Paul Little, FD Richard Hobbs, David Mant, Cliodna AM McNulty and Mark Mullee on behalf of the PRISM investigators

Incidence and clinical variables associated with streptococcal throat infections:

a prospective diagnostic cohort study

Abstract

Background
Management of pharyngitis is commonly based on features which are thought to be associated with Lancefield group A beta-haemolytic streptococci (GABHS) but it is debatable which features best predict GABHS. Non-group A strains share major virulence factors with group A, but it is unclear how commonly they present and whether their presentation differs.

Aim
To assess the incidence and clinical variables associated with streptococcal infections.

Design and setting
Prospective diagnostic cohort study in UK primary care.

Method
The presence of pathogenic streptococci from throat swabs was assessed among patients aged ≥5 years presenting with acute sore throat.

Results
Pathogenic streptococci were found in 204/597 patients (34%, 95% CI = 31 to 38%): 33% (68/204) were non-group A streptococci, mostly C (*n* = 29), G (*n* = 18) and B (*n* = 17); rarely D (*n* = 3) and *Streptococcus pneumoniae* (*n* = 1). Patients presented with similar features whether the streptococci were group A or non-group A. The features best predicting A, C or G beta-haemolytic streptococci were patient's assessment of severity (odds ratio [OR] for a bad sore throat 3.31, 95% CI = 1.24 to 8.83); doctors' assessment of severity (severely inflamed tonsils OR 2.28, 95% CI = 1.39 to 3.74); absence of a bad cough (OR 2.73, 95% CI = 1.56 to 4.76), absence of a coryza (OR 1.54, 95% CI = 0.99 to 2.41); and moderately bad or worse muscle aches (OR 2.20, 95% CI = 1.41 to 3.42).

Conclusion
Non-group A strains commonly cause streptococcal sore throats, and present with similar symptomatic clinical features to group A streptococci. The best features to predict streptococcal sore throat presenting in primary care deserve revisiting.

Keywords
pharyngitis; primary care; tonsillitis; streptococcus.

BACKGROUND

Pharyngitis is one of the commonest presentations in clinical practice and most patients are treated with antibiotics despite a Cochrane Review suggesting modest symptomatic benefit.[1] A reasonable strategy in reducing the public health threat of antibiotic resistance is to limit antibiotic use to the minority of individuals with streptococcal infections who are more likely to benefit[2–4] and avoid treatment in those unlikely to benefit. Lancefield group A beta-haemolytic streptococci (GABHS) is the most frequent major bacterial pathogen in pharyngitis and clinical scores to predict GABHS have some promise to be useful[5–7] including the simple 'Centor' criteria — 3 out of 4 of pus, cervical nodes, a history of fever and no history of cough, which are widely advocated in clinical practice guidance.[2,4,8–10] However these criteria have low specificity[8] leading to high rates of overall antibiotic use.[8] Furthermore small studies in typical primary care settings have suggested other features might be useful in refining the criteria; such as, shorter prior duration, severity of pain, and muscle ache.[11,7] The issue of which variables most strongly predict streptococcal infections is therefore still not settled.

Rapid streptococcal antigen tests to detect GABHS are used widely in developed countries to target treatment since GABHS is the most common major pathogen,[5] and the use of rapid tests may help practitioners reduce prescribing.[12,13] Other Lancefield groups (particularly C and G) have hitherto had much less emphasis,[14] and there are no rapid antigen tests available for detecting these groups. Although rheumatic fever is probably not caused by group C and G streptococci, the incidence of rheumatic fever has dramatically declined in developed countries[1] and antibiotic treatment to prevent rheumatic fever is an extremely inefficient use of healthcare resources.[4] The major virulence factors among group A streptococci are shared by group C and G streptococci, particularly the M proteins, peptidase, hylauronic capsule, and streptokinase[14,11] and similar numbers of cases of streptococcal septicaemia due to C and G streptococci are regularly reported.[15] However, such complications are rare, hence the major benefit of targeting streptococcal infections, which may apply to groups C, G, and A if clinical presentation is similar, is likely to be in limiting antibiotic treatment to individuals who will benefit from more rapid symptom resolution[1] and a shorter infective period.[2] A small study in two Norwegian practices

P Little, BA, MRCP, FRCGP, FMedSci, professor of primary care research, **M Mullee**, BSc(Hons), MSc, CStat MSC, senior lecturer in medical statistics, Primary Care and Population Science, Faculty of Medicine University of Southampton. **FDR Hobbs**, FMedSci, professor and head of Primary Care Health Sciences and director, NIHR School for Primary Care Research, University of Oxford. **D Mant**, FRCP, FRCGP, emeritus professor of general practice, Department of Primary Care Health Sciences, University of Oxford, Oxford. **C McNulty**, MRCPath FRCPathol, head of unit, Health Protection Agency Primary Care Unit, Microbiology Department, Gloucestershire Royal Hospital, Gloucester.

Address for correspondence
Paul Little, University of Southampton, Aldermoor Health Centre, Aldermoor Close, Southampton, SO16 5ST, UK.
E-mail: p.little@soton.ac.uk

Submitted: 20 December 2011; **Editor's response:** 31 January 2012; **final acceptance:** 14 June 2012.

How this fits in

This study suggests that it is not just Lancefield group A strains that cause significant illness in primary care: non-group A strains commonly cause streptococcal sore throats, and present with similar symptomatic clinical features to group A streptococci. This suggests that RADTs, which are widely used in many developed countries, are missing clinically important streptococci. The best features to predict streptococcal sore throat presenting in primary care deserve revisiting since features not commonly used in diagnosis (for example, rapid presentation, severity of inflammation) may be useful clinically.

suggested that Lancefield groups C and G presentations were similar to group A;[11] supported by Tiemstra *et al*.[3] Conversely a substantial study concluded that clinical presentations were different.[16] Thus both the relevance of C and G streptococci in symptomatic presentation and the clinical predictors require clarification. This study reports new data on the epidemiology of pathogens causing pharyngitis and the predictors of the presence of pathogenic streptococci for patients presenting with pharyngitis in primary care.

METHOD

Inclusion

Health professionals in general practices in the south and central areas of England recruited adults or children aged ≥5 years presenting with acute sore throat (<2 weeks), where the sore throat was the predominant clinical feature (or where the clinician felt that the pharyngitis was driving the illness presentation) and with an abnormality on examination of the throat (erythema with or without pus and anterior cervical glands), similar to a previous study in primary care.[17] Exclusions were other non-infective causes of sore throat (for example apthous ulceration, candida, or drugs), or unable to consent (for example dementia or uncontrolled psychosis).

Clinical data

Following informed consent baseline clinical data were collected by the recruiting health professional.[18,7,19] The clinical proforma collected information on age; sex; current smoking status; past history of quinsy;[20] data on symptom severity for the symptoms of sore throat, difficulty swallowing, fever, cough, coryza ('runny nose') headache, muscle ache, abdominal pain, diarrhoea vomiting, earache (each symptom was rated by the patient as 0 = no problem, 1 = slight problem, 2 = moderately bad problem, or 3 = severe problem). The doctor or nurse documented examination findings for oral temperature using TempaDOT™ thermometers,[21] the severity of tonsillar and pharyngeal inflammation, the presence of cervical glands, tonsillar exudate, fetor and palatal oedema.[7,18,19]

Throat swabs. At the training session in each practice clinicians were instructed in standard study procedures, including how to take a throat swab. Swabs were taken by the clinician and sent to a central laboratory for culture and sensitivity of all significant pathogens in line with National Standard Operating Procedures.[22,23] Mean time between specimen collection and receipt at laboratory was 2.9 days (data incomplete for 13 samples). The swabs were inoculated onto a blood agar plate and staph/strep agar plate (E&O Laboratories Ltd, Bonnybridge) and spread for single colonies. Plates were incubated anaerobically for 48 hours.[22,23] Plates were read after 24 hours incubation and negative cultures reincubated for an additional 24 hours. Suspected beta-haemolytic streptococcal isolates were identified via visual analysis of colony morphology and Lancefield grouping (PathoDx® Strep Grouping Kit, Oxoid, Basingstoke), in accordance with the National Standard Operating Procedures.[22,23] Antibiotic sensitivities were conducted using disc diffusion techniques.[24]

Sample size. The study was also designed to assess the accuracy of rapid antigen detection tests (not reported here) and the RADT element of this study limited the sample size: assuming sensitivity of 90%,[25] and that 25% of individuals have streptococcus (based on the study's piloting), to estimate the sensitivity with 95% confidence intervals (CIs) of +/-5% 139 patients with streptococci were needed: 556 patients in total. To estimate the predictive value of clinical variables a subgroup of 139 patients with a clinical presentation not associated with streptococcal infection would provide estimates of a negative predictive value of 90% with 95% CIs of +/-5%, and a subgroup of 93 individuals with streptococcal infection would provide estimates of a positive predictive value of 60% with 95% CIs of +/- 10%. The study estimated that a sample size of 455 patients would be sufficient to detect of

an odds ratio of 2 (assuming an alpha of 0.05 and beta of 0.2) for variables with a prevalence of 20–65% among patients without streptococcal infection.

Analysis. Clinical variables were included in a logistic regression model to assess their association with the presence of streptococci. Forward selection was used: variables were included if significant at the 10% level and retained in multivariate analysis if they remained significant at the 5% level, with no evidence of collinearity. All variables significant in univariate analysis were checked again in the final model. Cases with missing data for a particular analysis were excluded. For variables with several levels (for example, sore throat) to facilitate use in a simple clinical score (that is, ease of implementation), a cut off was normally made at or near an odds ratio of 2. Continuous variables were dichotomised using previous cut-offs (age <10 years; prior duration longer than the median of 3 days[7]). For duration there was a progressive reduced likelihood of infection with group A streptococci with longer prior duration however the study dichotomised at the median for ease of implementation. The study also presents a version of the final model with more categories for each variables (that is, not dichotomised, using ordered categorical variables). Such a model could potentially be used with computerised practices to document more precisely risk of streptococcal infection. Although for non-group A streptococci to date the study assumed Lancefield groups B, D, and also pneumococcus were not to be counted as significant pharyngeal pathogens, given the ongoing debates about this issue[3] the study also presents the multivariate analysis when these streptococci are included as potentially significant pathogens. Given the higher asymptomatic carriage rates of streptococci in children this study did not include age in the final multivariate models .

RESULTS

A total of 70 GPs and practice nurses in south and central England recruited 606 patients from March 2007 until January 2008. Recruitment took a year due to the limited duration of recruitment in many practices; the median time spent recruiting was 3 months. However, the median recruitment rate (the number of patients/months recruiting) was 4.7 patients per month; close to the expected rate from national data.[26] Sixty seven of 605 patients (11%) were aged <10 years, 106/604 (18%) were smokers, and 109/605 (32%) were male.

Of 606 patients recruited, 592 had microbiology results and 567 had useable baseline clinical data.

Pathogenic streptococci were found in 202 patients (34%): of these 136 were Lancefield group A beta-haemolytic streptococci, and 66/202 (33%) were non Lancefield group A streptococci: mainly groups C (*n* = 27), G (*n* = 18), and B (*n* = 17), but also D (*n* = 3) and pneumococcus (*n* = 1).

Table 1. Clinical variables in patients with Lancefield Group A beta-haemolytic streptococci (*n* = 136) compared with all other patients

	Patients with Group A (%)	Patients with no Group A (%)	Univariate OR (95% CI)	*P*-value	[a]Multivariate OR (CI)	*P*-value
Prior duration ≤3 days	94/135 (70)	213/454 (47)	2.59 (1.72 to 3.91)	<0.001	1.92 (1.23 to 3.01)	0.004
Cervical glands	121/133 (91)	332/449 (74)	3.55 (1.89 to 6.67)	<0.001	2.63 (1.32 to 5.23)	0.006
Severely inflamed tonsils	39/132 (30)	62/442 (14)	2.57 (1.62 to 4.07)	<0.001	1.63 (0.98 to 2.69)	0.059
Absence of runny nose	96/135 (71)	257/454 (57)	1.89 (1.24 to 2.86)	0.003	1.29 (0.81 to 2.05)	0.284
Age group <10 years	32/136 (24)	32/455 (7)	4.07 (2.38 to 6.94)	<0.001	3.49 (1.89 to 6.43)	<0.001
Sore throat (moderately bad or worse)	131/136 (96)	402/454 (89)	3.39 (1.33 to 8.66)	0.011	3.26 (1.11 to 9.53)	0.031
Absence of moderately bad cough	123/136 (90)	304/455 (67)	4.70 (2.57 to 8.60)	<0.001	4.02 (2.13 to 7.57)	<0.001
Purulent tonsils	70/135 (52)	151/454 (33)	2.16 (1.46 to 3.19)	<0.001	1.23 (0.79 to 1.91)	0.352
Fever (during last 24 hours)	109/136 (80)	269/455 (59)	2.79 (1.76 to 4.43)	<0.001	1.82(1.09 to 3.02)	0.021
Moderately bad muscle aches	52/135 (39)	116/454 (26)	1.83 (1.22 to 2.74)	0.004	1.85 (1.18 to 2.91)	0.008
Headache	100/136 (74)	278/454 (61)	1.76 (1.15 to 2.69)	0.009	1.28 (0.79 to 2.07)	0.318

[a]*Multivariate model controlled for prior duration cervical glands, severe sore throat, absence of cough, bad muscle aches, and fever. OR = odds ratio.*

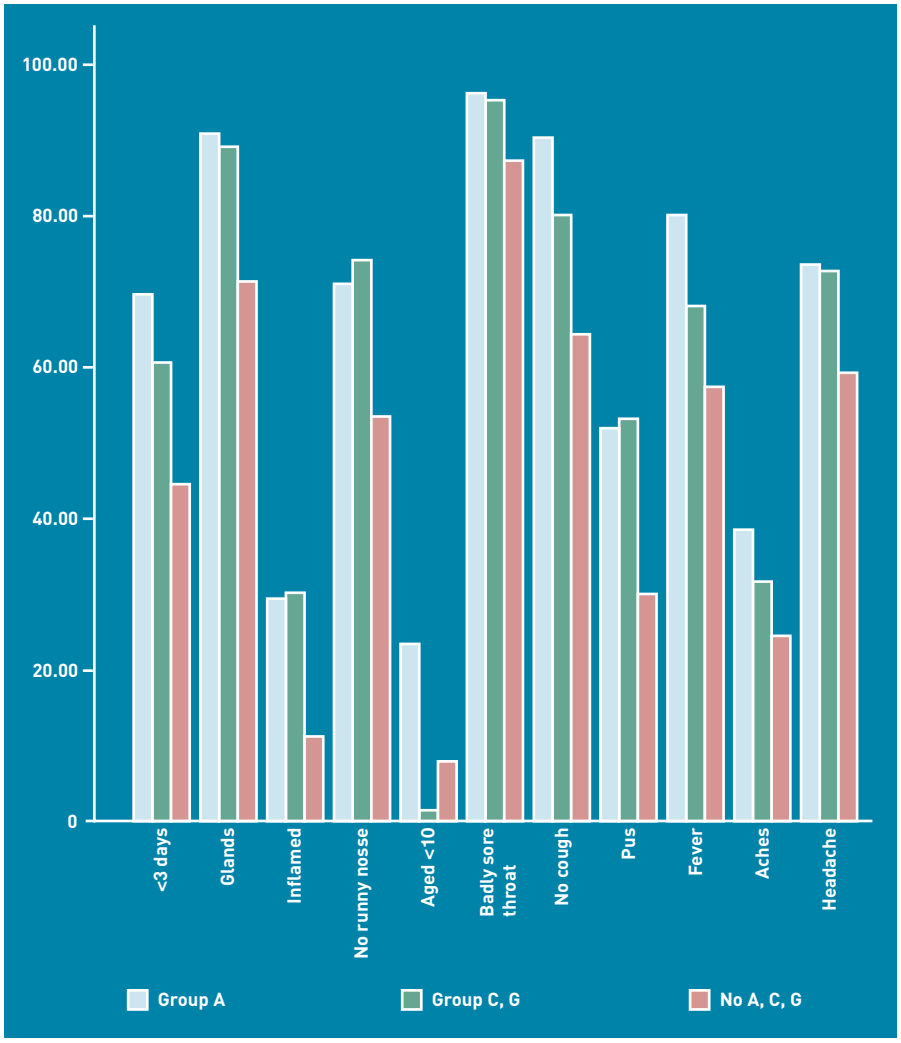


Figure 1. Percentage of symptom and signs at presentation for patients with group A Streptococci, group C or G streptococci, and no group A, C or G streptococci.

Patients who had group A beta-haemolytic strains when compared with all other patients were more likely to have short duration of illness (≤3 days), anterior cervical glands, be aged <10 years, have a moderately bad or worse sore throat, moderately bad or worse muscle aches, fever during the last 24 hours, and not have a bad cough (Table 1). Although purulent tonsils were predictive in univariate analysis they did not independently predict the presence of group A streptococci (Table 1).

Patients with group C and G beta-haemolytic strains presented with similar clinical features to individuals with group A beta-haemolytic strains (Table 2 and Figure 1), with the exception of age, where children were very unlikely to have C and G strains and more likely to have group A strains. Many of the same features associated with group A strains were associated with the presence of C and G streptococci .

The independent clinical features associated with combined group A , C, and G streptococci were: prior duration 3 days or less, moderately bad or worse muscle aches, moderately bad or worse sore throat, and the absence of a bad cough, severely inflamed tonsils, aged <10 years old, fever during the last 24 hours, and anterior cervical glands (Table 3). The absence of a 'runny nose' (coryza) was also very close to significance in multivariate analysis (P = 0.054). There were too few patients with group B infections to assess with confidence but many had similar

Table 2. Clinical variables in patients with Lancefield group C and G beta-haemolytic streptococci compared with patients having no growth of group A, C, or G beta-haemolytic streptococci

	Patients with non-group A (%)	Patients with no pathogenic streptococci (%)	Univariate OR (95% CI)	*P*-value	[a]Multivariate OR (CI)	*P*-value
Prior duration ≤3 days	29/45 (64)	184/409 (45)	2.22 (1.17 to 4.21)	0.015	1.74 (0.88 to 3.42)	0.110
Cervical glands	42/45 (93)	290/404 (72)	5.50 (1.67 to 18.11)	0.005	4.28 (1.27 to 14.4)	0.019
Severely inflamed tonsils	17/45 (38)	45/397 (11)	4.75 (2.41 to 9.35)	<0.001	3.66 (1.80 to 7.44)	<0.001
Absence of runny nose	34/45 (76)	223/409 (55)	2.58 (1.27 to 5.23)	0.009	2.20 (1.06 to 4.60)	0.035
Age group <10 years	0/45 (0)	32/410 (8)	0.0 (N/A)	N/A	N/A	N/A
Sore throat (moderately bad or worse)	44/45 (98)	358/409 (88)	6.27 (0.84 to 46.5)	0.073	4.05 (0.53 to 30.9)	0.178
Absence of moderately bad cough	36/45 (80)	268/410 (65)	2.12 (0.99 to 4.52)	0.052	1.40 (0.61 to 3.21)	0.430
Purulent tonsils	25/45 (56)	126/409 (31)	2.81 (1.50 to 5.24)	0.001	1.57 (0.76 to 3.23)	0.225
Fever (during last 24 hours)	34/45 (76)	235/410 (57)	2.30 (1.14 to 4.67)	0.021	1.61 (0.75 to 3.43)	0.219
Moderatelybad muscle aches	18/45 (40)	98/409 (24)	2.12 (1.12 to 4.00)	0.021	2.36 (1.20 to 4.65)	0.013
Headache	35/45 (78)	243/409 (59)	2.39 (1.15 to 4.96)	0.019	1.79 (0.82 to 3.92)	0.147

[a]All multivariate estimates adjusted for cervical glands, severity of inflammation, absence of coryza, muscle aches If other streptococci are included (B and D) then the significant predictors are prior duration, cervical glands, severity of inflammation, and the absence of coryza. OR = odds ratio.

Table 3. Clinical variables in patients with non-group A (C and G) and Group A compared with patients having no growth of C,G or A streptococci

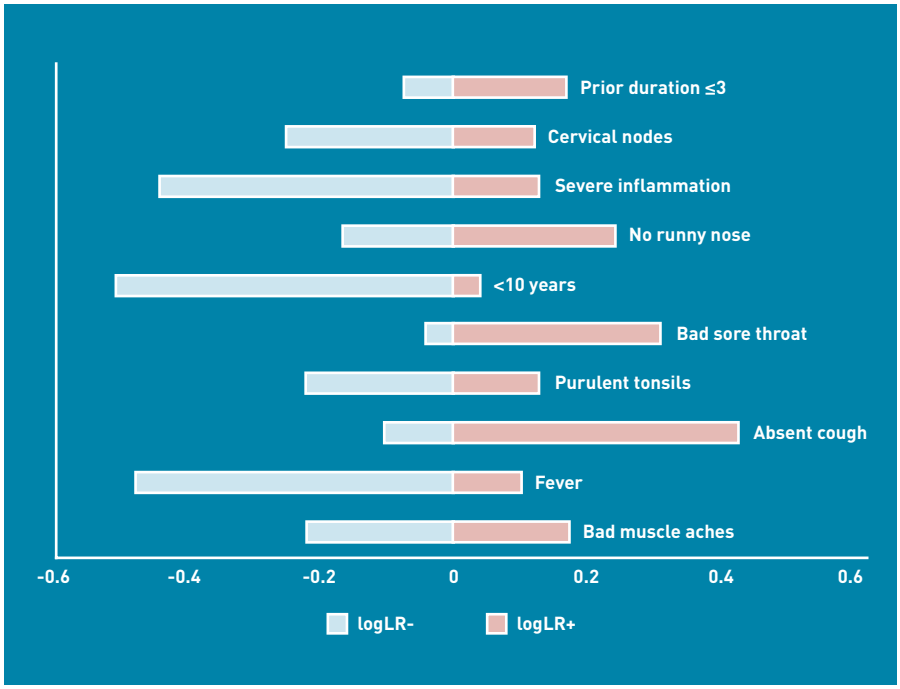
	Patients with group A, C or G streptococci (%)	Patients with no group A, C or G streptococci (%)	Univariate OR (95% CI)	*P*-value	[a]Multivariate OR (95% CI)	*P*-value
Prior duration ≤3 days	123/180 (68)	184/409 (45)	2.64 (1.82 to 3.82)	<0.001	1.92 (1.26 to 2.92)	0.002
Cervical glands	163/178 (92)	290/404 (72)	4.27 (2.41 to 7.57)	<0.001	2.93 (1.55 to 5.52)	0.001
Severely inflamed tonsils	56/177 (32)	45/397 (11)	3.62 (2.32 to 5.64)	<0.001	2.28 (1.39 to 3.74)	0.001
Absence of runny nose	130/180 (72)	223/409 (55)	2.17 (1.48 to 3.17)	<0.001	1.55 (0.99 to 2.41)	0.054
Age group ≤10 years	32/181 (18)	32/410 (8)	2.54 (1.50 to 4.29)	0.001	1.95 (1.05 to 3.62)	0.033
Sore throat (moderately bad or worse)	175/181 (97)	358/409 (88)	4.16 (1.75 to 9.87)	0.001	3.31 (1.24 to 8.83)	0.017
Absence moderately bad cough	159/181 (88)	268/410 (65)	3.83 (2.35 to 6.25)	<0.001	2.73 (1.56 to 4.76)	<0.001
Purulent tonsils	95/180 (53)	126/409 (31)	2.51 (1.75 to 3.60)	<0.001	1.06 (0.67 to 1.66)	0.814
Fever (during last 24 hours)	143/181 (79)	235/410 (57)	2.80 (1.86 to 4.21)	<0.001	1.69 (1.05 to 2.71)	0.030
Muscle aches moderately bad	70/180 (39)	98/409 (24)	2.02 (1.39 to 2.94)	<0.001	2.20 (1.41 to 3.42)	<0.001
Headache	135/181 (75)	243/409 (59)	2.00 (1.36 to 2.96)	<0.001	1.41 (0.89 to 2.25)	0.143

[a]All multivariate estimates adjusted for prior duration, cervical glands, severity of sore throat, severity of inflammation, the absence of cough, the absence of coryza, muscle aches and fever. If other streptococci are included (band D) then the significant predictors are short prior duration, cervical glands, severity of sore throat, severity of inflammation, absence of cough, absence of coryza, and muscle aches.

features in terms of a severe sore throat (17/17; 100%) purulent tonsils 10/17 (59%), 13/16 (81%) cervical glands, short prior duration 9/17 (53%), the absence of a bad cough 14/17 (82%), and no runny nose 13/17 (76%); however fever 10/17 (59%) was similar to those patients where no streptococci were isolated and only 3/17 (18%) had severely inflamed tonsils. A fuller model — where the variables in Table 3 are not dichotomised — is presented in Appendix 1 which supports the overall findings from the simpler models, with the exception of coryza (which is no longer significant).

There is considerable variation as to how well each indicator performs in helping rule in or rule out the presence of streptococci (Figure 2).

Figure 2. Log univariate likelihood ratios (log of likelihood ratio for a negative test (logLR-) and log of likelihood ratio for a positive test [log LR+]) for individual symptoms and signs at presentation for patients with either group A, C or G betahaemolytic streptococci.



Recruitment bias

Comparing patients from higher recruiting doctors (higher than the median: average 11.8 patients per month) with patients from lower recruiting doctors (an average 2.6 patients per month) there was no difference in the number of features that predicted streptococcal infections in multivariate analysis (Table 3, respectively a mean of 3.3 features and 3.4 features), suggesting little or no recruitment bias based on clinical characteristics.

DISCUSSION

Summary

This study documents that non-group A strains are a common cause of streptococcal sore throat in primary care, have a similar symptomatic presentations to group A presentations, and that the best predictors of streptococcal infection may not include some of the features traditionally used.

Funding

This study was funded by the UK Health Technology Assessment Programme, reference number HTA 05/10/01.

Ethical approval

Approved by MREC, reference number 06/MRE06/17.

Provenance

Freely submitted; externally peer reviewed.

Competing interests

CM leads the writing and review of the HPA management of Infection guide for primary care and is a member of the Department of Health Advisory Committee on Antimicrobial Resistance and Healthcare-Associated Infections and the Prescribing Sub-Group and Chair of the Public Education Sub-Groups of this Committee, and was also a member of the NICE self-limiting respiratory tract infection guideline development group.

Acknowledgements

The PRISM investigators were: University of Southampton — Paul Little, Ian Williamson, Mike Moore, Mark Mullee, Man Ying Edith Cheng, James Raftery, David Turner, Jo Kelly, Jane Barnett, Karen Middleton, Gerry Leydon; University of Birmingham — Richard Hobbs, Brendan Delaney, Olga Kostopoulou, Richard McManus, Razia Meer-Baloch; University of Oxford — David Mant, Paul Glasziou, Sue Smith, Diane Coulson; Health Protection Agency — Cliodna McNulty, Peter Hawtin. We are grateful for the doctors and patients who gave their time to make this possible.

Discuss this article

Contribute and read comments about this article on the Discussion Forum: **http://www.rcgp.org.uk/bjgp-discuss**

Strengths and limitations

The power to detect variables associated with group C and G streptococci was limited, although this is one of the largest studies to assess a broad range of clinical variables and the study found similar features to a smaller study reported previously.[11] Missing data was minimal (less than 5% for any analysis), and although consecutive recruitment of cases was difficult to enforce in practice, there was very little evidence of recruitment bias compared with expected rates of recruitment from national samples. Selection bias is a potentially important issue among low recruiting doctors, but the study found no evidence of clinical differences comparing higher and lower recruiting doctors. Overall fewer children than expected from historical data sets[27] were recruited which probably reflects reluctance of parents and/or GPs to expose children to a throat swab, but since the study elected not to include age per se in the model, the impact of this should be slight.

The time between taking a swab and receipt at the laboratory was slightly longer than expected, but Lancefield groups A, C, and G are not particularly sensitive to transport conditions, and the study found relatively high percentages of streptococci compared to previous literature. Since there was no indication from sentinel practices or microbiology laboratories to indicate a streptococcal epidemic, the high streptococcal percentages and more florid clinical signs compared to previous studies in a similar geographical area[28] may indicate changing consultation thresholds. Although the study indicates clinical features not traditionally incorporated in making diagnostic assessments may possibly not be important, further data sets are needed before recommending a key variable set.

The way variables are operationalised may also be important (for example, McIsaac[8,29] uses tonsillar swelling or exudate, Centor[18] just exudate, the study chose exudate since swelling is not necessarily an acute feature). The study used intermediate cut points where indicated rather than the extremes of each scale; however, since the judgement of intermediate points may be more variable, using the extremes (none or very) may be more sensible for developing a clinical prediction rule.

Comparison with existing literature

Traditionally clinicians have been predominantly interested in group A beta-haemolytic streptococci due to their association with major non-suppurative adverse outcomes, particularly rheumatic fever.[5] Hence the clinical predictors of group A infection[5–7] — especially pus, cervical nodes, a history of fever and no history of cough[30] — have been widely used in clinical guidelines.[2,4,31] Historical comparisons tentatively suggest that these variables may identify a group of patients who are more likely to benefit from antibiotics.[1] The study confirmed the importance of cervical glands and the absence of a bad cough and of fever.[7,8] However, this study documents that although the feature of purulence is associated with the presence of group A streptococci in univariate analysis, in this data set it is not independently predictive – and other features may be important, particularly the severity of both the sore throat and the inflammation, the prior duration (reflecting the more rapid severe onset), muscle aches, and possibly the absence of coryza. Some of these features have been identified previously in studies from typical primary care settings[7,11] but previous studies have been limited by lack of multivariate analysis or limited power.

The clinical presentation of group C and G streptococci suggests strongly that not only are these presentations unlikely to be due to commensal carriage, but that they are causing a similar clinical syndrome to group A streptococci. This supports those studies which observed similar symptomatic presentation.[11,3] If group C and G streptococci are clinically important, then rapid streptococcal antigen tests (which are targeted at group A beta-haemolytic streptococci only) will miss a significant proportion of streptococcal infection.

Implications for practice

Group C and G streptococci present with symptomatic illness in a similar manner to group A streptococci. Rapid antigen detection tests which are widely used in many developed countries to detect group A streptococci will miss these organisms. The best features to predict streptococcal sore throat presenting in primary care also deserve clarification since features not commonly used in diagnosis (for example, rapid presentation, severity of inflammation) may be useful clinically.

REFERENCES

1. Spinks A, Glaziou P, Del Mar C. Antibiotics for sore throat. *Cochrane Database Syst Rev* 2006; **(4):** CD000023.
2. Cooper R, Hoffman J, Bartlett J, *et al.* Principles of appropriate antibiotic use for acute pharyngitis in adults. *Ann Intern Med* 2001; **134(6):** 509–517.
3. Tiemstra J, Miranda R. Role of non-group a streptococci in acute pharyngitis. *J Am Board Fam Med* 2009; **22(6):** 663-669.
4. NICE guideline development group. *Prescribing of antibiotics for self-limiting respiratory tract infections in adults and children in primary care.* London: NICE, 2008. http://www.nice.org.uk/Guidance/CG69 (accessed 20 Sep 2012).
5. Del Mar C. Managing sore throat: a literature review I: Making the diagnosis. *Med J Austr* 1992; **156(8):** 572–575.
6. Dagnelie C, Bartelink M, Van Der Graaf Y, *et al.* Towards better diagnosis of throat infections with GABHS in general practice. *Br J Gen Pract* 1998; **48(427):** 959–962.
7. Dobbs F. A scoring system for predicting Group A streptococcal throat infection. *Br J Gen Pract* 1996; **46(409):** 461–464.
8. McIsaac W, Kellner J, Aufricht P, *et al.* Empirical Validation of Guidelines for the Management of Pharyngitis in Children and Adults. *JAMA* 2004; **291(13):** 1587–1595.
9. Cooper RJ, Hoffman JR, Bartlett JG, *et al.* Principles of appropriate antibiotic use for acute pharyngitis in adults: background. *Ann Emerg Med* 2001;**37**: 711–719. http://pages.medicine.ucsf.edu/impaact/images/principlespharyngitisaem.pdf (accessed 16 Oct 2012)
10. Vincent M, Celestin N, Hussain A. Pharyngitis. *Am Fam Phys* 2004; **69(6):** 1465–1470.
11. Lindbaek M, Hoiby E, Steinsholt I, Hjortdahl P. Clinical symptoms and signs in sore throat patients with large colony variant ß-haemolytic streptococci groups C or G versus group A. *Br J Gen Pract* 2005; **55(517):** 615–619.
12. Llor C, Madurell J, Balague-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(586):** e244–e251.
13. Worrall G, Hutchinson J, Sherman G, Griffiths J. Diagnosing streptococcal sore throat in adults a randomized controlled trial of in-office aids. *Can Fam Physician* 2007; **53(4):** 666–671.
14. Efstratiou A. Pyogenic streptococci of Lancefiled groups C and G as pathogens in man. *Soc Appl Bacteriol Symp Ser* 1997; **26:** 72S–79S.
15. Health Protection Agency. Health protection report: streptococcal bacteraemias. *HPA Weekly Report* 2011; **46(2012/02):** 1–23.
16. Meier C, Centor RM, Graham L Jr, Dalton HP. Clinical and microbiological evidence for endemic pharyngitis among adults due to group C streptococci. *Arch Intern Med* 1990; **150(4):** 825–829.
17. Little PS, Gould C, Williamson I, *et al.* Reattendance and complications in a randomised trial of prescribing strategies for sore throat: the medicalising effect of prescribing antibiotics. *BMJ* 1997; **315(7104):** 350–352.
18. Centor RM, Witherspoon JM, Dalton HP, *et al.* The diagnosis of strep throat in the emergency room. *Med Decis Making* 1981; **1(3):** 239–246.
19. Breese BB. A simple scorecard for the tentative diagnosis of streptococcal pharyngitis. *Am J Dis Child* 1977; **131(5):** 514–517.
20. Dunn N, Lane D, Everitt H, Little P. Use of antibiotics for sore throat and incidence of quinsy. *Br J Gen Pract* 2007; **57(534):** 45–49.
21. Rogers M. A viable alternative to the glass/mercury thermometer. *Paed Nurs* 1992; **4(9):** 53–55.
22. The Standards Unit. Health Protection Agency. UK standards for microbiology investigations. *Investigation of throat swabs.* London: HPA, 2012. http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1317132856329 (accessed 16 Oct 2012).
23. The Standards Unit. Health Protection Agency. UK standards for microbiology investigations. *Identification of Streptococcus species, Entrococcus species and morphologically similar organisms.* London: HPA, 2012. http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1313155001427 (accessed 16 Oct 2012).
24. British Society for Antimicrobial Chemotherapy. BSAC *Methods for antimicrobial susceptibility testing.* Version 11.1 May 2012. http://bsac.org.uk/wp-content/uploads/2012/02/Version-11.1-2012-Final-.pdf (accessed 16 Oct 2012).
25. Dean L, Perry K. *Group A streptococcus rapid antigen detection kits - a review of the evaluation literature*, 04123 edn. London: DOH, 2005.
26. HMSO, OPCS. *Morbidity statistics from general practice: Fourth National study 1991.* 1 edn. London: HMSO, 1994.
27. Petersen I, Johnson A, Islam A, *et al.* Protective effect of antibiotics against serious complications of common respiratory tract infections: retrospective cohort study with the UK General Practice Research Database. *BMJ* 2007; **335(7627):** 982.
28. Little PS, Williamson I, Warner G, *et al.* An open randomised trial of prescribing strategies for sore throat. *BMJ* 1997; **314(7082):** 722–727.
29. McIsaac W, Goel V, To T, Low D. The validity of a sore throat score in family practice. *CMAJ* 2000; **163(7):** 811–815.
30. Zwart S, Sachs A, Ruijs G, *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(7228):** 150–154.
31. Snow V, Mottur-Pilson C, Cooper R, Hoffman J. Principles of appropriate antibiotic use for acute pharyngitis in adults. *Ann Intern Med* 2001; **134(6):** 506–508.

Appendix 1. Clinical variables in patients with group A, C or G beta-haemolytic streptococci compared with patients having no growth of C,G or A beta-haemolytic streptococci using more levels for variables.

		Patients with group A, C or G streptococci (%)	Patients with no group A, C or G streptococci (%)	Univariate OR	*P*-value	Multivariate OR[a]	*P*-value
Prior duration	≥5 days	32/180(18)	181/409 (44)	1.0		1.0	
	3–4 days	74/180 (41)	131/409 (32)	3.2 (2.0 to 5.1)	<0.001	2.0 (1.2 to 3.5)	0.010
	1–2 days	74/180 (41)	97/409 (24)	4.3 (2.7 to 7.0)	<0.001	3.6 (2.0 to 6.5)	<0.001
Glands	None	15/178 (8)	114/404 (28)	1.0		1.0	
	Small	58/178 (33)	125/404 (31)	3.5 (1.9 to 6.6)	<0.001	2.4 (1.2 to 5.0)	0.019
	Medium	93/178 (52)	145/404 (36)	4.9 (2.7 to 8.9)	<0.001	3.0 (1.5 to 6.1)	0.002
	Large	12/178 (7)	20/404 (5)	4.6 (1.9 to 11.2)	0.001	1.2 (0.4 to 3.6)	0.768
Tonsils inflamed	None	21/177 (12)	109/397 (27)	1.0		1.0	
	Slight	29/177 (16)	110/397 (28)	1.4 (0.7to 2.5)	0.322	1.2(0.6 to 2.4)	0.670
	Moderately bad	71/177 (40)	133/397 (34)	2.8 (1.6 to 4.8)	<0.001	1.5 (0.8 to 2.9)	0.187
	Severe	56/177 (32)	45/397 (11)	6.5 (3.5 to 11.9)	<0.001	3.3 (1.6 to 7.0)	0.002
Runny nose	Severe	4/180 (2)	17/409 (4)	1.0		1.0	
	Moderately bad	12/180 (7)	63/409 (15)	0.81 (0.2 to 2.8)	0.741	0.9 (0.2 to 3.9)	0.904
	Slight	34/180 (19)	106/409 (26)	1.4 (0.4 to 4.3)	0.599	1.1 (0.3 to 4.4)	0.853
	None	130/180 (72)	223/409 (55)	2.5 (0.8 to 7.5)	0.109	1.6 (0.4 to 5.8)	0.506
Age group	≥21 years	93/181 (51)	265/411 (64)	1.0		1.0	
	11–20 years	56/181 (31)	114/411 (28)	1.4 (0.9 to 2.1)	0.097	1.1(0.7 to 1.8)	0.741
	≤10 years	32/181 (18)	32/411 (8)	2.8 (1.7 to 4.9)	<0.001	2.4 (1.2 to 4.7)	0.015
Sore throat	Slight	6/181 (3)	51/409 (12)	1.0		1.0	
	Moderately bad	80/181 (44)	199/409 (49)	3.4 (1.4 to 8.3)	0.006	3.0 (1.1 to 8.5)	0.033
	Severe	95/181 (53)	159/409 (39)	5.1 (2.1 to 12.3)	<0.001	3.8 (1.3 to 10.9)	0.012
Cough	Severe	1/181 (1)	34/410 (8)	1.00		1.0	
	Moderately bad	21/181 (12)	108/410 (26)	6.6 (0.9 to 51)	0.070	3.7 (0.5 to 30)	0.225
	Slight	42/181 (23)	94/410 (23)	15 (2 to 115)	0.008	6.6 (0.8 to 53)	0.077
	None	117/181 (65)	174/410 (42)	23 (3 to 169)	0.002	8.6 (1.1 to 68)	0.041
Purulent tonsils		95/180(53)	126/409(31)	2.5(1.8 to 3.6)	<0.001	0.79 (0.5 to 1.3)	0.365
Fever (last 24 hours)	None	38/181 (21)	175/410 (43)	1.0		1.0	
	Slight	59/181 (33)	114/410 (28)	2.4 (1.5 to 3.8)	<0.001	1.7 (1.0 to 2.9)	0.073
	Moderately bad	63/181 (35)	88/410 (21)	3.3 (2.0 to 5.3)	<0.001	1.5 (0.8 to 2.7)	0.184
	Severe	21/181 (12)	33/410 (8)	2.9 (1.5 to 5.6)	0.001	1.0 (0.4 to 2.2)	0.946
Muscle aches	None	61/180 (34)	206/409 (50)	1.0		1.0	
	Slight	49/180 (27)	105/409 (26)	1.6 (1.0 to 2.5)	0.044	1.5 (0.9 to 2.5)	0.166
	Moderately bad	50/180 (28)	75/409 (18)	2.3 (1.4 to 3.6)	0.001	2.6 (1.5 to 4.6)	0.001
	Severe	20/180 (11)	23/409 (6)	2.9 (1.5 to 5.7)	0.001	3.7 (1.6 to 8.8)	0.002
Headache	None	46/181 (25)	166/409 (41)	1.0		1.0	
	Slight	55/181 (30)	127/409 (31)	1.6 (1.0 to 2.5)	0.054	1.2 (0.7 to 2.2)	0.484
	Moderately bad	59/181 (33)	85/409 (21)	2.5 (1.6 to 4.0)	<0.001	1.7 (0.9 to 3.2)	0.079
	Severe	21/181 (12)	31/409 (8)	2.4 (1.3 to 4.7)	0.006	1.3 (0.6 to 3.0)	0.538

[a]all multivariate estimates adjusted for prior duration, cervical glands, severity of sore throat, severity of inflammation, absence of cough, absence of coryza, muscle aches and fever. OR = odds ratio.