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What is the optimal strategy for managing primary care patients with an uncomplicated acute sore throat? Comparing the consequences of nine different strategies using a compilation of previous studies

Ronny Gunnarsson ,[1,2,3,4] Ulrich Orda,[5] Bradley Elliott,[6] Clare Heal,[7] Chris Del Mar[8]

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For numbered affiliations see end of article.

Correspondence to
Professor Ronny Gunnarsson; ronny.gunnarsson@infovoice.se

ABSTRACT

Objective Identifying optimal strategies for managing patients of any age with varying risk of acute rheumatic fever (ARF) attending for an apparently uncomplicated acute sore throat, also clarifying the role of point-of-care testing (POCT) for presence of group A beta-haemolytic *Streptococcus* (GABHS) in these settings.

Design We compared outcomes of adhering to nine different strategies for managing these patients in primary healthcare.

Setting and participants The nine strategies, similar to guidelines from several countries, were tested against two validation data sets being constructs from seven prior studies.

Main outcome measures The proportion of patients requiring a POCT, prescribed antibiotics, prescribed antibiotics having GABHS and finally having GABHS not prescribed antibiotics, if different strategies had been adhered to.

Results In a scenario with high risk of ARF, adhering to existing guidelines would risk many patients ill from GABHS left without antibiotics. Hence, using a POCT on all of these patients minimised their risk. For low-risk patients, it is reasonable to only consider antibiotics if the patient has more than low pain levels despite adequate analgesia, 3–4 Centor scores (or 2–3 FeverPAIN scores or 3–4 McIsaac scores) and a POCT confirming the presence of GABHS. This would require testing only 10%–15% of patients and prescribing antibiotics to only 3.5%–6.6%.

Conclusions Patients with high or low risk for ARF needs to be managed very differently. POCT can play an important role in safely targeting the use of antibiotics for patients with an apparently uncomplicated acute sore throat.

Strengths and limitations of this study

- ► This study investigated both overprescribing of antibiotics where the risk for rheumatic fever is low as well as undertreatment in scenarios where the risk is high, however, defining a specific cut-off for high risk is left to the reader.
- ► This study assumes that bacteria other than group A beta-haemolytic *Streptococcus* can be ignored for patients attending primary healthcare at their first visit for an apparently uncomplicated acute sore throat and the conclusions are only valid for this type of patient.
- ► The consequences of applying different strategies were evaluated using two data sets constructed from seven prior studies.

BACKGROUND

An acute sore throat is a common reason for visits to a primary healthcare (PHC) provider.[1–3] Commonly, this is caused by viruses or group A beta-haemolytic *Streptococcus* (GABHS).

Fear of acute rheumatic fever and other complications

A sore throat caused by GABHS can result in suppurative complications, such as peritonsillar abscess (quinsy), otitis media, sinusitis and skin infections, as well as non-suppurative ones, such as acute rheumatic fever (ARF) and poststreptococcal glomerulonephritis. Suppurative complications after a sore throat are unusual and rarely dangerous in high-income countries.[4]

ARF, and the subsequent rheumatic heart disease (RHD), is the most serious and feared complication with a worldwide estimated 319 400 deaths in 2015.[5] Hence, historically an emphasis was put on the risk and prevention of ARF. Most high-income countries has seen a step decline in the incidence of ARF. However, the risk for ARF in high-income countries may still have to be considered in a few high-risk individuals such as immigrants

from low-income countries as well as some groups of first nation people.[5] The estimated age-standardised prevalence of RHD per 100 000 population was for low-income countries 444 and for high-income countries 3.4, respectively.[5]

Antibiotic treatment of patients with a sore throat reduces the incidence of ARF.[6–8] Adherence to secondary prophylaxis after one episode of ARF is poor,[9] emphasising the importance of preventing the first episode. Some recommendations before the era of point-of-care testing (POCT) were to swab for GABHS and treat accordingly, however, this caused delay and often an additional consultation. Subsequently, it became common practice in many high-income countries to prescribe penicillin routinely to patients attending with a sore throat despite a step decline in the incidence of ARF.

Other bacteria than GABHS

Streptococcus dysgalactiae subspecies Equisimilis (SDSE), *Fusobacterium necrophorum* (FN) and other bacteria are commonly found.[10–14] FN may also cause the rare Lemierre's disease.[15 16] It has been suggested that prescribing antibiotics to patients with an uncomplicated acute sore throat harbouring FN may reduce the incidence of Lemierre's syndrome,[17] although there are to date no empirical studies supporting this. Case-control studies conclude SDSE and FN are not as important as GABHS in patients with an apparently uncomplicated acute sore throat.[18 19] Furthermore, most empirical studies show antibiotics have no effect on symptom relief in the absence of GABHS,[20–22] with a few exceptions showing a borderline effect in adult patients with SDSE.[23 24] Despite this some practitioners perceive anything bacterial requires antibiotic treatment.[25]

Clinical scoring algorithms

Various scoring algorithms were developed to identify patients with a lower probability of having GABHS, including the Centor criteria,[26 27] the FeverPAIN scores[28 29] and the McIsaac scores.[26 30 31] However, these algorithms are poorly adopted in clinical practice which may contribute to inappropriate antibiotic prescribing.[32–34]

Changes over time in high-income countries

A century ago, most countries had high incidences of ARF. However, this has declined dramatically over time in high-income countries.[35] There are some exceptions, such as Australia and New Zealand, which still have high incidences of ARF in some risk groups.[7 36]

In high-income countries, the main reason for antibiotic treatment is to reduce symptoms. Intervention studies show a minor reduction of symptoms in patients with a sore throat with a combination of presumed viral or bacterial origin.[37] Antibiotics have a modest effect in reducing acute symptoms if GABHS is present in children,[20 21 38] and in children and adults combined.[22 39 40] Placebo controlled studies that performed a separate analysis for GABHS-positive and GABHS-negative patients found a statistically significant effect of antibiotics in GABHS-positive patients but not in those GABHS-negative.[20–22 40] A subgroup analysis in a recent meta-analysis found a better effect of antibiotics if GABHS is present.[37]

However, antibiotics have adverse effects such as increased antibiotic resistance, allergies, short-term gastrointestinal disturbances,[41] candidiasis,[41] potentially a reduction in development of long-term immunity against GABHS,[42] increased risk for colorectal cancer,[43 44] increased risk for rheumatic arthritis[45] and possibly also increased risk for obesity.[46–48] The modest reduction in acute symptoms has to be weighed against these potential negative effects.

Modern guidelines and their impact in high-income countries

There is now a plethora of different guidelines in high-income countries advising against routine use of antibiotics.[49 50] Existing guidelines for management of patients with a sore throat focus on GABHS.[51 52] However, they vary widely.[53 54] While guidelines are important in theory and likely to have some impact,[55] some practitioners seem to develop their own individual approach to manage patients presenting with a sore throat that differs significantly from any guideline.[25 32 56–61] Some practitioners prescribe antibiotics to all, or nearly all, patients with a sore throat, perhaps in an attempt to reduce risks, to meet patient expectations or to reduce risks of litigation.[62] However, the art of medicine is rarely about achieving zero risk but rather to weigh different risks and benefits.

The problem is twofold. First, that there are contradicting guidelines for managing patients with a sore throat and second, that many practitioners do not adhere to any of them and instead rely on their own approach and clinical judgement. General practitioner (GPs) are highly skilled in improvising when faced with complex problems such as frail patients with multimorbidity or patients having a mixture of biomedical and psychosocial problems. In these situations, the GP makes a very good compromise between different guidelines or develops a plan where no guideline exists. These situations cannot be resolved without a high degree of improvisation requiring a strong belief in one's own clinical judgement. However, most patients attending for a sore throat are relatively young and do not have relevant comorbidities so typically this problem is strait forward. A very simple and specific guideline, such as those for the uncomplicated acute sore throat, leave no room for improvisation, but this may not be compatible with the nature of many, otherwise highly skilled, GPs.[63]

Point-of-care testing

Throat swabs send for bacteriology are hampered by the delay in obtaining results.[64] However, high-quality POCTs, delivering a result in minutes, are more useful.[34 65 66] Some studies find little benefit of POCT in a low risk setting.[29] Other studies, in a mixture of high-risk and low-risk patients, suggest they produce a modest reduction of antibiotic prescribing[67–69] but importantly,

they make antibiotic prescribing better targeted.[69] The adoption of POCT varies due to concerns with accuracy of the test, although this concern may be misplaced due to misconceptions:

1. The belief that a rapid POCT is not sensitive enough to reliably rule out the presence of GABHS. The POCT has, traditionally been compared with culture as reference standard,[70] a technique introduced in 1903.[71] Modern POCT has been perceived to have a sensitivity below 90% when compared with culture as reference standard.[70 72] However, using more advanced reference standards has shown that, when there is diagnostic discrepancy between modern POCT and culture, POCT are more likely to be correct.[73 74] Several modern POCT may have higher sensitivity than culture. There are also new small POCT molecular tests with a >95% sensitivity compared with in-house PCR.[75] Hence, modern high-quality POCT does not have a sensitivity inferior to culture, though this remains an educational challenge.
2. There is a belief that the POCT cannot distinguish between carriers and patients ill from GABHS, thus rendering the POCT useless. However, this is a misunderstanding of the problem. A high-quality POCT, used correctly, showing no presence of GABHS has a negative predictive value near 99% irrespective of the proportion of carriers of GABHS.[65 76–78] Carriers will only influence the clinical value of a POCT positive for GABHS (the positive predictive value) but, in most patients the test will be negative and hence very reliable and clinically useful.[65] Hence, a modern POCT will always work well as a stopping rule to stop incorrect antibiotic prescribing.[66]
3. An assumption that patients ill from a non-GABHS bacterium should be treated with antibiotics, making the POCT useless since these bacteria are not detected by the type of POCT mostly used in today's PHC. This is linked to the misconception that anything that is bacterial requires antibiotics.[25]

To rely on clinical symptoms and signs alone, ignoring the additional information from a modern high-quality POCT, increases antibiotic prescribing[34 66] and leaves a significant proportion of patients ill from GABHS without antibiotics, which may not be acceptable in a situation with an elevated risk for ARF.[34]

The remaining dilemma

In many high-income countries, 40%–80% of patients attending PHC for an apparently uncomplicated acute sore throat are prescribed antibiotics.[33 79–84] Furthermore, many patients in a high-risk setting attending for a sore throat, and with proven presence of GAHS, are not prescribed antibiotics.[34] This makes it worth to investigate the consequences of using different strategies in a constructed data validation set with known prevalence of GABHS. Our goal was to identify optimal strategies for scenarios with low as well as high risk of ARF.

METHODS

Selection of strategies to be evaluated

Most guidelines in high-income countries advice against the routine use of antibiotics in patients with minor discomfort. Hence, strategies using a cut-off of ≥2 or ≥3 Centor criteria to guide the use of POCT and antibiotic prescribing were evaluated and the consequences were estimated. These strategies does not include the scenario where you want to identify all patients with a GABHS infection irrespective of the magnitude of symptoms, as in patients at high risk of ARF. Furthermore, the strategies mentioned above do not cover the situation where avoidance of antibiotic use is the main focus. Hence, the strategies of prescribing antibiotics to all patients, using a POCT on all patients, never considering antibiotic use and including analgesics in a decision tree were also evaluated. Some of these strategies correspond to existing guidelines (table 1—with no ambition to identify all guidelines aligning with the strategies to be evaluated).

Data set for validation of strategies

We identified seven publications stating the proportion of patients harbouring GABHS split into Centor scores 0–4 and providing actual numbers or detailed proportions. Two publications, Wigton *et al*[85] and Fine *et al*[26] were retrospective chart reviews where only patients who had their throat swabbed were included. Two studies by Pallon *et al*[86 87] included patients first triaged by a nurse to sort out those with less probability for harbouring GABHS. Previous studies prospectively including unselected patients[13 34 69] had a higher prevalence of patients with 0 Centor criteria compared with the publications including selected patients.[26 85–87] Consequently, we decided to create two separate validation data sets, each being the weighted average of included studies (table 2).

Monitoring of adverse events and safety procedures

Due to the nature of this study, no adverse events were expected nor observed.

Outcome measures and statistical analysis

The outcome measures were the proportion of patients requiring a POCT, prescribed antibiotics, prescribed antibiotics and having GABHS and finally having GABHS not prescribed antibiotics. This was calculated for the following strategies: (A) prescribe antibiotics to all patients, (B) test all patients and prescribe antibiotics if positive, (C) prescribe antibiotics if Centor criteria is 2–4 (as in Scotland,[50]) (D) prescribe antibiotics if Centor criteria is 3–4 (as in Australia[88] ESCMID Europe[52] and UK,[49]) (E) if Centor criteria is 2–4 test patient and prescribe antibiotics if positive, (F) if Centor criteria is 3–4 test patient and prescribe antibiotics if positive (as in Sweden[89] and the USA,[90]) (G) if Centor criteria is 2–4 and pain is more than mild after analgesics test patient and prescribe antibiotics if positive, (H) if Centor criteria is 3–4 and pain is more than mild after analgesics test

Table 1 Some existing guidelines for managing patients with an uncomplicated acute sore throat and low risk for acute rheumatic fever

Guideline	Short summary of the threshold to prescribe antibiotics	Statement about throat swabbing	Statement about analgesics*
Therapeutic guidelines Australia[88]	It is reasonable to prescribe antibiotics if symptoms are severe (Centor scores are not mentioned but the described symptoms correspond well with 3–4 Centor criteria)	(Throat swabs are not mentioned at all)	Paracetamol or **Non-steroidal anti-inflammatory drugs** (NSAIDs) can be used
European Society of Clinical Microbiology and Infectious Diseases (ESCMID)[52]	Consider antibiotics if 3–4 Centor criteria	Throat swabs are not necessary but may be used in patients with 3–4 Centor criteria.	All patients may try systemic paracetamol or ibuprofen.
Netherlands[91]	Only to patients with peritonsillar infiltrate/abscess.	Throat swabs should be avoided	Paracetamol in adequate dose
The Scottish Intercollegiate Guidelines Network (SIGN)[50]	The Centor clinical prediction score should be used to assist the decision on whether to prescribe an antibiotic (no cut-off is provided but seems like Centor 2–4)	Throat swabs should be avoided	Ibuprofen (paracetamol if intolerant to ibuprofen)
Sweden[89]	Only consider antibiotics if 3–4 Centor criteria and if a point of care test for GABHS is positive	Only if 3–4 Centor criteria and if antibiotics is considered.	All patients may try analgesics.
UK[49]	Consider antibiotics if 3–4 Centor criteria or 4–5 FeverPAIN scores.	Throat swabbing has no clear advantage.	All patients may try systemic paracetamol or ibuprofen.
USA[90]	Prescribe antibiotics if 3–4 Centor criteria and if a point of care test for GABHS is positive	Only if 3–4 Centor criteria.	Adults should be offered analgesics

*Analgesics are mentioned in all guidelines as a parallel information but it is not being a direct part of a decision tree like 'don't consider antibiotics if analgesics reduce pain significantly so no pain or only mild pain remains'.
GABHS, group A beta-haemolytic *Streptococcus*.

patient and prescribe antibiotics if positive, (I) never test nor prescribe antibiotics (as in the Netherlands).[91]

Patient and public involvement

Patients were not involved in the development of plans for design, outcome measures or implementation of the study conduct. No patients were asked to advise on the interpretation or writing of results.

RESULTS

The strategies to prescribe antibiotics to all patients (row A in table 3) or to test all patients and prescribe antibiotics to all with a positive test (row B in table 3) would have ensured all of those having GABHS were given antibiotics (the rightmost column in row A and B in table 3). The lowest rate of antibiotic prescribing is achieved using the strategy of no antibiotic use (row I in table 3). If any use of antibiotics is allowed, the lowest prescribing rate, 3.5%–6.6%, would have been achieved by the strategy to only test if Centor criteria is 3–4, the pain is more than mild after adequate dose of analgesics and then only prescribe antibiotics if the test is positive (row H in table 3).

DISCUSSION

Consequences of adhering to different strategies vary dramatically and the choice of optimal strategy should be guided by the local prevalence of RHD as a marker of risk in the local setting. However, local healthcare providers may have different opinions as to which prevalence of RHD constitutes high, moderate or low risk. Hence, we suggest management in these different settings without defining a specific cut of in the prevalence of RHD to constitute a high-risk, moderate-risk or low-risk setting.

Strength and limitations of the data set for validation

The data sets for validation of strategies constitute a mix of studies including children and/or adults from various countries and continents. However, reasonable variations in the validation data sets would not alter the conclusions in this study.

Suggested management if the risk for ARF is high

Primary prevention of ARF is the main goal in this scenario. Hence, none of patients at high risk of ARF and harbouring GABHS, irrespective of Centor scores, should miss out on antibiotics (the rightmost column in table 3).We have seen that not testing patients in a high risk setting leaves a significant proportion of patients at high risk of ARF truly ill from GABHS without antibiotics.[34] The strategy best achieving adequate antibiotic cover is to test all patients if POCTs are available (row B in table 3). Prescribing antibiotics to all patients attending for a sore throat (row A in table 3) would be the second best strategy if POCTs are unavailable. However, the latter strategy will lead to many unnecessary antibiotic prescriptions to patients not harbouring GABHS.

Suggested management if the risk for ARF is moderate

In this setting, it might be acceptable that patients with mild symptoms are left untreated despite some of them harbouring GABHS. The best strategy is to test all patients (row B in table 3) if POCTs are easily available. The

Table 2 Previous data sets with detailed information on prevalence of GABHS related to the number of Centor criteria

				0 centor criteria		1 centor criteria		2 centor criteria		3 centor criteria		4 centor criteria	
				Prevalence*	GABHS post†	Prevalence*	GABHS post†	Prevalence*	GABHS post†	Prevalence*	GABHS post†	Prevalence*	GABHS post†
Year	n	Study	Age year	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)
Prospective studies including unselected patients attending primary healthcare													
2015	312	Centor[13]	15–30	13 (39)	5.1 (2)	33 (104)	4.8 (5)	34 (106)	5.7 (6)	14 (44)	14 (6)	6.1 (19)	11 (2)
2016	101	Orda[34]	3–15	34 (34)	12 (4)	39 (39)	21 (8)	15 (15)	53 (8)	8.9 (9)	56 (5)	4.0 (4)	25 (1)
2021	281	Gunnarsson‡[69]	0–96	23 (65)	28 (18)	34 (96)	15 (14)	27 (76)	36 (27)	12 (35)	57 (20)	3.2 (9)	78 (7)
-	694	Validation set A		20 (138)	17 (24)	34 (239)	11 (27)	28 (197)	21 (41)	13 (88)	35 (31)	4.6 (32)	31 (10)
Prospective studies only including patients selected by nurse triage or retrospective chart reviews/registers only including patients where the practitioner decided to take a throat swab													
1986	405	Wigton[85]	>12	7.6 (39)	2.6 (1)§	27 (137)	14 (19)§	31 (160)	23 (37)§	2.3 (12)	45 (5)§	11 (57)	54 (31)§
2012	142081	Fine[26]	>3	9.6 (13 603)	7 (952)§	32 (45 080)	12 (5410)§	33 (47 167)	21 (9905)§	19 (26 769)	38 (10 172)§	6.7 (9462)	57 (5393)§
2021	77	Pallon[87]	0–14	7.8 (6)	33 (2)	25 (19)	32 (6)	29 (22)	59 (13)	39 (30)	57 (17)	0 (0)	-
2021	220	Pallon[86]	15–44	7,3 (16)	13 (2)	23 (50)	12 (6)	31 (69)	23 (16)	25 (54)	44 (24)	14 (31)	58 (18)
-	142783	Validation set B		9.6 (13 664)	7.0 (957)	32 (45 286)	12 (5441)	33 (47 418)	21 (9971)	19 (26 865)	38 (10 218)	6.7 (9550)	57 (5442)

*Proportion of patients having this number of Centor criteria fulfilled.
†Proportion of patients with this number of Centor criteria harbouring GABHS.
‡Additional information was obtained after contact with the authors to clarify the proportion of patients harbouring GABHS split into Centor categories.
§Exact numbers of individuals are calculated from stated percentages. In this process, we calculate to the nearest whole integer. We then calculate new percentages from these exact numbers. Our percentages differs slightly from Wigton and Fine's papers. Wigton and Fine provide percentages with low precision presumably resulting in an insignificant rounding error. This explains the small insignificant difference in percentages.
GABHS, group A beta-haemolytic *Streptococcus*.

Table 3 Different strategies for managing patients with a sore throat and their consequences

Different strategies for testing presence of GABHS and prescribing antibiotics (AB)	Resembling guidelines in	Validation data set	Requiring testing for GABHS*	Requiring antibiotic prescribing†	Proportion of those prescribed antibiotics harbouring GABHS‡	Proportion of those harbouring GABHS not prescribed antibiotics§
A.Prescribe AB to all patients	(None)	A B	0.0% 0.0%	100% 100%	19% 22%	0.0% 0.0%
B.Test all patients—AB only if test is positive	(None)	A B	100% 100%	19% 22%	100% 100%	0.0% 0.0%
C.No testing. Prescribe AB if Centor is 2–4	Scotland	A B	0.0% 0.0%	46% 59%	26% 31%	38% 20%
D.No testing. Prescribe AB if Centor is 3–4	Australia European Society of Clinical Microbiology and Infectious Diseases (ESCMID) UK	A B	0.0% 0.0%	17% 26%	34% 43%	69% 51%
E.Test if Centor is 2–4—AB only if test is positive	(None)	A B	46% 59%	12% 18%	100% 100%	38% 20%
F.Test if Centor is 3–4—AB only if test is positive	Sweden USA	A B	17% 26%	5.9% 11%	100% 100%	69% 51%
G.Test if Centor is 2–4 and pain is more than mild after analgesics—AB only if test is positive¶	(None)	A B	27% 35%	7.1% 11%	100% 100%	63% 52%
H.Test if Centor is 3–4 and pain is more than mild after analgesics—AB only if test is positive¶	(None)	A B	10% 15%	3.5% 6.6%	100% 100%	82% 71%
I.Never test nor prescribe AB. Only advice on analgesics.	Netherlands	A B	0.0% 0.0%	0.0% 0.0%	–	100% 100%

*Proportion of patients tested when following the strategy for testing and prescribing antibiotics.
†Should be as low as possible in patients with no elevated risk for ARF or any other risk factors such as known immunodeficiency.
‡Should be as high as possible as we mainly have solid evidence for the effectiveness of antibiotics in the presence of GABHS.
§Should be as low as possible in patients at elevated risk for ARF.
¶Some patients have mild pain before analgesics and analgesics is assumed to further reduce the need for antibiotics.[97] We assume 40% can be managed solely by using proper analgesics if the pain level and use of analgesics is an active part of a decision tree. These patients need no testing nor antibiotics as long as they have a low risk for ARF.
ARF, acute rheumatic fever; GABHS, group A beta-haemolytic *Streptococcus*.

second best strategy, if POCTs are available but of limited supply, is to adhere to the strategy described in row E, test if the patient has 2–4 Centor scores and prescribe antibiotics to all patients with a positive test. The consequences would be that a similar proportion of patients are prescribed antibiotics as if everyone was tested but only roughly half of the patients require testing. The downside is that 20%–38% of patients with a sore throat harbouring GABHS miss out on antibiotics. The third best option, if POCTs are completely unavailable, would be to prescribe antibiotics to all patients attending for a sore throat. Again, the downside is the overtreatment as described above.

Suggested management if the risk for ARF is negligible

Here the use of antibiotics for preventing ARF is unnecessary, and is of small benefit for reducing symptoms.[37] Hence, the primary goal is to safely reduce antibiotic usage as much as possible. The optimal management in this situation is patient-centred care where the clinician presents available evidence of the benefits and harms of antibiotics. This is followed by a joint discussion whether antibiotics are worthwhile here, in other words, shared decision making.[92]

The Netherlands have the most restrictive guideline prohibiting any antibiotic prescribing to otherwise healthy patients attending for an uncomplicated acute sore throat.[91] Despite this GPs in the Netherlands prescribe antibiotics to approximately 50% of patients attending with a sore throat[83 84] suggesting that this overly restrictive guideline has limited influence. It will be difficult to deny antibiotic treatment for those having intense symptoms despite adequate analgesics, presence of GABHS and requesting antibiotics. Hence, stating that otherwise healthy patients with uncomplicated acute sore throat should never be prescribed antibiotics at their first visit is unlikely to work in reality and potentially unethical. A sensible compromise that can work in real life should be made.

The main reason for considering antibiotics is to reduce pain and fatigue, and there is no need for antibiotics if analgesics work well in low-risk patients. Many current guidelines recommend the use of analgesics for symptomatic treatment (table 1) but none of the guidelines presented

in table 1 include analgesics in a decision tree for antibiotic prescribing. Analgesics should be part of a decision tree for low risk patients where antibiotics should only be considered if the patient has more than low pain after adequate analgesics, 3–4 Centor criteria[26 27] (or 2–3 FeverPAIN scores[28 29] or 3–4 McIsaac scores[26 30 31]) and a positive test confirming the presence of GABHS. Adhering to this recommendation results in the lowest rate of antibiotic prescribing if antibiotics are going to be used at all (row H in table 3). This strategy only requires a small proportion of patients being tested (10%–15%) and an even smaller proportion prescribed antibiotics (3.5%–6.6%).

Children versus adults

Asymptomatic carriers of GABHS are more common in children than in adults in most settings. However, the proportion of carriers in children can in some settings be very low and similar to the carrier rates seen in adults.[34] Carriers will only influence the clinical value of a POCT positive for GABHS (the positive predictive value) but, in most patients the test will be negative and hence very reliable and clinically useful.[65] The conclusion is that a modern POCT will always work well, in children and adults, as a stopping rule to stop incorrect antibiotic prescribing.[66]

ARF and RHD are more common in children but may occur also in adults. The main goal is to keep antibiotic prescribing at a minimum in a low risk setting while ensuring no patients attending for a sore throat and harbouring GABHS is left without antibiotics in a high risk setting. These goals are exactly the same for children as well as adults. Although adhering to our recommendations may result in a few unnecessary antibiotic prescriptions to children the same strategies were identified as optimal for children and adults.

Suggestions for future research

Highly skilled GPs successfully managing complex problems in patients with multimorbidity do not seem to comply well with existing simple guidelines for managing patients attending for an apparently uncomplicated acute sore throat. The drivers for GPs to make decisions are complex, and the relevance of the patient's expectations should not be underestimated.

A possible alternative might be to allow healthcare providers other than medical practitioners manage otherwise healthy patients at their first visit for an apparently uncomplicated acute sore throat. Studies evaluating nurse management of these patients,[93–95] however have been, due to methodological problems, inconclusive. A study using community pharmacies to manage these patients by adhering to the algorithm described in row F in table 3 resulted in antibiotic prescribing to only 9.8% of all patients.[96] This is very similar to our result of 5.9%–11% if this strategy had been adhered to. However, using healthcare providers other than medical practitioners must be further tested, preferably in a well-designed randomised controlled trial, to ensure it does not compromise patient safety or adequate patient education.

CONCLUSIONS

For patients at high risk of ARF, we suggest that the safe strategy is to test all patients with an apparently uncomplicated acute sore throat for presence of GABHS. Prescribing antibiotics to all patients at high risk would be the second best option if POCTs are unavailable, although this results in significant overprescribing of antibiotics.

In patients at low risk of ARF at their first visit we suggest adopting shared decision making and inform the patient that the most effective use of antibiotics is achieved by using the following strategy: primarily utilising analgesics as part of a decision tree where antibiotics should only be considered if the patient has more than low pain after adequate analgesics, 3–4 Centor criteria (or 2–3 FeverPAIN scores or 3–4 McIsaac scores) and a positive POCT confirming the presence of GABHS.

It should be emphasised that these strategies may not be optimal in patients with signs of complications, in patients returning after a previous visit now being unwell, in patients with significant comorbidities and in hospitalised patients.

Author affiliations
[1]School of Public Health and Community Medicine - General Practice/Family Medicine, Göteborgs universitet Institutionen för medicin, Goteborg, Sweden
[2]Research, Development, Education and Innovation, Primary Health Care, Västra Götalandsregionen, Göteborg, Sweden
[3]Centre for Antibiotic Resistance Research (CARe), University of Gothenburg, Göteborg, Sweden
[4]The primary health care clinic for homeless people, Närhälsan, Region Västra Götaland, Göteborg, Sweden
[5]Mount Isa Hospital, North West Hospital and Health Service, Mount Isa, Queensland, Australia
[6]Hinchinbrook Health Care, Ingham, Queensland, Australia
[7]School of Medicine and Dentistry, James Cook University, Mackay, Queensland, Australia
[8]Faculty of Health Sciences and Medicine, Bond University, Gold Coast, Queensland, Australia

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ORCID iD
Ronny Gunnarsson http://orcid.org/0000-0001-9183-3072

REFERENCES

1 André M, Vernby A, Odenholt I, *et al*. Diagnosis-prescribing surveys in 2000, 2002 and 2005 in Swedish general practice: consultations, diagnosis, diagnostics and treatment choices. *Scand J Infect Dis* 2008;40:648–54.
2 Tyrstrup M, Beckman A, Mölstad S, *et al*. Reduction in antibiotic prescribing for respiratory tract infections in Swedish primary care- a retrospective study of electronic patient records. *BMC Infect Dis* 2016;16:709.
3 Armstrong GL, Pinner RW. Outpatient visits for infectious diseases in the United States, 1980 through 1996. *Arch Intern Med* 1999;159:2531–6.
4 Little P, Stuart B, Hobbs FDR, *et al*. Predictors of suppurative complications for acute sore throat in primary care: prospective clinical cohort study. *BMJ* 2013;347:f6867.
5 Watkins DA, Johnson CO, Colquhoun SM, *et al*. Global, regional, and national burden of rheumatic heart disease, 1990-2015. *N Engl J Med* 2017;377:713–22.
6 Catanzaro FJ, Stetson CA, Morris AJ, *et al*. The role of the streptococcus in the pathogenesis of rheumatic fever. *Am J Med* 1954;17:749–56.
7 Lennon D, Anderson P, Kerdemilidis M, *et al*. First presentation acute rheumatic fever is preventable in a community setting: a school-based intervention. *Pediatr Infect Dis J* 2017;36:1113–8.
8 Robertson KA, Volmink JA, Mayosi BM. Antibiotics for the primary prevention of acute rheumatic fever: a meta-analysis. *BMC Cardiovasc Disord* 2005;5:11.
9 Kevat PM, Reeves BM, Ruben AR, *et al*. Adherence to secondary prophylaxis for acute rheumatic fever and rheumatic heart disease: a systematic review. *Curr Cardiol Rev* 2017;13:155–66.
10 Lindbaek M, Høiby EA, Lermark G, *et al*. Clinical symptoms and signs in sore throat patients with large colony variant beta-haemolytic streptococci groups C or G versus group A. *Br J Gen Pract* 2005;55:615–9.
11 Tiemstra J, Miranda RLF. Role of non-group a streptococci in acute pharyngitis. *J Am Board Fam Med* 2009;22:663–9.
12 Little P, Moore M, Hobbs FDR, *et al*. Primary care streptococcal management (PriSM) study: identifying clinical variables associated with Lancefield group A β-haemolytic streptococci and Lancefield non-group a streptococcal throat infections from two cohorts of patients presenting with an acute sore throat. *BMJ Open* 2013;3:e003943.
13 Centor RM, Atkinson TP, Ratliff AE, *et al*. The clinical presentation of Fusobacterium-positive and streptococcal-positive pharyngitis in a university health clinic: a cross-sectional study. *Ann Intern Med* 2015;162:241–7.
14 Hedin K, Bieber L, Lindh M, *et al*. The aetiology of pharyngotonsillitis in adolescents and adults - Fusobacterium necrophorum is commonly found. *Clin Microbiol Infect* 2015;21:263 e1–7.
15 Lemierre A. On certain septicaemias due to anaerobic organisms. *The Lancet* 1936;227:701–3.
16 Osowicki J, Kapur S, Phuong LK, *et al*. The long shadow of Lemierre's syndrome. *J Infect* 2017;74:S47–53.
17 Bank S, Christensen K, Kristensen LH, *et al*. A cost-effectiveness analysis of identifying Fusobacterium necrophorum in throat swabs followed by antibiotic treatment to reduce the incidence of Lemierre's syndrome and peritonsillar abscesses. *Eur J Clin Microbiol Infect Dis* 2013;32:71–8.
18 Gunnarsson RK, Manchal N. Group C beta haemolytic Streptococci as a potential pathogen in patients presenting with an uncomplicated acute sore throat - A systematic literature review and meta-analysis. *Scand J Primary Health Care* 2020:1–12.
19 Malmberg S, Petrén S, Gunnarsson R, *et al*. Acute sore throat and *Fusobacterium necrophorum* in primary healthcare: a systematic review and meta-analysis. *BMJ Open* 2021;11:e042816–9.
20 Pichichero ME, Disney FA, Talpey WB, *et al*. Adverse and beneficial effects of immediate treatment of Group A beta-hemolytic streptococcal pharyngitis with penicillin. *Pediatr Infect Dis J* 1987;6:635–43.
21 Krober MS, Bass JW, Michels GN. Streptococcal pharyngitis. placebo-controlled double-blind evaluation of clinical response to penicillin therapy. *JAMA* 1985;253:1271–4.
22 De Meyere M, Mervielde Y, Verschraegen G, *et al*. Effect of penicillin on the clinical course of streptococcal pharyngitis in general practice. *Eur J Clin Pharmacol* 1992;43:581–5.
23 Petersen K, Phillips RS, Soukup J, *et al*. The effect of erythromycin on resolution of symptoms among adults with pharyngitis not caused by group A Streptococcus. *J Gen Intern Med* 1997;12:95–101.
24 Zwart S, Sachs AP, Ruijs GJ, *et al*. Penicillin for acute sore throat: randomised double blind trial of seven days versus three days treatment or placebo in adults. *BMJ* 2000;320:150–4.
25 Hedin K, Strandberg EL, Gröndal H, *et al*. Management of patients with sore throats in relation to guidelines: an interview study in Sweden. *Scand J Prim Health Care* 2014;32:193–9.
26 Fine AM, Nizet V, Mandl KD. Large-scale validation of the centor and McIsaac scores to predict group A streptococcal pharyngitis. *Arch Intern Med* 2012;172:847–52.
27 Centor RM, Witherspoon JM, Dalton HP, *et al*. The diagnosis of strep throat in adults in the emergency room. *Med Decis Making* 1981;1:239–46.
28 Little P, Moore M, Hobbs FDR, *et al*. Primary care streptococcal management (PriSM) study: identifying clinical variables associated with Lancefield group A β-haemolytic streptococci and Lancefield non-group a streptococcal throat infections from two cohorts of patients presenting with an acute sore throat. *BMJ Open* 2013;3:e003943.
29 Little P, Hobbs FDR, Moore M, *et al*. Clinical score and rapid antigen detection test to guide antibiotic use for sore throats: randomised controlled trial of PRISM (primary care streptococcal management). *BMJ* 2013;347:f5806.
30 McIsaac WJ, White D, Tannenbaum D, *et al*. A clinical score to reduce unnecessary antibiotic use in patients with sore throat. *CMAJ* 1998;158:75–83.
31 McIsaac WJ, Goel V, To T, *et al*. The validity of a sore throat score in family practice. *CMAJ* 2000;163:811–5.
32 Linder JA, Chan JC, Bates DW. Evaluation and treatment of pharyngitis in primary care practice: the difference between guidelines is largely academic. *Arch Intern Med* 2006;166:1374–9.
33 Gulliford MC, Dregan A, Moore MV, *et al*. Continued high rates of antibiotic prescribing to adults with respiratory tract infection: survey of 568 UK general practices. *BMJ Open* 2014;4:e006245.
34 Orda U, Mitra B, Orda S, *et al*. Point of care testing for group A streptococci in patients presenting with pharyngitis will improve appropriate antibiotic prescription. *Emerg Med Australas* 2016;28:199–204.
35 Howie JG, Foggo BA. Antibiotics, sore throats and rheumatic fever. *J R Coll Gen Pract* 1985;35:223–4.
36 Australian Institute of Health and Welfare. Rheumatic heart disease and acute rheumatic fever in Australia: 1996-2012. Cardiovascular diseases series. Canberra 2013.
37 Spinks A, Glasziou PP, Del Mar CB. Antibiotics for treatment of sore throat in children and adults. *Cochrane Database Syst Rev* 2021;12:CD000023.
38 Nelson JD. The effect of penicillin therapy on the symptoms and signs of streptococcal pharyngitis. *Pediatr Infect Dis* 1984;3:10–13.
39 Middleton DB, D'Amico F, Merenstein JH. Standardized symptomatic treatment versus penicillin as initial therapy for streptococcal pharyngitis. *J Pediatr* 1988;113:1089–94.
40 Dagnelie CF, van der Graaf Y, De Melker RA. Do patients with sore throat benefit from penicillin? A randomized double-blind placebo-controlled clinical trial with penicillin V in general practice. *Br J Gen Pract* 1996;46:589–93.
41 Gillies M, Ranakusuma A, Hoffmann T, *et al*. Common harms from amoxicillin: a systematic review and meta-analysis of randomized placebo-controlled trials for any indication. *CMAJ* 2015;187:E21–31.
42 Pichichero ME. The development of immunity sequelae or the carrier state following streptococcal pharyngitis. *Pediatr Ann* 1992;21:829–34.
43 Armstrong D, Dregan A, Ashworth M, *et al*. The association between colorectal cancer and prior antibiotic prescriptions: case control study. *Br J Cancer* 2020;122:912–7.
44 Wan Q-Y, Zhao R, Wang Y, *et al*. Antibiotic use and risk of colorectal cancer: a meta-analysis of 412 450 participants. *Gut* 2020;69:2059–60.
45 Armstrong D, Dregan A, Ashworth M, *et al*. Influence of prior antibiotic use on risk of rheumatoid arthritis: case control study in general practice. *Rheumatology* 2020;59:1281–7.
46 Miller SA, Wu RKS, Oremus M. The association between antibiotic use in infancy and childhood overweight or obesity: a systematic review and meta-analysis. *Obes Rev* 2018;19:1463–75.
47 Rasmussen SH, Shrestha S, Bjerregaard LG, *et al*. Antibiotic exposure in early life and childhood overweight and obesity: a systematic review and meta-analysis. *Diabetes Obes Metab* 2018;20:1508–14.
48 Leong KSW, Derraik JGB, Hofman PL, *et al*. Antibiotics, gut microbiome and obesity. *Clin Endocrinol* 2018;88:185–200.
49 National Institute for Health and Care Excellence (NICE). NICE Guideline [NG84] - Sore throat (acute): antimicrobial prescribing 2018.
50 Scottish Intercollegiate Guidelines Network (SIGN). SIGN Guideline [117] - Management of sore throat and indications for tonsillectomy. A national clinical guideline 2010.

51 Shulman ST, Bisno AL, Clegg HW, *et al*. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the infectious diseases Society of America. *Clin Infect Dis* 2012;55:1279–82.
52 ESCMID Sore Throat Guideline Group, Pelucchi C, Grigoryan L, *et al*. Guideline for the management of acute sore throat. *Clin Microbiol Infect* 2012;18:1–27.
53 Hoare KJ, Ward E, Arroll B. International sore throat guidelines and international medical graduates: a mixed methods systematic review. *J Prim Health Care* 2016;8:20–9.
54 Mustafa Z, Ghaffari M, Methods D. Diagnostic methods, clinical guidelines, and antibiotic treatment for group A streptococcal pharyngitis: a narrative review. *Front Cell Infect Microbiol* 2020;10:563627.
55 Gunnarsson R, Ebell MH, Wächtler H, *et al*. Association between guidelines and medical practitioners' perception of best management for patients attending with an apparently uncomplicated acute sore throat: a cross-sectional survey in five countries. *BMJ Open* 2020;10:e037884–10.
56 Rico-Ferreira P, Palazón-Bru A, Calvo-Pérez M, *et al*. Nonadherence to guidelines for prescribing antibiotic therapy to patients with tonsillitis or pharyngotonsillitis: a cross-sectional study. *Curr Med Res Opin* 2015;31:1319–22.
57 Cars H, Håkansson A. To prescribe-or not to prescribe-antibiotics. District physicians' habits vary greatly, and are difficult to change. *Scand J Prim Health Care* 1995;13:3–7.
58 Pitts J, Vincent S. What influences doctors' prescribing? Sore throats revisited. *J R Coll Gen Pract* 1989;39:65–6.
59 Gröndal H, Hedin K, Strandberg EL, *et al*. Near-patient tests and the clinical gaze in decision-making of Swedish GPs not following current guidelines for sore throat - a qualitative interview study. *BMC Fam Pract* 2015;16:81.
60 Neumark T, Brudin L, Mölstad S. Use of rapid diagnostic tests and choice of antibiotics in respiratory tract infections in primary healthcare-a 6-y follow-up study. *Scand J Infect Dis* 2010;42:90–6.
61 Reinholdt KB, Rusan M, Hansen PR, *et al*. Management of sore throat in Danish general practices. *BMC Fam Pract* 2019;20:75.
62 Panthöfer S. Do doctors prescribe antibiotics out of fear of malpractice? *The HEDG Working Paper series* 2016;16:1–35.
63 Tyrstrup M, André M, Brorsson A, *et al*. A study of guidelines for respiratory tract infections and their references from Swedish GPs: a qualitative analysis. *Scand J Prim Health Care* 2020;38:83–91.
64 Cheung L, Pattni V, Peacock P, *et al*. Throat swabs have no influence on the management of patients with sore throats. *J Laryngol Otol* 2017;131:977–81.
65 Orda U, Gunnarsson R, Orda S, *et al*. Etiologic predictive value of a rapid immunoassay for the detection of group A streptococci antigen from throat swabs in patients presenting with a sore throat. *Int J Infect Dis* 2016;45:32–5.
66 Gunnarsson MS, Sundvall P-D, Gunnarsson R. In primary health care, never prescribe antibiotics to patients suspected of having an uncomplicated sore throat caused by group A beta-haemolytic streptococci without first confirming the presence of this bacterium. *Scand J Infect Dis* 2012;44:915–21.
67 Llor C, Madurell J, Balagué-Corbella M, *et al*. Impact on antibiotic prescription of rapid antigen detection testing in acute pharyngitis in adults: a randomised clinical trial. *Br J Gen Pract* 2011;61:e244–51.
68 Worrall G, Hutchinson J, Sherman G, *et al*. Diagnosing streptococcal sore throat in adults: randomized controlled trial of in-office AIDS. *Can Fam Physician* 2007;53:666–71.
69 Gunnarsson RK, Orda U, Elliott B, *et al*. Improving antibiotics targeting using PCR point-of-care testing for group A streptococci in patients with uncomplicated acute sore throat. *Aust J Gen Pract* 2021;50:76–83.
70 Stewart EH, Davis B, Clemans-Taylor BL, *et al*. Rapid antigen group A streptococcus test to diagnose pharyngitis: a systematic review and meta-analysis. *PLoS One* 2014;9:e111727.
71 Ferretti J, Kohler W. History of streptococcal research. In: Ferretti JJ, Stevens DL, Fischetti VA, eds. *Streptococcus pyogenes: basic biology to clinical manifestations*. Oklahoma City, 2016.
72 Lean WL, Arnup S, Danchin M, *et al*. Rapid diagnostic tests for group A streptococcal pharyngitis: a meta-analysis. *Pediatrics* 2014;134:771–81.
73 Lindbaek M, Høiby EA, Lermark G, *et al*. Which is the best method to trace group A streptococci in sore throat patients: culture or GAS antigen test? *Scand J Prim Health Care* 2004;22:233–8.
74 Cohen JF, Cohen R, Bidet P, *et al*. Rapid-antigen detection tests for group A streptococcal pharyngitis: revisiting false-positive results using polymerase chain reaction testing. *J Pediatr* 2013;162:1282–4.
75 Cohen DM, Russo ME, Jaggi P, *et al*. Multicenter clinical evaluation of the novel Alere I Strep a isothermal nucleic acid amplification test. *J Clin Microbiol* 2015;53:2258–61.
76 Gunnarsson RK, Lanke J. The predictive value of microbiologic diagnostic tests if asymptomatic carriers are present. *Stat Med* 2002;21:1773–85.
77 Gunnarsson RK. *Dissertation: microbiologic diagnostic tests when asymptomatic carriers are present. aspects of the use of conventional throat and nasopharyngeal cultures as examples*. Sweden: University of Gothenburg, 2001.
78 Orda U, Gunnarsson RK, Orda S. Etiologic predictive value of a rapid immunoassay for detection of group A streptococci antigen from throat swabs in patients presenting with a sore throat. North American Primary Care Research Group (NAPCRG) Annual Meeting. Colorado Springs, US, 2016. Available: https://www.youtube.com/watch?v=YHMeQuKOYpw
79 Luo R, Sickler J, Vahidnia F, *et al*. Diagnosis and management of group A streptococcal pharyngitis in the United States, 2011-2015. *BMC Infect Dis* 2019;19:193.
80 Tran J, Danchin M, C Steer A, *et al*. Management of sore throat in primary care. *Aust J Gen Pract* 2018;47:485–9.
81 Patel C, Green BD, Batt JM, *et al*. Antibiotic prescribing for tonsillopharyngitis in a general practice setting: can the use of modified Centor criteria reduce antibiotic prescribing? *Aust J Gen Pract* 2019;48:395–401.
82 Dallas A, van Driel M, Morgan S, *et al*. Antibiotic prescribing for sore throat: a cross-sectional analysis of the ReCEnT study exploring the habits of early-career doctors in family practice. *Fam Pract* 2016;33:302–8.
83 Damoiseaux RAMJ, Venekamp RP. [Prescribing antibiotics for sore throat: a persistent habit]. *Ned Tijdschr Geneeskd* 2015;159:A9419.
84 Tyrstrup M, van der Velden A, Engstrom S, *et al*. Antibiotic prescribing in relation to diagnoses and consultation rates in Belgium, the Netherlands and Sweden: use of European quality indicators. *Scand J Prim Health Care* 2017;35:10–18.
85 Wigton RS, Connor JL, Centor RM. Transportability of a decision rule for the diagnosis of streptococcal pharyngitis. *Arch Intern Med* 1986;146:81–3.
86 Pallon J, Rööst M, Sundqvist M, *et al*. The aetiology of pharyngotonsillitis in primary health care: a prospective observational study. *BMC Infect Dis* 2021;21:971.
87 Pallon J, Sundqvist M, Rööst M, *et al*. Presence of microorganisms in children with pharyngotonsillitis and healthy controls: a prospective study in primary healthcare. *Infection* 2021;49:715–24.
88 Antibiotic. Egf. *Acute pharyngitis and/or tonsillitis. therapeutic guidelines (eTG Complete)*. Melbourne: Therapeutic Guidelines Limited, 2014.
89 Handläggning AV faryngotonsilliter I öppenvård – NY rekommendation. *Information från Läkemedelsverket* 2012;6:18–25.
90 Harris AM, Hicks LA, Qaseem A, *et al*. Appropriate antibiotic use for acute respiratory tract infection in adults: advice for high-value care from the American College of physicians and the centers for disease control and prevention. *Ann Intern Med* 2016;164:425–34.
91 de Jongh E, Opstelten W, Werkgroep NHG-Standaard Acute keelpijn. [Revision of the Dutch College of General Practitioners practice guideline 'Acute sore throat']. *Ned Tijdschr Geneeskd* 2015;159:A9456.
92 Coxeter P, Del Mar CB, McGregor L, *et al*. Interventions to facilitate shared decision making to address antibiotic use for acute respiratory infections in primary care. *Cochrane Database Syst Rev* 2015;11:CD010907.
93 Cox C, Jones M. An evaluation of the management of patients with sore throats by practice nurses and GPs. *Br J Gen Pract* 2000;50:872–6.
94 Fabrellas N, Sánchez C, Juvé E, *et al*. A program of nurse algorithm-guided care for adult patients with acute minor illnesses in primary care. *BMC Fam Pract* 2013;14:61.
95 Stuhr JK, Lykkegaard J, Kristensen JK. Danish GPs' and practice nurses' management of acute sore throat and adherence to guidelines. *Fam Pract*2018.
96 Thornley T, Marshall G, Howard P, *et al*. A feasibility service evaluation of screening and treatment of group A streptococcal pharyngitis in community pharmacies. *J Antimicrob Chemother* 2016;71:3293–9.
97 Kenealy T. Sore throat. *BMJ Clin Evid* 2007;2007