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Antibiotics for the uncomplicated acute sore throat to prevent invasive group A Streptococcus - a critical analysis of current evidence

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ABSTRACT

Objective: Group A Streptococcus (GAS) can cause mild and severe infections. The most feared infection is invasive GAS (iGAS) infection. The objective of this study was to estimate to what extent the population incidence of iGAS infections can be reduced by providing antibiotic treatment to patients with an uncomplicated acute sore throat.

Methods: Compilation of existing relevant evidence linking antibiotic treatment of patients with an uncomplicated acute sore throat to the population prevalence of iGAS were identified. This information was combined with epidemiologic data from 2024 for the entire Swedish population. The primary outcome measure was the proportion of iGAS preventable by prescribing antibiotics to patients with uncomplicated acute sore throat. Secondary outcomes were the number of patients who need to have their throat swabbed and be prescribed antibiotics to prevent one case of iGAS. The outcome was stratified in different strategies, based on the Centor score, a commonly used clinical scoring algorithm for patients with an uncomplicated acute sore throat.

Results: Up to 6.7% of iGAS cases in children and ≤2.8% in adults can be prevented, assuming all patients with an uncomplicated acute sore throat attending a health care provider have a throat swab and those harboring GAS are prescribed antibiotics. Swabbing only patients fulfilling 3-4 Centor criteria and prescribing antibiotics if GAS is present would prevent ≤1.6% of iGAS cases in children and ≤1.2% in adults. The number needed to treat (NNT) for preventing one case of iGAS was for throat swabbing 45,000-110,000 and for antibiotic prescribing 12,000-110,000.

Conclusions: A few iGAS infections are preventable by prescribing antibiotics to patients with an uncomplicated acute sore throat but this achievement is associated with large unintended consequences, such as side effects and a substantially increased workload for primary care. We propose that prevention of iGAS should not be a reason for prescribing antibiotics to patients with an uncomplicated acute sore throat.

Introduction

Invasive group A Streptococcal (iGAS) infection is a severe condition in which GAS can be identified from a normally sterile body site. Sometimes, the definition also includes cases where GAS has been identified in a normally non-sterile body site combined with a severe clinical presentation, such as streptococcal toxic shock syndrome, necrotizing fasciitis, pneumonia, septic arthritis, meningitis, peritonitis, osteomyelitis, myositis, and puerperal sepsis [1].

Important risk factors for iGAS infection include chronic underlying diseases (e.g. cancer immunosuppression lymphoedema and indwelling devices), prior infection with respiratory viruses—particularly influenza A, exposure to specific virulent GAS strains, living in low-income households or being homeless, having many children in the household, pregnancy and conditions that compro-

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mise the integrity of the skin barrier—such as varicella (chickenpox) in children and ulcers in adults [2–6]. Half of children and more than 90% of adults with an iGAS infection have at least one risk factor [7].

In recent years, the incidence of iGAS has increased in several countries [6,8]. iGAS infections have a high mortality, and permanent sequelae are common among survivors. Therefore, prevention and early detection of iGAS infections are of utmost importance. One strategy to prevent iGAS is to reduce the transmission of GAS in the community. GAS is transmitted via respiratory droplets from sneezing or coughing, through direct skin to skin contact, or indirectly via contaminated surfaces [3]. Transmission can occur from individuals with acute GAS-related illness, such as an acute sore throat or skin infections, and from asymptomatic carriers harboring the bacteria in their throat without signs of illness.

An initially uncomplicated acute sore throat can in rare cases progress to a severe iGAS infection, and this raises the question whether early antibiotic treatment of an initially uncomplicated sore throat would have prevented the development of iGAS in the same person. However, most iGAS cases presents primarily as an invasive disease [7,9].

Antibiotic treatment of patients with an uncomplicated acute sore throat will reduce transmission of GAS in the community and, this is believed to reduce the population incidence of iGAS [10–12]. However, to date no estimation has been presented as to what proportion of iGAS cases that can be prevented with this approach.

Available information does not allow an exact estimation of the scope for preventing iGAS infections by focusing on antibiotic treatment to patients with an uncomplicated acute sore throat. Hence, the objective of this study was to critically evaluate available evidence and use this to calculate an approximate estimate of how various strategies of managing patients with an uncomplicated acute sore throat may reduce the population incidence of iGAS.

Material and methods

The incidence and proportion of infections being caused by GAS differs significantly between children and adults. Therefore, all estimates and calculations were stratified for children and adults. The definition of children varies in previous publications used to underpin this study. Hence, children were in this study defined as younger than 15-20 years of age.

Different strategies

Clinical guidelines vary considerably about how to manage patients with an acute sore throat. The most restrictive approaches are seen in The Netherlands and Belgium, where guidelines advise against any antibiotic treatment for uncomplicated cases [13,14]. However, guidelines in most other countries permit antibiotic use in selected patients with an uncomplicated acute sore throat. In many high-income countries this is done by a three-step sorting mechanism. Firstly, an initial triage, sometimes over the phone. Secondly, those not having an obvious mild viral illness may be subjected to a clinical scoring to select patients for a throat swab and then thirdly, prescribing antibiotics if the throat swab shows presence of GAS (Figure 1).

One of the most used clinical scoring algorithms is the Centor score, where 1 point is allocated to each of the four criteria history of fever, swollen tender anterior lymph nodes, tonsillar exudate, and absence of cough [15]. Consequently, we evaluated different preventive strategies applied by the health care system using varying cut-offs in Centor scores as a guide for obtaining a throat swab.

We assume that GAS is transmitted from carriers of GAS in the throat, individuals with an uncomplicated acute sore throat and individuals with skin infections like impetigo or pyoderma. Furthermore, we assume that antibiotics to an individual with GAS will reduce transmission of GAS from this individual. The various strategies using different cut-off for obtaining a throat swab will determine which patients with an uncomplicated acute sore throat will be eligible for antibiotic prescribing. This information enables us to estimate the effect antibiotics to patients with an uncomplicated acute sore throat will have on reducing the population incidence of iGAS.

Preventing iGAS

Preventing iGAS in the society can happen through four main approaches: 1) Prescribing antibiotics to patients with an uncomplicated acute sore throat to prevent iGAS in the same patient, 2) Prescribing antibiotics to patients with an uncomplicated acute sore throat to reduce transmission of GAS in the community, 3) Prescribing antibiotics to asymptomatic carriers of GAS to reduce transmission of GAS in the community, and 4) Prescribe antibiotics to patients with skin infections caused by GAS.

For oral phenoxymethylpenicillin eradication of GAS is achieved in 14% of asymptomatic throat carriers based on a data set of children and adults combined [16]. For this, and many other practical reasons, the third option is deemed unsuitable. However, we still need to consider the possibility of carriers transmitting GAS.

We have collated available information to make an approximate estimate of the preventive effect of the first and second approach while also considering that transmission of GAS happens from asymptomatic throat carriers of GAS and from individuals with skin infections.

Current knowledge being the basis for relevant assumptions

We compiled current knowledge, or lack thereof, and made informed assumptions about the general population, sore throat patients seeking health care, transmission of GAS in the community and the possibility of preventing iGAS infections (Tables 1 and 2). The scientific evidence underpinning the assumptions, labeled A to Q, are described in detail in Supplementary File 1.

Applied example and outcome measures

At the end of 2024, Sweden had approximately 2.3 million children and 8.3 million adults. In the same year, the incidence of iGAS was unusually high, with 163 reported cases in children and 1152 in adults. We used these Swedish figures and the assumptions stated in Tables 1 and 2 to calculate the outcome measures: 1) the proportion of iGAS infections possible to prevent, 2) the number of episodes of an uncomplicated acute sore throat to have a throat swab to prevent one case of iGAS, and 3) the number of episodes of an uncomplicated acute sore throat to have an antibiotic prescription to prevent one case of iGAS.

The first outcome measure includes the entire population irrespective if they contact a health care provider for an episode of an uncomplicated acute sore throat prior to their iGAS infection. The second and third outcome measure only includes patients contacting a health care provider with an episode of an uncomplicated acute sore throat. Details on how these outcomes were calculated are provided in Supplementary File 1.

Sources from where iGAS patients acquire GAS

We know that cases with iGAS must have acquired their GAS either from a patient with a sore throat, from an asymptomatic throat carrier of GAS or from an individual with a skin infection. By

Table 1
Strategies and assumptions regarding episodes of an uncomplicated acute sore throat.

			Test patients[a] for presence of GAS and prescribe antibiotics (AB) only if the test is positive									
	Strategy I: Prescribe AB to all patients[a] with a sore throat		II: Test all patients		III: Test patients with Centor 1-4		IV: Test patients with Centor 2-4		V: Test patients with Centor 3-4		VI: Test patients with Centor 4	
	Children	Adults	Children	Adults	Children	Adults	Children	Adults	Children	Adults	Children	Adults
A) Population incidence rate (episodes per 1000 person-years)[b]	1000	690	1000	690	1000	690	1000	690	1000	690	1000	690
B) Episodes where persons contact a health care provider (%)[b]	35%	41%	35%	41%	35%	41%	35%	41%	35%	41%	35%	41%
C) Episodes where persons attend health care and throat swab is obtained (%)[b]	0.0%	0.0%	100%	100%	74%	83%	36%	50%	14%	18%	2.9%	5.4%
D) Episodes where persons attend health care and tested positive for GAS (%)[b]	—	—	33%	13%	37%	13%	52%	17%	55%	26%	20%	27%
E) GAS related sore throat episodes NOT prescribed antibiotics and transmitting GAS (%)[b,c]	35%	15%	35%	15%	35%	15%	35%	15%	35%	15%	35%	15%
F) GAS related sore throat episodes prescribed antibiotics and transmitting GAS (%)[b,d]	20%	11%	20%	11%	20%	11%	20%	11%	20%	11%	20%	11%
G) Transmission of GAS from episodes of sore throat (transmissions per 1000 person-years)[e]	100	12	100	12	100	21	110	21	110	22	120	22

AB, antibiotics; GAS, group A Streptococcus.
[a] Patients refer to episodes of an uncomplicated acute sore throat where a person contact health care, usually primary care.
[b] Evidence for these assumptions are explained in the Supplementary File 1.
[c] This includes all episodes of an uncomplicated acute sore throat caused by GAS in the population irrespective if they contact health care.
[d] This includes all episodes of an uncomplicated acute sore throat caused by GAS contacting health care and prescribed AB.
[e] This is calculated from existing evidence as described in Supplementary File 1.

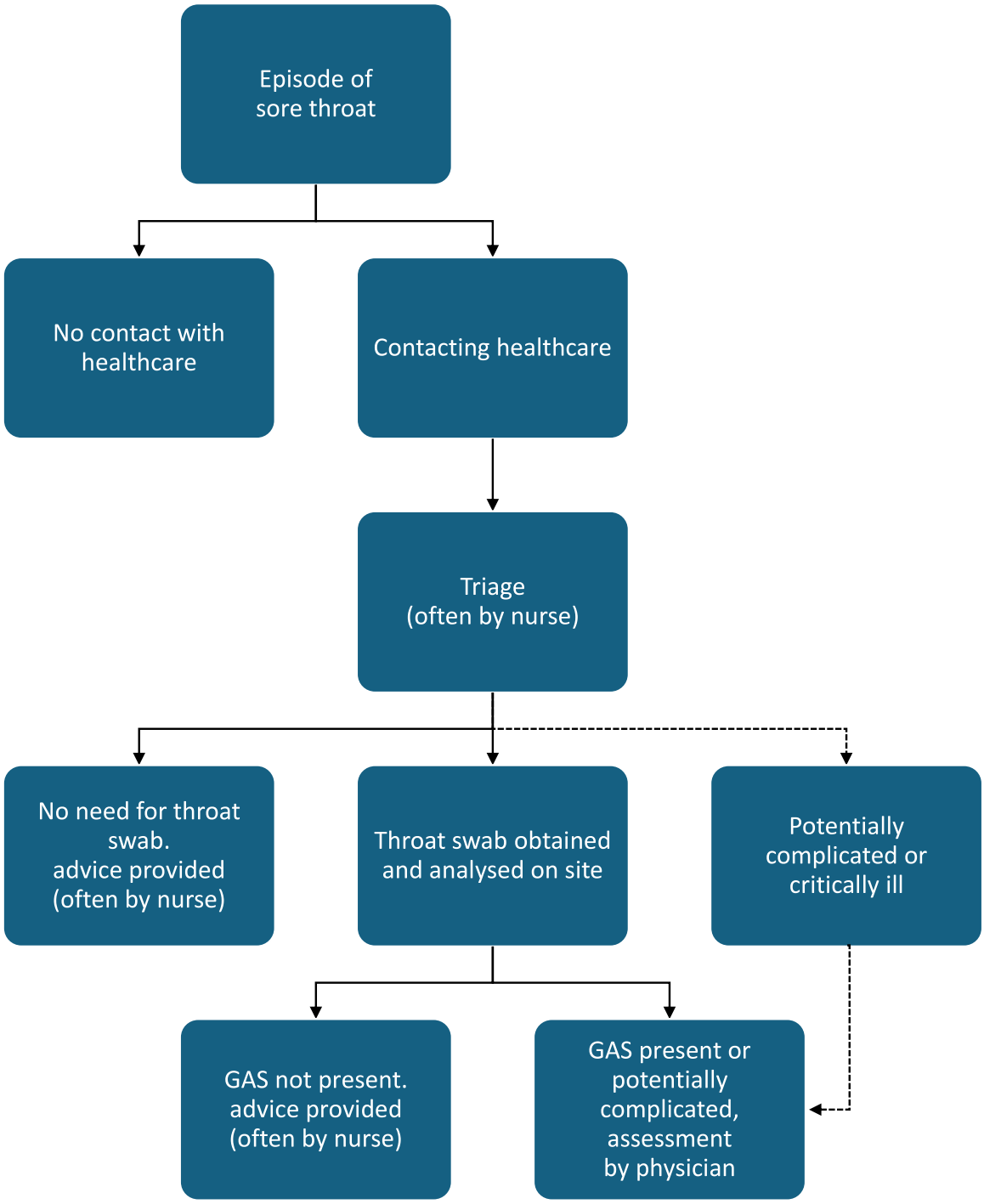

Figure 1. Flow chart in Swedish primary care for patients with an acute sore throat episode. Abbreviation: GAS, group A Streptococcus.

estimating the incidence of sore throat episodes, episodes of carrying GAS in the throat and the incidence of skin infection episodes, and the probability for these to transmit GAS, we could estimate the sources of GAS for cases of iGAS (Supplementary File 1).

Sensitivity analysis

We conducted a large number of sensitivity analyses to explore the impact of uncertainties in our assumptions. This involved making reasonable alterations to explore how these would change the overall outcomes. Supplementary File 1 provides details on which sensitivity analyses that were made and Supplementary File 2 shows the outcome of them.

In most years prior to the COVID-19 pandemic, the incidence of iGAS was substantially lower than in 2024. Hence, we also model a scenario in which the annual incidence of iGAS is reduced to half of the 2024 level.

Results

The 2024 incidence of iGAS infections in Sweden were for 7.2 for children and 14 for adults per 100,000 individuals.

Table 2
Assumptions regarding episodes of GAS throat carriage, skin infections and iGAS.

	Children	Adults
Assumptions regarding episodes of asymptomatic carriage of GAS in the throat		
H) Population incidence rate (annual episodes per 1000 person years)[a]	610	110
I) Proportion of episodes of asymptomatic GAS carriage that transmit GAS (%)[a]	5.5%	3.3%
J) Episodes of asymptomatic GAS carriage transmitting GAS (transmissions per 1000 person years)[b]	34	3.8
Assumptions regarding episodes of impetigo or pyoderma		
K) Population incidence rate (episodes per 1000 person years)[a]	40	6.2
L) Episodes where a person contacts a health care provider (%)[a]	80%	80%
M) Episodes where GAS is involved (%)[a]	5.0%	5.0%
N) Episodes where GAS is involved and antibiotics are prescribed (%)[a]	70%	70%
O) Transmission of GAS from episodes of impetigo or pyoderma (transmissions per 1000 person years)[b]	0.42	0.065
Assumptions regarding episodes of iGAS infections		
P) Episodes of iGAS contacting health care with preceding uncomplicated acute sore throat (%)[a]	15%	6.7%
Q) Probability that antibiotics for uncomplicated acute sore throat prevents subsequent iGAS infection (%)[c]	50%	50%

GAS, group A Streptococcus; iGAS, invasive group A Streptococcus.
[a] This evidence is described in Supplementary File 1.
[b] This is calculated from existing evidence (described in Supplementary File 1).
[c] There is poor evidence for this assumption and the rationale for our assumption is described in Supplementary File 1.

Sources for GAS

We estimate that in Sweden 77% of children and 85% of adults with iGAS acquired their GAS from a case with an acute sore throat, the rest mainly acquired it from a carrier of GAS (Table 3). In Sweden, skin infections, like impetigo or pyoderma, contributes very little to the transmission of GAS in the society (Table 3). Prescribing antibiotics more widely to patients with an uncomplicated acute sore throat will to some extent increase the relative contribution of asymptomatic carriers as a source of GAS to patients with iGAS (Table 3).

Preventing iGAS

Prescribing antibiotics to all patients presenting to a health care provider with an acute sore throat has the potential to prevent 4.5% of iGAS cases in children and 1.9% in adults (Table 4). The extensive sensitivity analysis shows that if assumptions are altered this might change to be between 2.4-6.7% for children and 1.0-2.9% for adults (Table 4).

Using a cut-off in the number of Centor criteria to obtain a throat swab and prescribe antibiotics only to those having presence of GAS reduces the proportion of iGAS cases that can be prevented (Table 4). If the threshold for performing a throat swab in Sweden was lowered from the current 3-4 Centor criteria to 2-4, the extent of iGAS cases that could potentially be prevented would increase (Table 4). In 2024, making this adjustment in Sweden would have prevented an estimated 2.5 cases of iGAS in children and 7.1 cases of iGAS in adults. However, this approach would have required a substantial increase in the annual number of episodes of a sore throat requiring assessments with a throat swab, increasing from 110,000 to 290,000 in children and from 420,000 to 1,200,000 in adults (Table 4).

The number of episodes of an uncomplicated acute sore throat that need to be swabbed to prevent one case of iGAS varies between 45,000 and 110,000 depending on the Centor score cut-off used to guide throat swabbing (Table 4). The corresponding NNT for antibiotic prescribing to prevent one case of iGAS varies between 12,000 and 110,000 (Table 4). These estimates change slightly in the sensitivity analyses (Table 4).

Sensitivity analysis

Despite altering many assumptions to maximize the preventive effect, less than 7% of iGAS cases in children and less than 3% in adults are preventable by antibiotic treatment of patients with an uncomplicated acute sore throat (Table 4 and Supplementary File 2). Maximum prevention of iGAS requires that all patients presenting to a health care provider with a sore throat are tested and prescribed antibiotics if GAS is present. In more realistic scenarios where the cut-off for testing is 2-4 Centor scores $\leq$3.9% of iGAS cases in children and $\leq$2.1% in adults can be prevented (Table 4).

Discussion

This study shows that prescribing antibiotics to patients with uncomplicated acute sore throat will reduce transmission of GAS in the society and this will reduce the population incidence of iGAS infections. The proportion of iGAS cases that can be prevented by antibiotics is smaller than might be expected. The main reasons for this are 1) most individuals in the society with an acute sore throat don't contact health care (Supplementary File 1), 2) individuals with an uncomplicated acute sore throat are most contagious initially during the first days and half of patients are contacting a health care provider at day three or later diminishing the scope for stopping transmission of GAS (Supplementary File 1), and 3) 15-25% of iGAS cases acquire their GAS from individuals who are asymptomatic throat carriers of GAS, a group that should not be prescribed antibiotics.

In theory, some of the factors limiting the effectiveness of antibiotics in reducing iGAS could be addressed by providing the general population with "standby" antibiotics to keep at home and initiate immediately upon developing a sore throat. However, there are strong arguments against such an approach. A substantial proportion of the population would likely not use the antibiotics as intended, and there is no evidence that this strategy would reduce iGAS incidence by more than a marginal extent. Moreover, the potential drawbacks would be considerable, with antibiotic stewardship representing only one of several major concerns. To date, no scientific publication or clinical guideline has proposed implementing such a strategy.

Current Swedish guidelines [17], in line with many guidelines in other countries, advise performing a throat swab in patients with 3-4 Centor criteria and prescribing antibiotics if the swab shows presence of GAS. In Sweden, and many other countries, there is an ongoing discussion among clinicians and policymakers about these criteria. Some suggest expanding the criteria for throat swabbing to include patients with 2-4 Centor criteria, or even all patients without apparent signs of viral infection, to reduce the population incidence of iGAS [11,12]. Such strategies will prevent a few more iGAS cases but also lead to unintended consequences such as short-term

Table 3
Sources of GAS for patients with iGAS.

	Strategy I: Prescribe AB to all patients[a] with a sore throat		Test patients [a] for presence of GAS and prescribe antibiotics (AB) only if the test is positive: II: Test all patients		III: Test patients with Centor 1-4		IV: Test patients with Centor 2-4		V: Test patients with Centor 3-4		VI: Test patients with Centor 4	
	Children	Adults	Children	Adults	Children	Adults	Children	Adults	Children	Adults	Children	Adults
GAS acquired from person carrying GAS in the throat	25%	24%	25%	24%	25%	15%	24%	15%	23%	15%	22%	15%
GAS acquired from person with acute sore throat[b]	75%	76%	75%	76%	75%	85%	76%	85%	77%	85%	77%	85%
GAS acquired from person with impetigo or pyoderma[c]	0.31%	0.41%	0.31%	0.41%	0.30%	0.26%	0.29%	0.26%	0.28%	0.26%	0.27%	0.25%

Abbreviations: AB, antibiotics; GAS, group A Streptococcus; iGAS, invasive group A Streptococcus.
[a] Patients refers to patients attending health care, usually primary care, for an uncomplicated acute sore throat.
[b] This includes all episodes of an uncomplicated acute sore throat caused by GAS in the population irrespective if they contact health care.
[c] This includes all episodes of impetigo or pyoderma caused by GAS in the population irrespective if they contact health care.

side effects, long-term side effects [18,19] and crowding-out with subsequent opportunity costs driven by a substantially increased workload for primary health care.

Strengths and limitations of the study

We deliberately put many details in two Supplementary Files to ensure the article itself is readable. The article may be seen as a guide to introduce the problem and present an overview of necessary assumptions and the main results. This is likely sufficient for many readers. All details are fully presented in the comprehensive Supplementary Files for the interested reader.

One limitation of this study is that the incidence data for iGAS in Sweden already reflect the current antibiotic prescribing patterns. Therefore, our estimates may slightly underestimate the full preventive potential of broader antibiotic treatment strategies. However, this effect appears small, and Table 4 suggests that current Swedish guidelines, if fully adhered to, would only account for a reduction in iGAS cases of 1.1% in children and 0.76% in adults.

Our analysis is based on the Swedish population and its national incidence of iGAS infections a particular year. Other countries may have a different incidence of iGAS infections. Even so, the overall finding that iGAS infections only to a small extent can be prevented is likely to be valid in most high-income countries.

There is no prior study clarifying whether antibiotic treatment for an uncomplicated acute sore throat can prevent the same patient from developing iGAS. Given that the preventive effect from antibiotics can range from 0-100% we found it reasonable to test the consequences of assuming this effect was 25%, 50%, and 75% respectively (Supplementary File 1). Other assumptions are supported by evidence of varying quality. Therefore, we did extensive sensitivity analyses altering most assumptions and exploring the consequences of this. Hence, our figures should be interpreted as indicative rather than exact. We also recognize that GAS transmission is a dynamic process influenced by heterogeneity in contact patterns, superspreading events, and temporal variation. Nevertheless, we believe that the conclusion, that only a very small proportion of iGAS cases can be prevented by treating patients attending a health care provider with an uncomplicated acute sore throat with antibiotics, remains robust.

We made multiple sensitivity analyses in Supplementary File 2 and present the consequences of changing one assumption each time. We did not explore the consequences of combining multiple simultaneous changes in assumptions. If that was done, most likely some alterations would increase, and others would decrease the chances of preventing iGAS. It is highly unlikely that multiple simultaneous changes in assumptions would all work in the same direction as to increase or decrease the proportion of iGAS cases that can be prevented.

In our calculations we estimate the effect of prescribing antibiotics. We are aware that compliance is not 100%. However, this is accounted for in the publications underpinning the assumed effect of antibiotic prescribing (Supplementary File 1).

Our results indicate that expanding the criteria for throat swabbing would increase the number of patients currently contacting a health care provider who qualify for a throat swab test. Furthermore, broadly applying wider criteria may, in the long term, encourage more proactive care-seeking behavior in the population. While an increase in consultations for uncomplicated acute sore throat would yield a small improvement in the prevention of iGAS cases, it would also drive the health care workload (Table 4).

We used Sweden as a model and our results is likely to be similar in most high-income countries. The situation is very different in low-income settings where skin infections are more prevalent, and our results may not be valid in such settings.

Table 4
Results and sensitivity analyses using Sweden as example.

	Strategy I: Prescribe AB to all patients[a] with a sore throat		Test patients[a] for presence of GAS and prescribe antibiotics (AB) only if the test is positive									
			II: Test all patients		III: Test patients with Centor 1-4		IV: Test patients with Centor 2-4		V: Test patients with Centor 3-4		VI: Test patients with Centor 4	
	Children	Adults	Children	Adults	Children	Adults	Children	Adults	Children	Adults	Children	Adults
Using all assumptions as stated in Tables 1 and 2												
Proportion of iGAS infections possible to prevent	4.5%	1.9%	4.5%	1.9%	3.8%	1.7%	2.6%	1.4%	1.1%	0.76%	0.21%	0.24%
No. of episodes of sore throat contacting health care	820,000	2,400,000	820,000	2,400,000	820,000	2,400,000	820,000	2,400,000	820,000	2,400,000	820,000	2,400,000
No. of episodes of sore throat requiring a throat swab	–	–	820,000	2,400,000	600,000	2,000,000	290,000	1,200,000	110,000	420,000	24,000	130,000
No. of episodes to throat swab to prevent one case of iGAS	–	–	110,000	110,000	98,000	97,000	69,000	74,000	64,000	48,000	68,000	45,000
No. of episodes prescribed antibiotics to prevent one case of iGAS	110,000	110,000	36,000	14,000	36,000	13,000	36,000	13,000	35,000	13,000	34,000	12,000
= Sensitivity analyses making the largest change in the proportion of iGAS that can be prevented are shown below[b] =												
1a) Lowering the population incidence rate, measured as episodes per 1000 person-years, of acute sore throat (for children from 1023 to 345 and for adults from 693 to 135)												
Proportion of iGAS infections possible to prevent	3.3%	1.1%	3.3%	1.1%	2.8%	1.1%	2.0%	0.91%	0.83%	0.51%	0.17%	0.18%
No. of episodes to throat swab to prevent one case of iGAS	–	–	51,000	37,000	45,000	29,000	31,000	22,000	29,000	14,000	29,000	12,000
No. of episodes prescribed antibiotics to prevent one case of iGAS	51,000	37,000	17,000	4800	17,000	3800	16,000	3735	16,000	3600	14,000	3300
2a) Lowering the proportion of sore throat episodes contacting health care (for children from 35% to 18% and for adults from 41% to 21%)												
Proportion of iGAS infections possible to prevent	2.4%	1.0%	2.4%	1.0%	2.0%	0.87%	1.4%	0.69%	0.57%	0.39%	0.11%	0.13%
No. of episodes to throat swab to prevent one case of iGAS	–	–	110,000	110,000	96,000	100,000	68,000	76,000	64,000	49,000	66,000	45,000
No. of episodes prescribed antibiotics to prevent one case of iGAS	110,000	110,000	36,000	14,000	36,000	13,000	35,000	13,000	35,000	13,000	33,000	12,000
2b) Increasing the proportion of sore throat episodes contacting health care (for children from 35% to 53% and for adults from 41% to 62%)												
Proportion of iGAS infections possible to prevent	6.7%	2.8%	6.7%	2.8%	5.6%	2.7%	3.9%	2.1%	1.6%	1.2%	0.32%	0.37%
No. of episodes of sore throat contacting health care	1,300,000	3,600,000	1,300,000	3,600,000	1,300,000	3,600,000	1,300,000	3,600,000	1,300,000	3,600,000	1,300,000	3,600,000
No. of episodes of sore throat requiring a throat swab	–	–	1,300,000	3,600,000	910,000	3,000,000	450,000	1,800,000	170,000	640,000	36,000	190,000
No. of episodes to throat swab to prevent one case of iGAS	–	–	110,000	110,000	99,000	96,000	70,000	73,000	65,000	47,000	69,000	45,000
No. of episodes prescribed antibiotics to prevent one case of iGAS	110,000	110,000	37,000	14,000	37,000	12,000	36,000	12,000	36,000	12,000	35,000	12,000
12a) Lowering the proportion of iGAS episodes where antibiotics for preceding acute sore throat prevents subsequent iGAS (for children from 50% to 25% and for adults from 50% to 25%)												
Proportion of iGAS infections possible to prevent	2.3%	0.96%	2.3%	0.96%	1.9%	0.88%	1.3%	0.69%	0.55%	0.39%	0.11%	0.13%
No. of patients to throat swab to prevent one case of iGAS	–	–	220,000	210,000	200,000	190,000	140,000	150,000	130,000	96,000	130,000	88,000
No. of patients to prescribe antibiotics to prevent one case of iGAS	220,000	210,000	73,000	28,000	72,000	25,000	71,000	25,000	70,000	25,000	66,000	24,000
12b) Increasing the proportion of iGAS episodes where antibiotics for preceding acute sore throat prevents subsequent iGAS (for children from 50% to 75% and for adults from 50% to 75%)												
Proportion of iGAS infections possible to prevent	6.8%	2.9%	6.8%	2.9%	5.7%	2.6%	3.9%	2.1%	1.6%	1.1%	0.32%	0.36%
No. of patients to throat swab to prevent one case of iGAS	–	–	74,000	72,000	65,000	65,000	46,000	50,000	43,000	32,000	46,000	31,000
No. of patients to prescribe antibiotics to prevent one case of iGAS	74,000	72,000	24,000	9300	24,000	8500	24,000	8400	24,000	8400	23,000	8300

AB, antibiotics; GAS, group A Streptococcus; iGAS, invasive group A Streptococcus.

[a] Patients refer to patients attending health care, usually primary care, for an uncomplicated acute sore throat.

[b] The sensitivity analysis is described in detail in Supplementary File 1 and the outcome of all sensitivity analyses are described in Supplementary File 2. Only the five sensitivity analyses deviating the most from the main results are displayed in this table, the rest are found in Supplemental file 2. The numbering at the beginning relates to the sensitivity analyses in Supplementary File 1 and 2.

Comparison with existing literature

It has been proposed that antibiotic treatment could be considered for GAS carriers during community outbreaks of iGAS [20]. One guideline from the UK mentions that antibiotic treatment of asymptomatic individuals might be considered if more than one case of iGAS is found in a nursing home [1]. That said, there is only weak evidence supporting the use of prophylactic antibiotics to prevent iGAS infection among close contacts of confirmed cases [21]. Antibiotic treatment of close contacts to patients with an iGAS infection will not have any noticeable impact on the population's overall incidence of iGAS infections.

Some experts have expressed an opinion that prescribing antibiotics to patients with uncomplicated acute sore throat may prevent subsequent iGAS infection in the same individual [20,22]. Erlacher *et al.* [23] do not think iGAS is preventable. Gustavsson *et al.* [24] concludes that all patients with preceding confirmed streptococcal tonsillitis developed iGAS despite adequate antibiotic treatment. These publications merely consider preventing iGAS in the same individual and do not consider a reduction in transmission of GAS in the community as a mechanism to reduce the population incidence of iGAS.

Our study is, to our knowledge, the first to provide an approximate estimate for the possibility of preventing iGAS by antibiotic treatment to patients with an uncomplicated acute sore throat. We accounted both for reduced incidence of iGAS when preceded by a sore throat and for a reduced transmission of GAS in the community. The latter effect is likely larger than the potential effect of preventing iGAS in the same patient.

Conclusions

The present study indicates that only a very small proportion of iGAS infections can be prevented by prescribing antibiotics to patients with an uncomplicated acute sore throat. As most of these patients experience a mild self-limiting illness, an important question is to what extent antibiotics, given their potential side effects, should be recommended to many patients to protect a few other patients.

Widening the criteria for throat swabbing would significantly increase the burden on health care services (Table 4). This raises concerns about the unintended consequence of reducing access to care for other groups of patients. Furthermore, the decision in this matter should not be based merely on cost-effectiveness but should also take resource availability into account [25]. Thus, determining the threshold for throat swabbing and treating patients with uncomplicated acute sore throat is not just a scientific issue, it is also a matter of policy and prioritization making it a political issue. This study contributes with important new facts that will facilitate those discussions.

Irrespective if the criteria for testing and prescribing antibiotics are widened, this study emphasizes the importance of recognizing early signs of iGAS, or any other severe infection. There are simple flow charts to accomplish this in patients presenting to a health care provider with an acute sore throat [26].

A detailed analysis of the practicalities of different pathways to increase prevention of iGAS combined with a robust health economic analysis and an analysis of available resources, preferably as a time needed to treat analysis [25], is imperative.

In the longer term, future research should focus on development of a safe and effective vaccine against GAS. This has the potential to both reduce illness caused by GAS and antibiotic prescribing [27]. Until a safe and effective GAS vaccine is available, health systems must carefully weigh the benefits of broader testing and treatment against harms and resource constraints.

Declaration of competing interests

The authors have no competing interests to declare.

CRediT authorship contribution statement

Ronny Gunnarsson: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Software, Validation, Writing – original draft, Writing – review & editing. **Erik Wiezell:** Conceptualization, Formal analysis, Methodology, Validation, Writing – review & editing. **Carl Wikberg:** Conceptualization, Methodology, Validation, Writing – review & editing, Formal analysis. **Pär-Daniel Sundvall:** Conceptualization, Formal analysis, Methodology, Validation, Writing – review & editing. **Karin Rystedt:** Conceptualization, Formal analysis, Methodology, Validation, Writing – review & editing.

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Ethics approval was not sought since this study is based on data from previous publications and publicly available statistics.

Data sharing

This study is based on already published knowledge and relevant references have been cited.

Declaration of generative AI and AI-assisted technologies in the writing process

Gemini version 3 was used after the manuscript was written to enhance the language of one paragraph in the discussion.

Transparency statement

Authors affirms that the manuscript is an honest, accurate, and transparent account of the study being reported and that no important aspects of the study have been omitted.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2026.108818.

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