics provide care for patients with a limited number of conditions, including sore throat. This data set included 238 656 patient encounters where physician assistants or nurse practitioners collected standardized information from the history and physical examination based on algorithm-driven care. Clinicians enter codified data in real time, and the records are stored in a common database.

MinuteClinic providers have shown more than 99% adherence to a recognized protocol for acute pharyngitis: the Strep Pharyngitis Algorithm from the Institute for Clinical Systems Improvement (14, 15). Guided by the algorithm, clinicians collect structured information about relevant signs and symptoms, acquire rapid testing on all patients with pharyngitis, ordering confirmatory testing when the rapid test results are negative), and treat only patients with positive test results for GAS pharyngitis. All visits in this data set contained complete information about age; all signs and symptoms included in 2 traditional, validated clinical scores (the Centor and McIsaac scores); and test results (Table 1) (4, 16).

Our study included patients with a chief symptom of sore throat or symptoms of pharyngitis with testing performed for GAS pharyngitis. Patients who reported having been treated for GAS pharyngitis within the previous month and those younger than 15 years were excluded. When patients contributed more than 1 visit to the data set, only the first visit was included. MinuteClinic policy is to care only for patients who are generally well-appearing; those with concern for sepsis are referred to emergent care centers.

Test Methods

All clinic locations used the QuickVue In-Line Strep A test (Quidel, San Diego, California), which was waived under the Clinical Laboratory Improvement Amendments. The confirmatory test was a throat culture (43%) or streptococcal DNA probe (57%), which is often considered equal to culture and is widely used in the United States (17, 18). Patients were categorized as positive for GAS pharyngitis if the rapid or confirmatory test results were positive.

Statistical Analysis

The analysis was restricted to 9 MinuteClinic markets from 6 states (Georgia, Indiana, Maryland, Minnesota, North Carolina, and Tennessee) with a minimum of 7000 patient visits each for pharyngitis during the study. Two thirds of the patients were selected randomly for derivation and the rest for validation. We repeated all steps used on the derivation set with the validation set to compare results. To enable integration of contemporaneous, local epidemiologic data on GAS pharyngitis, we used a previously validated biosurveillance variable reflecting disease incidence, the recent local proportion positive (RLPP) (8), expressed using the following equation (Appendix, available at www.annals.org).

$$\frac{(\text{Patients with pharyngitis who tested positive for GAS pharyngitis in market A in the previous 14 d})}{(\text{Total patients with pharyngitis tested for GAS pharyngitis in market A in the previous 14 d})}$$

The RLPP was assigned for each patient visit on the basis of location and date.

Variable Selection

Our a priori hypothesis was that the original variables from the Centor and McIsaac scores would dominate the home score. Because the purpose of the home score is to focus on information that can be supplied by the patient combined with biosurveillance-derived knowledge, we excluded physical examination variables (tender anterior cervical lymph nodes and exudates) from the Centor and McIsaac scores and added the RLPP variable. A stepwise selection model with 15 home score predictors (sex, absence of cough, pain when swallowing, history of fever, exposure to GAS pharyngitis, stomachache, difficulty sleeping, ear pain, postnasal discharge, hoarseness, headache, nausea, vomiting, and lack of rhinorrhea confirmed the hypothesis, identifying the same home variables from the original Centor and McIsaac scores (fever, absence of cough, and age) and RLPP.

Home Score Calculation

The home score (range, 8–62) is based on demographic, historical, and biosurveillance data only, not physical examination data. To calculate the home score for each patient, we used the results of logistic regression based on the final model to calculate the predicted probability (0–100) of GAS pharyngitis. The home score can be calculated from the following equation, where f = −1 if fever is present, f = 1 if fever is not present, c = 1 if cough is present, and c = −1 if cough is not present.

$$\frac{100}{1+\exp\left[(2.05+\mathrm{f}\,(0.44)+\mathrm{c}*(0.27)-3.60\,(\mathrm{RLPP})+0.0002\,(\mathrm{age\ in\ y})\right]}$$

For example, for a 41-year-old patient with fever and cough who presented when the RLPP was 0.19, the home score would be 23.

For each home score of 0 to 100, we calculated the percentage of patients who actually tested positive for GAS pharyngitis and examined the relationship between the home score and positivity for GAS pharyngitis. Standard metrics (sensitivity, specificity, and positive and negative predictive values) compared performance of the home score with the Centor and McIsaac scores and the clinical biosurveillance score (Table 1) (8). The Centor and McIsaac scores rely on elements derived from the history and physical examination. To calculate the Centor score, patients receive 1 point for each of the following factors: fever; absence of cough; presence of tonsillar exudates; and swollen, tender anterior cervical lymph nodes. The Centor score is the sum of these points (range, 0–4).

The McIsaac score (range, 0–5) adjusts the Centor score to account for the increased incidence of GAS pharyngitis in children and decreased incidence in older adults by adding 1 point to the Centor score for those younger than 15 years and subtracting 1 point for those aged 45 years or older. The clinical biosurveillance score (range, 4–79) adjusts the Centor score on the basis of real-time biosurveillance data about the recent local incidence of GAS pharyngitis (Appendix). We calculated the clinical biosurveillance score by adjusting a

patient's Centor score with the RLPP by using the equations in the Appendix Table (available at www.annals.org).

Hypothetical Outcomes

We computed the number of patients who, according to the home score, were at low risk for GAS pharyngitis and therefore might avoid or delay a trip to a medical provider. The Centers for Disease Control and Prevention advocates the American College of Physicians guideline based on the Centor score for management of acute pharyngitis in adults. This guideline recommends that adult patients who are unlikely to have GAS pharyngitis (Centor score, 0–1) should be neither tested nor treated (5). We calculated the Centor scores for these patients as well as the following outcomes: the numbers of visits saved and additional missed cases of GAS pharyngitis compared with the existing American College of Physicians and Centers for Disease Control and Prevention approach.

Analyses ranged across a spectrum of risk thresholds for GAS pharyngitis. We extrapolated results to project the effect on 12 million national visits for pharyngitis annually. We tabulated outcomes across a wide range of home score thresholds from 10 to 30. Metrics include the number of patients who were correctly and incorrectly diagnosed with GAS pharyngitis and the estimated number of patients nationally whose management would be affected by the home score.

The Boston Children's Hospital Committee on Clinical Investigation approved this database analysis. JMP Pro software, version 10.0.0 (SAS Institute, Cary, North Carolina), was used for statistical analyses.

Role of the Funding Source

This work was supported by the Centers for Disease Control and Prevention and the National Library of Medicine, National Institutes of Health. The funding sources had no role in the study design, data analysis, data interpretation, writing of the manuscript, or decision to submit the manuscript for publication.

Results

Of the 132 821 patient visits to 1 of the 9 locations with at least 7000 patient visits, 6726 visits from patients treated in the previous month, 39 279 visits from patients younger than 15 years, and 15 040 repeated visits were excluded, leaving 71 776 visits for calculation of the home score (Figure). Of these, two thirds were used for the derivation set (n = 48 089) and one third for the validation set (n = 23 687).

Among the 48 089 retail health visits for patients aged 15 years or older in the derivation set, 11 614 (24%) tested positive for GAS pharyngitis. In the validation set, 5728 of 23 687 (24%) tested positive. Table 2 shows the characteristics of the derivation and validation sets for age, sex, and clinical signs and symptoms of pharyngitis by GAS pharyngitis result for those aged 15 years or older. Table 2 also contains information about the epidemiologic conditions of GAS pharyngitis (RLPP) when the patient visits took place. In both groups, patients who tested positive for GAS pharyngitis were more likely to present with tonsillar

exudates, swollen anterior cervical lymph nodes, absence of cough, and fever in the previous 24 hours. Table 3 shows the sensitivity, specificity, and positive and negative predictive values of a range of home score thresholds for the derivation and validation sets.

Home Score Performance

Table 4 shows outcomes of patients when using strategies based on the low-risk thresholds where neither testing nor treatment would occur. Two thresholds for the home score and the low-risk thresholds for the Centor and McIsaac scores of less than 2 are shown. If the home score is less than 10, the negative predictive value is 0.90, which means that 90% of the patients identified as low risk by the home score would have tested negative for GAS pharyngitis.

Table 5 summarizes the outcomes if patients were managed on the basis of a home score determined to be low risk. For example, if the home score were less than 10, for every missed patient with GAS pharyngitis, 27 health care visits could be saved in which patients would have been neither tested nor treated for GAS pharyngitis. At a national scale, this would save 230 000 visits annually. This cutoff also could be expected to miss an additional 8500 cases annually of GAS pharyngitis compared with a conventional Centor score--based approach. However, most patients with GAS pharyngitis have a self-limited course.

Complications from missed cases include acute rheumatic fever, which is rare in adults; acute glomerulonephritis that would not be prevented even with antibiotics; and abscess formation, highlighting the importance of close follow-up and recognition of patients who seem ill. At a higher home score threshold of 15, a total of 61 000 additional patients would be missed nationally in 1 year but 780 000 visits would be saved.

Discussion

Clinical prediction models tend to rely on elements gleaned from a patient’s history, physical examination, and preliminary laboratory data to calculate the likelihood of disease and then provide physicians with recommendations about whether to test or treat patients for specific conditions (19–22). Recent, local epidemiology is an important predictor of the risk for communicable diseases among symptomatic patients but is rarely if ever integrated quantitatively into prediction models (8, 23–25). We have internally validated a fusion model using population health data and information supplied directly by patients, using both biosurveillance and participatory medicine approaches to make a common diagnostic decision The model, based on history and recent, local disease patterns without physical examination information, could help clinicians and patients estimate the likelihood of disease before a clinical encounter and help steer these patients to timely, appropriate care when needed. In some instances, patients unlikely to have GAS pharyngitis might avoid, or at least delay, an emergency or outpatient visit.

Anhang Price and colleagues (26) and Kellermann and colleagues (27) have shown the feasibility of Web-based triaging by patients and parents of children with influenza-like illness. Although their study showed great sensitivity in detecting children at risk for complications of influenza, it had low specificity. Our analysis of GAS pharyngitis offers an

opportunity for improving specificity via home triage that incorporates clinical symptoms with relevant, real-time biosurveillance. One other advantage of a home triage system for well-appearing adults with pharyngitis is that acute decompensation is much less probable in this population than in children with influenza.

Even without information from physical examination findings, the home score approaches the accuracies and overall performances of the existing validated scores. Clinicians could use the home score to interact with patients online or over the telephone. There may also be circumstances in which it would be safe for patients themselves to be guided by a home score application.

For example, a home score less than 10 (low risk) might yield the recommendation of supportive measures, such as fever control, rest, and hydration. A tailored message could recommend that these patients recheck their home score in 24 to 48 hours. Because the home score is dynamic, a change in symptoms or local epidemiology could result in a different recommendation.

Patients with higher scores might be advised to seek care for further evaluation and possibly testing. Presenting the absolute risk for GAS pharyngitis and the corresponding recommendation could decrease ambulatory visits that would have been unlikely to result in diagnostic testing for this condition but would have contributed to increased cost, reduced efficiency of the health system, and opportunity cost for the patient. An additional public health benefit could be reduced antibiotic exposure, lessening selection for drug-resistant strains and perturbation of the normal microflora.

Patient-generated data for care and research are becoming increasingly common with further penetration of consumer technology and use of patient portals, personally controlled health records, and mobile health applications (28–30). Although the GAS pharyngitis home score shows the potential value of these data, safe and effective implementation requires key logistic and workflow decisions.

First, the strategy requires national, regional, or local approaches to making the biosurveillance data available at the point of care. Because so many patients are tested for GAS pharyngitis, most hospitals and many large group practices would have sufficient data to generate their own RLPPs. Second, implementers can decide whether a computerized decision-support system based on patient-entered data advises patients directly or is used to guide their providers' decisions through a shared portal or application.

The home score could help clinicians estimate the risk for GAS pharyngitis in children. However, because the American Academy of Pediatrics recommends that all pediatric patients with pharyngitis be tested for GAS pharyngitis, we did not include children younger than 15 years in the analyses about visits saved.

Our study has limitations. Analyses were performed retrospectively, although all data were collected prospectively. Data are not available to calculate interobserver agreement or reliability. Patients entering their symptoms at home could answer differently during a MinuteClinic encounter. These data do not reflect the incidence of other pathogens that can

cause pharyngitis, such as *Fusobacterium necrophorum*, which may be particularly severe in young adults and adolescents and is one pathogen that may cause the Lemierre syndrome (31).

Our data do not allow evaluation of streptococcal carriage, although all patients in this data set were symptomatic with a sore throat; thus, those testing positive would be treated clinically. Performance of the score in a home setting would be best if the patients resembled the MinuteClinic clientele who were included in this study. We recommend that any application using the home score limit it to patients without signs or symptoms of serious illness.

We cannot account for baseline immunity to GAS pharyngitis within the population nor the local emergence of hypervirulent GAS pharyngitis strains or infectious causes of community-acquired pharyngitis, which may vary across regions. Data more recent than 2008 were not available for analysis, but the approach to patients with pharyngitis by MinuteClinics has not changed. The same electronic medical record, algorithm-driven approach, and testing methods are still used, with consistently high provider adherence to protocol. One possible limitation is that the prevalence of GAS pharyngitis among MinuteClinic patients could have changed over time, although one generalizable strength of our model is that it considers a range of prevalence of GAS pharyngitis.

Logistically, integration of a home score might result in lower testing rates by providers, which could weaken the RLPP as a reliable surveillance indicator; therefore, it would be necessary to maintain testing on an intentional sample of patients each week to account for this. The RLPP, as a surveillance variable, is a trailing indicator, so the accuracy of the home score could decrease if GAS pharyngitis rates rapidly changed. To mitigate this effect, we used a 14-day RLPP rather than a 3- or 7-day RLPP, all of which had similar accuracy in the study population.

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Appendix: Calculation of the RLPP and the Clinical Biosurveillance Score

Calculation of the RLPP

The RLPP is a biosurveillance variable that we created previously to reflect the real-time epidemiology of GAS pharyngitis. To calculate the RLPP, we included test results from the study population as well as from younger patients. We included data from patients younger than 15 years when calculating the overall local incidence data because they contribute to the epidemiologic context of the clinically analyzed population. The RLPP is a moving window.

To calculate the 14-day RLPP for a patient seen on 15 January 2007, for example, we divided the number of positive GAS pharyngitis test results by the number of tests sent in that market from 1 to 14 January 2007. We calculated 3-, 7-, and 14-day RLPPs and compared them using the Pearson correlation coefficients. The 3-, 7-, and 14-day RLPPs were strongly correlated (14 vs. 7: r^2= 0.79 [$P < 0.001$]; 7 vs. 3: $r^2 = 0.63$ [$P < 0.001$]; and 14 vs. 3: $r^2 = 0.48$ [$P < 0.001$]), so we used the 14-day RLPP for subsequent analyses because it provides a realistic time frame to generate reliable, contemporaneous local data on GAS pharyngitis.

In the derivation set, an individual patient’s 14-day RLPP was calculated on the basis of a mean of 227 patients (SD, 115; 95% CI, 226 to 228; median, 198 patients [interquartile range, 132 to 334]) tested in that area in the previous 14 days. The median RLPP was 0.25 (interquartile range, 0.20 to 0.30; overall range, 0.08 to 0.51). The RLPP substantially fluctuated across time and location (8).

Calculation of the Clinical Biosurveillance Score

The clinical biosurveillance score can be calculated by adjusting a patient’s Centor score on the basis of the RLPP, as defined by the equations in the Appendix Table(8). For example, for a patient with a Centor score of 2 who presents when the RLPP is 0.33, the clinical biosurveillance score would be 8.8 + 64 * (0.33), which equals 30.

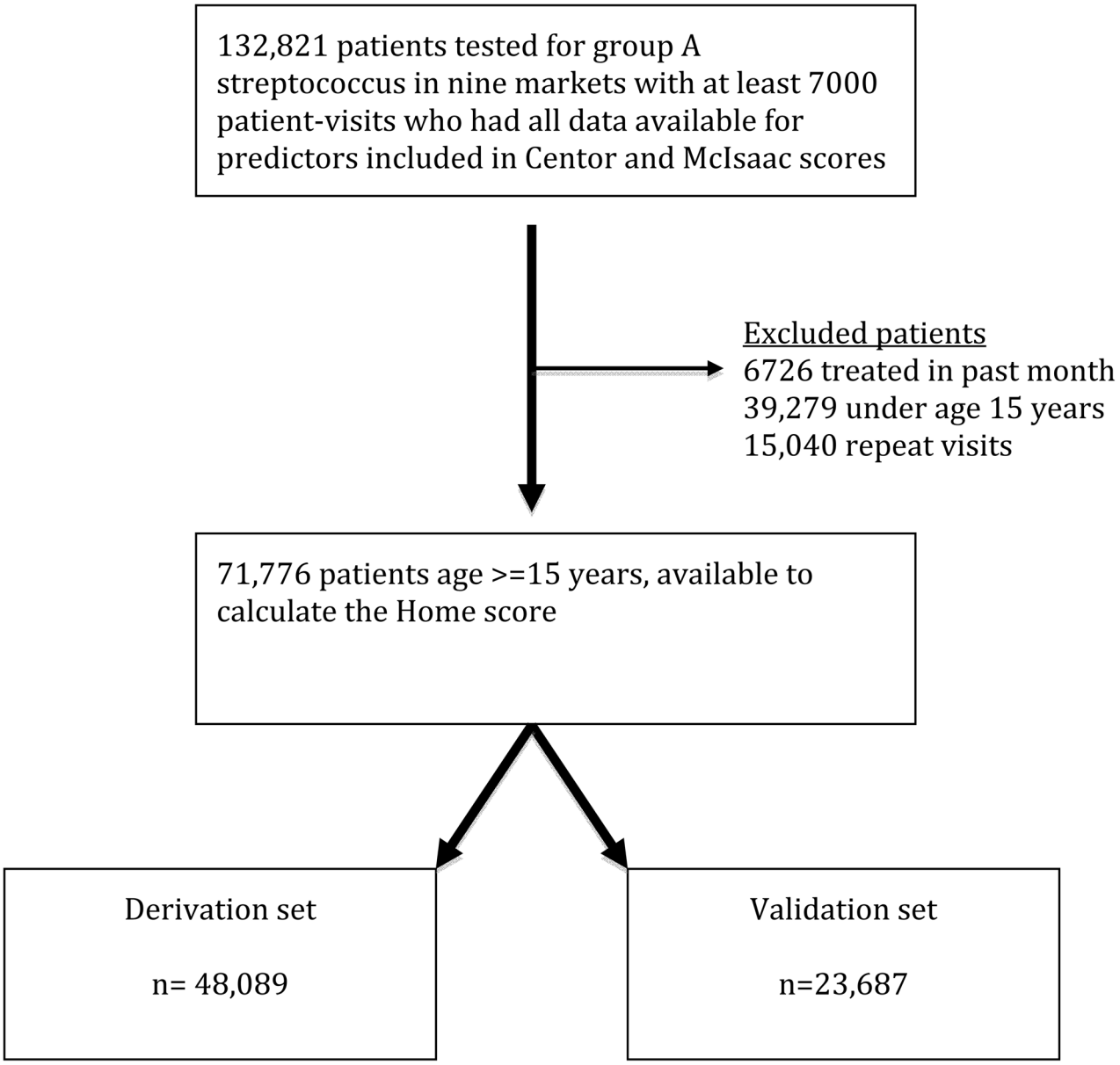

Figure 1.
Patient flow diagram

Table 1

Data Elements Used to Compute the Centor, McIsaac, Clinical Biosurveillance, and Home Scores*

Variable	Centor Score	McIsaac Score	Clinical Biosurveillance Score	Home Score
Historical elements				
Fever	X	X	X	X
Absence of cough	X	X	X	X
Age	–	X	–	X
Physical examination findings				
Swollen, tender anterior cervical lymph nodes	X	X	X	–
Tonsillar exudate	X	X	X	–
Biosurveillance data				
RLPP	–	–	X	X

RLPP = recent local proportion positive.

* For details on how to calculate these scores, see the Methods section.

Table 2

Clinical Characteristics of Patients in the Derivation and Validation Sets*

Characteristic	Derivation Set (*n* = 48 089)			Validation Set (*n* = 23 687)		
	Overall (*n* = 48 089)	GAS Pharyngitis–Positive (*n* = 11 614)	GAS Pharyngitis–Negative (*n* = 36 475)	Overall (*n* = 23 687)	GAS Pharyngitis–Positive (*n* = 5728)	GAS Pharyngitis–Negative (*n* = 17 959)
Mean age, (median [IQR]), *y*	34 (33 [24–41])	33 (33 [25–40])	34 (33 [24–42])	34 (33 [24–41])	33 (33 [25–40])	34 (33 [24–42])
Women	32 481 (68)	7565 (65)	24 916 (68)	15 940 (67)	3801 (66)	12 139 (68)
Fever	14 770 (31)	5340 (46)	9430 (26)	7304 (31)	2517 (44)	4787 (27)
Absence of cough	32 558 (68)	8795 (76)	23 763 (65)	15 986 (67)	4314 (75)	11 672 (65)
Anterior cervical lymphadenopathy	29 060 (60)	9004 (78)	20 056 (55)	14 229 (60)	4399 (77)	9830 (55)
Tonsillar exudate	10 397 (22)	4717 (41)	5680 (16)	5017 (21)	2267 (40)	2750 (15)
Mean RLPP (median [IQR])	0.25 (0.25 [0.20–0.30])	0.27 (0.26 [0.22–0.31])	0.25 (0.24 [0.19–0.29])	0.25 (0.25 [0.20–0.30])	0.27 (0.26 [0.21–0.31])	0.25 (0.24 [0.19–0.29])

GAS = group A streptococcal; IQR = interquartile range; RLPP = recent local proportion positive.

*Data presented as numbers (percentages) unless otherwise specified.

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Table 3

Sensitivity, Specificity, and Positive and Negative Predictive Values of Derivation (n = 48 089) and Validation (n = 23 687) Sets at a Range of Home Score Thresholds

Home Score	Sensitivity, %		Specificity, %		Positive Predictive Value, %		Negative Predictive Value, %	
	Derivation Set	Validation Set	Derivation Set	Validation Set	Derivation Set	Validation Set	Derivation Set	Validation Set
<10	99	99	4	1	25	24	90	87
<15	90	91	22	18	27	26	87	86
<20	70	74	50	44	31	30	84	84
<25	51	50	71	70	36	35	82	82
<30	40	37	81	81	40	38	81	80

Table 4

Overall Performance of Models at Thresholds for Identifying Patients at Risk for GAS Pharyngitis in the Derivation Set

Model and Threshold	True Positive, *n*	False Positive, *n*	False Negative, *n*	True Negative, *n*	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Home score								
<10	11 453	35 101	161	1374	0.99	0.04	0.25	0.90
<15	10 424	28 608	1190	7867	0.90	0.22	0.27	0.87
Centor score <2	9310	18 849	2304	17 626	0.80	0.48	0.33	0.88
McIsaac score <2	8739	16 671	2875	19 804	0.75	0.54	0.34	0.87

GAS = group A streptococcal.

Table 5

Patient Outcomes When the Home Score Classifies Adult Patients as Low Risk*

Home Score	Outcomes of Patients in Derivation Set		National Estimates of Outcomes		
	Visits Saved, *n*†	Additional Cases Missed Compared With the Centor Approach, *n*	Visits Saved, *n (million)*†	Additional Cases Missed Compared With the Centor Approach, *n*	Visits Saved per Missed Case, *n*
≤10 (*n* = 1535)	1374	53	0.23	8500	27
≤15 (*n* = 9061)	4947	374	0.78	61 000	13
≤20 (*n* = 21 630)	18 157	1963	2.9	320 000	9
≤25 (*n* = 31 563)	25 927	3641	4.2	590 000	7
≤30 (*n* = 36 429)	29 447	4775	4.8	780 000	6

*Derivation set, *n* = 48 089.

†Patients correctly classified as group A streptococcal pharyngitis–negative.

Appendix Table

Equations for Calculating the Clinical Biosurveillance Score by Adjusting a Patient's Centor Score on the Basis of the RLPP

Centor Score	Clinical Biosurveillance Score Adjustment
0	1.5 + 29* RLPP
1	4.2 + 37*RLPP
2	8.8 + 64*RLPP
3	20 + 88*RLPP
4	28 + 121*RLPP

RLPP = recent local proportion positive.