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Influence of the duration of penicillin prescriptions on outcomes for acute sore throat in adults:

the DESCARTE prospective cohort study in UK general practice

Abstract

Background
Guidelines recommend 10-day treatment courses for acute sore throat, but shorter courses may be used in practice.

Aim
To determine whether antibiotic duration predicts adverse outcome of acute sore throat in adults in routine care.

Design and setting
A secondary analysis of the DESCARTE (Decision rule for the Symptoms and Complications of Acute Red Throat in Everyday practice) prospective cohort study of 12 829 adults presenting in UK general practice with acute sore throat.

Method
A brief clinical proforma was used to collect symptom severity and examination findings at presentation. Outcomes were collected by notes review, a sample also completed a symptom diary. The primary outcome was re-consultation with new/non-resolving symptoms within 1 month. The secondary outcome was 'global' poorer symptom control (longer than the median duration or higher than median severity).

Results
Antibiotics were prescribed for 62% (7872/12 677) of participants. The most commonly prescribed antibiotic was phenoxymethylpenicillin (76%, 5656/7474) and prescription durations were largely for 5 (20%), 7 (57%), or 10 (22%) days. Compared with 5-day courses, those receiving longer courses were less likely to re-consult with new or non-resolving symptoms (5 days 15.3%, 7 days 13.9%, 10 days 12.2%, 7-day course adjusted risk ratio (RR) 0.92 [95% confidence interval [CI] = 0.76 to 1.11] and 10-days RR 0.86 [95% CI = 0.59 to 1.23]) but these differences did not reach statistical significance.

Conclusion
In adults prescribed antibiotics for sore throat, the authors cannot rule out a small advantage in terms of reduced re-consultation for a 10-day course of penicillin, but the effect is likely to be small.

Keywords
antibiotics, penicillin; cohort studies; drug prescribing; duration of prescribing; outcomes; sore throat; symptom control.

INTRODUCTION

Acute sore throat is a common illness in everyday primary care practice and most patients are still prescribed antibiotics.[1–3] Current UK guidelines recommend a 'no' or 'delayed' prescribing approach,[4] but when antibiotics are indicated then guidelines recommend 10 days of penicillin in order to reduce the risk of relapse.[5–8] This recommendation for long antibiotic courses first appeared in the 1950s, at a time when streptococcal complications were common and was based on observing the eradication of streptococci in asymptomatic carriers.[9–13] However, this evidence may not be directly applicable to modern care in more economically developed countries for a number of reasons: streptococcal disease has changed over time, studies were largely in children,[10–13] used low doses of penicillin,[10] were restricted to those with proven streptococcal infection,[10,11] used stringent assessments of compliance,[12] and used bacteriological rather than clinical cure.[10,11] Only one study found a significant increase in recurrent symptoms after a shorter antibiotic course.[12] In a study in adults comparing placebo with 3 and 7 days of antibiotic treatment, 7 days gave superior symptom control and bacteriological eradication rates. Recurrent sore throats were most frequent in the 3-day group, but there was no difference in re-attendance rates between the groups.[14] A Cochrane Review of longer penicillin courses versus short courses of other antibiotic classes in children found superior symptomatic benefit with short courses with comparable other outcomes.[15] There are potential harms arising from greater exposure to courses of penicillin, which is linked to subsequent carriage of resistant pneumococci[16] and carriage of resistant commensal organisms.[17] Not all guidelines recommend such prolonged treatment. The Dutch guidelines recommend 7-day treatment and no longer recommends 10 days for eradication of bacteria.[18] So if shorter courses lead to effective symptom relief without an increase in recurrence it should be possible to significantly reduce the volume of antibiotics prescribed.

Systematic reviews and randomised trials of antibiotics for acute sore throat have

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How this fits in

Antibiotics are not usually indicated for acute sore throat. When streptococcal infection is probable, or the risk of complications high, antibiotics are indicated and a 10-day course is usually recommended. The authors found evidence that a shorter duration of antibiotic prescription (5 days) is associated with similar symptomatic outcomes, and without increased risk of re-consultation, when compared with longer courses of antibiotics. A randomised controlled trial is required to confirm these findings, then exposure to antibiotics could potentially be reduced.

found only a modest effect on symptoms.[19] However, prescribing antibiotics may still be indicated in some instances.[19] It is important not to deny the benefit of antibiotics to patients at significant risk of severe illness or complications. Evidence about appropriate duration of the antibiotic treatment for acute sore throat in adults in the modern era is needed.

The authors therefore aimed to describe current antibiotic prescribing for sore throat in UK practice and to investigate whether duration of treatment or class of antibiotic was associated with adverse symptomatic outcome or increased re-consultation during the subsequent month. The authors used a large observational cohort that had been recruited to investigate potential prediction of septic complications of acute sore throat.[20]

METHOD

Overall study design

As previously reported, the DESCARTE (Decision rule for the Symptoms and Complications of Acute Red Throat in Everyday practice) study was a large prospective cohort of patients presenting with acute sore throat in routine primary care in the UK (N = 14 610),[20,21] a simple one-page paper and/or web-based case report form (CRF) was used to document clinical features at presentation.[21] The study included two nested consecutive diagnostic cohorts (n = 1107) to develop and validate a clinical score to predict bacterial infection,[22] and a randomised trial (n = 1781) that compared the use of the clinical score and the targeted use of a rapid antigen detection test with delayed antibiotic prescribing.[23] Trial participants were not included in the present analysis because their treatment had been allocated according to the trial protocol. Analysis was therefore in the 12 677/12 829 participants not in the clinical trial and in whom antibiotic status was recorded.[21] Initial recruitment was among six local networks (based in Southampton, Bristol, Birmingham, Oxford, Cardiff, and Exeter) but was extended nationally during the last 18 months of recruitment.

Patient inclusion criteria

Inclusion criteria was defined as previously well individuals aged ≥16 years, presenting with acute (≤14 days) sore throat as the main symptom, with an abnormal examination of the pharynx (identical criteria to the authors' previous studies).[24,25] Exclusion criteria were severe mental health problems (for example, cognitive impairment and unable to consent or assess history) and known immune suppression.

Baseline clinical proforma

Age, sex, current smoking status, prior duration of illness, and the presence and severity of baseline symptoms (sore throat, difficulty swallowing, fever during the illness, runny nose, cough, feeling unwell, diarrhoea, vomiting, abdominal pain, headache, muscle ache, sleep disturbance, earache) were documented on the CRF. Symptoms were recorded using 4-point Likert scales (none, a slight problem, a moderately bad problem, a severe problem), and the presence of signs (pus, nodes, cervical nodes, temperature, fetor, palatal oedema, difficulty speaking due to sore throat). The recruiting physician recorded antibiotic type and duration in the CRF.

Illness progression and/or non-resolution Progression and/or non resolution of illness

This was defined as re-consultation with non-resolving symptoms or development of a new respiratory diagnosis/symptom/sign within a month of the index presentation; similar to outcomes used previously in a trial of antibiotics for lower respiratory infection in adults[26] and in a cohort of children, and ascertained using notes review.[27] This outcome was collected retrospectively by practice staff or research staff who were not blinded to the treatment used. Since the outcome was derived from notes review it is available for the whole cohort not just those with diaries.

Documentation of symptomatic outcome

A symptom diary was randomly allocated to a proportion of those recruited to the study to achieve the pre-specified target of 1800 diaries. The diary was similar to that used in other studies.[24,25] Patients completed the

Table 1. Baseline characteristics by duration of antibiotic prescription in the whole cohort

	Duration of antibiotic prescription		
	5 days	7 days	10 days
Baseline clinical assessment			
Severity of sore throat/ difficulty swallowing on a 4-point Likert scale, mean (SD)	3.27 (0.65)	3.26 (0.67)	3.18 (0.63)
Severity of all baseline symptoms on a 4-point Likert scale, mean (SD)	2.18 (0.40)	2.15 (0.40)	2.12 (0.41)
FeverPAIN score,[a] mean (SD)	1.72 (1.30)	1.94 (1.32)	2.36 (1.18)
Centor score,[b] mean (SD)	1.85 (1.09)	2.06 (1.10)	2.33 (1.01)
Prior duration in days, mean (SD)	4.61 (3.57)	4.68 (4.22)	4.11 (3.36)
Age in years, mean (SD)	33.16 (14.05)	33.88 (14.21)	32.35 (13.75)
Female sex, *n*/*N* (%)	984/1466 (67.1)	2832/4187 (67.6)	1102/1632 (67.5)
Smoker, *n*/*N* (%)	356/1464 (24.3)	966/4168 (23.2)	285/1621 (17.6)
Fever in last 24 hours, *n*/*N* (%)	962/1458 (66.0)	2816/4171 (67.5)	1152/1630 (70.7)
Temperature °C, mean (SD)	36.86 (0.72)	36.93 (0.72)	36.99 (0.68)
Pus on tonsils, *n*/*N* (%)	648/1460 (44.4)	2131/4170 (51.1)	1050/1627 (64.5)
Severely inflamed tonsils, *n*/*N* (%)	209/1371 (15.2)	816/3945 (20.7)	325/1546 (21.0)
Prior medical problems, *n* (%)	0.27 (0.52)	0.25 (0.52)	0.23 (0.49)
Return within 4 weeks with new or worsening symptoms, *n*/*N* (%)	222/1449 (15.3)	577/4135 (13.9)	198/1620 (12.2)
Return within 4 weeks with complications, *n*/*N* (%)	13/1449 (0.9)	55/4135 (1.3)	22/1620 (1.3)

[a]FeverPAIN score comprises fever in the past 24 hours, purulence, rapid attendance (within 3 days), inflamed tonsils, and no cough or cold symptoms. [b]Centor score comprises a history of fever, pus on tonsils, enlarged glands, and absence of cough. SD = standard deviation.

diary each night until symptoms resolved, or up to 14 nights. Each symptom — sore throat, difficulty swallowing, feeling unwell, fevers, sleep disturbance — was scored (0 = no problem, to 6 = as bad as it could be). Symptomatic outcomes were only available for those returning diaries.

Sample size

Sample size calculations for the main study were based on the prediction of complications, a rare outcome. For the proposed analysis of diary data, a sample of 1800 patients allowing for 20% loss to follow-up of diaries (900 of whom would not be expected to have antibiotics), would have power to detect variables with prevalences of 20% to 80% with an odds ratio of 2 for adverse symptomatic outcome among the no antibiotic group. Adverse symptomatic outcome was defined as severe symptoms or prolonged symptoms.

Outcomes

The primary outcome was re-consultation, with progression or non-resolution of illness within 1 month of the index consultation. Secondary outcomes were only determined in those with diary data; worse symptomatic outcomes (above median for either duration or severity of illness); duration of moderately bad symptoms; and symptom severity on day 2–4.). All outcomes were reported in relation to prescribed antibiotic duration.

Analysis

All analyses were based on reported treatment at the index consultation. The subgroup analyses reported in this paper were specified in advance. Duration of symptoms was analysed using Cox regression. Linear regression was used for symptom severity, and a generalised linear regression model with a log link for re-consultation and adverse symptomatic outcome. The authors have reported both the univariate statistics and the relationships after controlling for the severity of all baseline symptoms, antibiotic type (immediate or delayed), and clustering of patients by practice. To control for potential confounding by indication, the authors calculated a propensity score based on predictors of antibiotic prescribing. The propensity score was calculated based on variables that were significant predictors ($P<0.05$) of antibiotic prescribing strategy (5 days/7 days/10 days) in a multinomial logit model (mlogit in Stata), and was then included as an additional covariate in the prior models. This method was chosen in preference to propensity score matching, because the outcome measure is categorical and therefore the analysis is more complex than for binary logistic models, where propensity score matching might make sense.[28] The predicted probability from this model was then used as the propensity score in the analysis of the relationship between prescribing strategy and the study outcome measures. In order to explore whether those with higher probability of streptococcal infection experienced differential benefit from antibiotics, the authors used the Centor score and the FeverPAIN score. The Centor score, derived from hospital outpatients, is used to predict the probability of streptococcal infection, has been shown to be related to response to antibiotics, and is widely used internationally.[29,30] The FeverPAIN score may also be used to predict the probability of streptococcal infection (A, C, and G) in community samples, and has been shown to be highly predictive of time-to-symptom-resolution and symptom severity.[22] The FeverPAIN score is estimated using fever in the past 24 hours, purulence, rapid attendance (within 3 days), inflamed

Table 2. Re-consultation with new or worsening symptoms in the month following the index consultation, according to duration of antibiotic prescribed and antibiotic class[a]

	Reported new or worsening symptoms, *n* (%)	Univariate risk ratio (95% CI, *P*-value)	Risk ratio controlling for baseline severity and clustering (95% CI, *P*-value)	Risk ratio controlling for propensity score (95% CI), *P*-value	Risk ratio controlling for propensity score in the imputed dataset (95% CI), *P*-value
Duration of antibiotic prescription					
5 days (reference category)	222/1449 (15.3)	1.00	1.00	1.00	1.00
7 days	577/4135 (13.9)	0.91 (0.75 to 1.05) *P* = 0.201	0.93 (0.78 to 1.08) *P* = 0.321	0.92 (0.76 to 1.11) *P* = 0.377	0.92 (0.76 to 1.10) *P* = 0.360
10 days	198/1620 (12.2)	0.80 (0.67 to 0.95) *P* = 0.013	0.81 (0.55 to 1.19) *P* = 0.287	0.86 (0.59 to 1.23) *P* = 0.408	0.85 (0.59 to 1.23) *P* = 0.395
Antibiotic class					
Phenoxymethylpenicillin (reference category)	725/5624 (12.9)	1.00	1.00	1.00	1.00
Other antibiotics	302/1847 (16.3)	1.27 (1.12 to 1.44) *P*<0.001	1.28 (1.11 to 1.47) *P* = 0.001	1.27 (1.11 to 1.49) *P* = 0.002	1.26 (1.09 to 1.45) *P* = 0.001

[a]*All models controlled for immediate or delayed prescribing and clustering of patients by practice.*

tonsils, and no cough or cold symptoms. The authors tested for an interaction between Centor/FeverPAIN and symptom severity. The authors also used the Centor/FeverPAIN score to dichotomise the sample into those more or less likely to have a streptococcal infection, with a cut-off point of ≥3 for Centor, which is widely used to direct antibiotic prescribing and for FeverPAIN 0–2 versus ≥3. For Centor, the probability of a streptococcus swab positive result is 15% for those with a score of 2, and 32% for those with a score of ≥3.[29] For FeverPAIN, the risk of a positive streptococcal swab is 26% for those with a score of 0, 1, or 2 and 60% for those with a score of ≥3.[22] Results are presented both for complete cases and for models, with significant predictors of the propensity score imputed using a chained equations multiple imputation model. Outcome measures were not imputed as it was not possible to distinguish between individuals who were missing data because they did not complete a diary when asked, and those who were not asked to complete one. Analyses were carried out in Stata version 12.1.

RESULTS

A total of 14 610 adult patients were recruited between 10 November 2006 and 1 June 2009, from 616 general practices. In all, 1629/2876 (57%) of those requested returned the symptom diary. There were no substantial differences in baseline characteristics between those returning the symptom diary and the main sample.[31] The inter-rater reliability for assessing return with non-resolution of symptoms was good (κ 0.84).[21] Those receiving shorter courses of antibiotics were less likely to have a history of fever in the past 24 hours and less likely to have severely inflamed tonsils or pus on the tonsils (Table 1), and hence a lower Centor and FeverPAIN score. Those receiving antibiotics other than penicillin also had less severe symptoms (Appendix 1). Those given immediate antibiotics had more severe symptoms at baseline and were more likely to have a history of fever and severe inflammation or pus on tonsils.[31]

Immediate antibiotics were prescribed for 6088/12 677 (48%), and delayed antibiotics for 1784/12 677 (14%). The most commonly prescribed antibiotic was phenoxymethylpenicillin (76%, 5656/7474), and the majority of these prescriptions were for three durations: 5 (20%), 7 (57%), or 10 (22%) days. The proportions of antibiotic class and duration in those returning a diary were not different from the main sample (Appendix 2). From the diary data of those reporting taking the antibiotics (*n* = 956), those prescribed a course of 10 days reported taking antibiotics for 9.33 days (standard deviation [SD] 1.73), those prescribed a course of 7 days

Table 3. Adverse symptomatic outcome (greater than median symptom severity in days 2–4, or greater than median duration of symptoms) according to duration of antibiotic prescribed and antibiotic class

	Poor symptomatic outcome, *n* (%)	Univariate risk ratio (95% CI, *P*-value)	Risk ratio controlling for baseline severity, antibiotic type (immediate or delayed), and clustering (95% CI, *P*-value)[a]	Risk ratio controlling for propensity score (95% CI, *P*-value)	Risk ratio controlling for propensity score in imputed dataset (95% CI, *P*-value)
Duration of antibiotic prescription					
5 days (reference category)	105/185 (56.8)	1.00	1.00	1.00	–
7 days	312/535 (58.3)	1.03 (0.89 to 1.19) *P* = 0.713	1.03 (0.89 to 1.20) *P* = 0.685	1.06 (0.91 to 1.23) *P* = 0.443	1.06 (0.91 to 1.23) *P* = 0.462
10 days	108/168 (64.3)	1.13 (0.96 to 1.34) *P* = 0.148	1.13 (0.95 to 1.35) *P* = 0.162	1.22 (1.02 to 1.46) *P* = 0.026	1.22 (1.02 to 1.46) *P* = 0.026
Antibiotic class					
Phenoxymethylpenicillin (reference category)	419/714 (58.7)	1.00	1.00	1.00	1.00
Other antibiotics	125/206 (60.7)	1.03 (0.91 to 1.17) *P* = 0.603	1.04 (0.91 to 1.18) *P* = 0.547	0.98 (0.84 to 1.12) *P* = 0.807	0.94 (0.68 to 1.32) *P* = 0.733

[a] *For duration, the model also controls for whether the antibiotics prescribed were immediate or delayed.*

reported taking antibiotics for 7.01 days (SD 2.14), and those prescribed a course of 5 days reported taking them for 5.75 days (SD 2.04).

When adjusting for propensity to prescribe antibiotics, those prescribed longer courses of antibiotics re-consulted less often during the month following the index consultation, compared with those prescribed a 5-day prescription. However, this difference was not statistically significant (7 days: risk ratio [RR] 0.92, 95% confidence interval [CI] = 0.76 to 1.11, *P* = 0.377; 10 days RR 0.86, 95% CI = 0.59 to 1.23, *P* = 0.408). Similar results were observed when adjusting for baseline severity and controlling for clustering of patients by practice (Table 2). Antibiotics other than penicillin were associated with a significantly greater risk of re-consultation (Table 2).

When controlling for propensity to prescribe or baseline severity and using 5-day prescription as comparator (Table 3), outcomes were similar in those prescribed 7 days of antibiotics. In those prescribed antibiotics for 10 days, adverse symptomatic outcomes were similar when controlling for baseline differences (RR 1.13, 95% CI = 0.95 to 1.35, *P* = 0.162), but were slightly worse when adjusting for propensity to prescribe (RR 1.22, 95% CI = 1.02 to 1.46, *P* = 0.026). Those prescribed phenoxymethylpenicillin experienced similar symptomatic outcomes compared with those receiving antibiotics other than penicillin (Table 3).

When tested independently, neither the severity of symptoms on day 2–4, nor the duration of moderately bad symptoms, was related to duration of prescription issued nor the class of antibiotic prescribed (Figure 1, Tables 4 and 5).

With the exception of the mean symptom severity score, there was no evidence of an interaction between FeverPAIN score and outcomes related to the duration of antibiotic prescription. There was no evidence of any interaction between FeverPAIN score and outcomes related to antibiotic type (further data available from authors on request). There was no evidence of any interaction between Centor score and outcomes related to the duration of antibiotic prescription, or on outcomes related to antibiotic type (further data available from authors on request).

DISCUSSION

Summary

This large observational cohort of patients enabled the authors to explore the effect of prescribing antibiotics in routine practice on re-consultation and symptom resolution. Although a 7-day course is most often prescribed, 5- and 10-day courses each accounted for approximately one-fifth of prescriptions. Compared with a 5-day course, those prescribed a 10-day course appeared to have slightly worse global

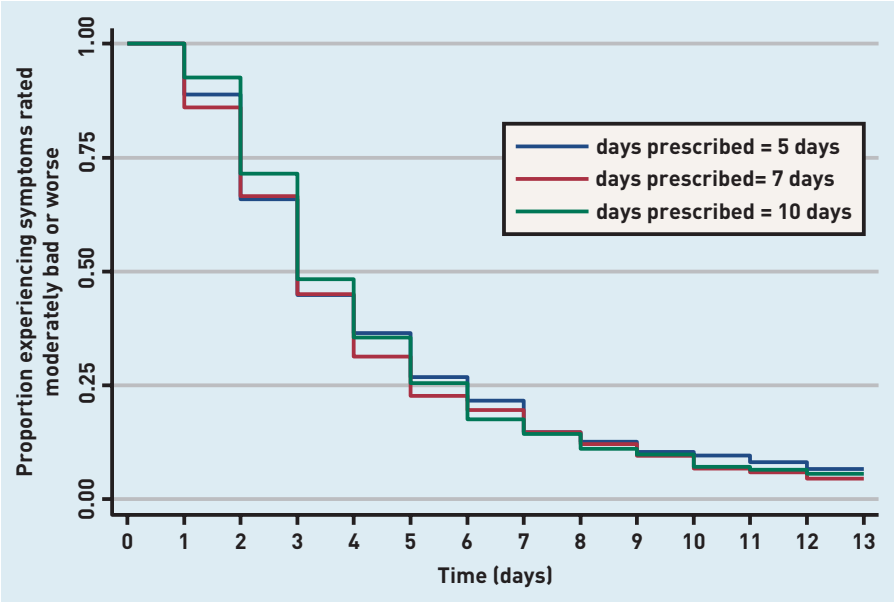

Figure 1. Proportion experiencing symptoms rated moderately bad or worse, according to duration of prescribed antibiotics.

symptomatic outcome (longer than the median duration or higher than median severity) after adjustment for propensity to prescribe. The re-consultation rate was higher with shorter courses, but this difference did not reach statistical significance. Current guidelines recommending penicillin treatment for 10 days are not supported by these findings where the purpose is to provide symptom relief rather than bacterial eradication.

There is no evidence that phenoxymethylpenicillin is inferior to other antibiotic classes for symptom control, and, given low rates of penicillin non-susceptibility of typical bacterial pathogens, it should be the first-choice antibiotic. The implications for symptomatic benefit and re-consultation are similar for those predicted to be more or less likely to have a streptococcal throat infection using symptom scores.

Strengths and limitations

The study was designed using a simple template to minimise selection bias and thus to produce a large generalisable prospective cohort. Recruitment of patients with acute illness is constrained by time issues and, in common with other studies of acute infection,[32–34] documentation of those not approached was poor (because time pressure to recruit also meant time pressure to document non-recruitment). The large sample prospectively recruited in routine practice with the inclusion of diary data enabled the study of different antibiotic classes and duration of prescription both on re-consultation and on symptomatic outcomes, which is likely to reflect the real-life experience of patients. As previously reported[31] there is evidence of a greater propensity to prescribe for those with more severe symptoms at baseline, and a longer duration of antibiotics was also more likely in those with more severe symptoms. The authors have adjusted for propensity to prescribe and for baseline severity of symptoms in this analysis but cannot rule out residual confounding. Those who completed and returned the symptom diary may represent a more adherent population more generally, so estimates of medication adherence may be inflated compared with the general population. The assessors of re-consultation were not blinded to the treatment allocation, which

Table 4. Symptom severity on day 2–4, according to duration of antibiotic prescribed and antibiotic class

	Symptom severity, mean (SD)	Difference (95% CI), *P*-value	Difference controlling for clustering, and antibiotic type and baseline severity score (95% CI), *P*-value	Difference controlling for propensity score, (95% CI), *P*-value	Difference controlling for propensity score in the imputed dataset (95% CI), *P*-value
Duration of antibiotic prescription					
5 days (reference category)	2.00 (1.22)	–	–	–	–
7 days	1.99 (1.21)	–0.01 (–0.22 to 0.19, *P*= 0.896)	0.01 (–0.18 to 0.19, *P*= 0.935)	0.06 (–0.13 to 0.25, *P*= 0.520)	0.05 (–0.14 to 0.24, *P*= 0.587)
10 days	2.10 (1.20)	0.10 (–0.15 to 0.35, *P*= 0.426)	0.13 (–0.14 to 0.41, *P*= 0.330)	0.21 (–0.06 to 0.48, *P*= 0.119)	0.20 (–0.06 to 0.48, *P*= 0.130)
Antibiotic class					
Phenoxymethylpenicillin (reference category)	2.01 (1.22)	–	–	–	–
Other antibiotics	2.02 (1.15)	0.01 (–0.17 to 0.20, *P*= 0.897)	0.02 (–0.17 to 0.21, *P*= 0.826)	0.00 (–0.20 to 0.19, *P*= 0.965)	–0.02 (–0.21 to 0.16, *P*= 0.796)

SD = standard deviation.

Table 5. Duration of moderately bad symptoms, according to duration of antibiotic prescribed and antibiotic class

	Duration of moderately bad symptoms, median days (IQR)	Univariate risk ratio, (95% CI, *P*-value)	Hazard ratio controlling for clustering, antibiotic (immediate or type (delayed), and baseline severity score (95% CI, *P*-value)	Hazard ratio controlling for propensity score, (95% CI, *P*-value)	Hazard ratio controlling for propensity score in imputed dataset, (95% CI, *P*-value)
Duration of antibiotic prescription					
5 days (reference category)	3 (2–5)	1.00	1.00	1.00	1.00
7 days	3 (2–5)	1.06 (0.89 to 1.27) *P* = 0.527	1.05 (0.91 to 1.23) *P* = 0.488	1.05 (0.90 to 1.23) *P* = 0·513	1.07 (0.91 to 1.25) *P* = 0.418
10 days	3 (2–5)	0.99 (0.79 to 1.24) *P* = 0.957	0.99 (0.83 to 1.20) *P* = 0.963)	0.92 (0.74 to 1.14) *P* = 0.432	0.92 (0.73 to 1.15) *P* = 0.460
Antibiotic class					
Phenoxymethylpenicillin (reference category)	3 (2–5)	1.00	1.00	1.00	1.00
Other antibiotics	3 (2–5)	0.94 (0.80 to 1.10) *P* = 0.435	0.94 (0.82 to 1.07) *P* = 0.350	1.03 (0.88 to 1.21) *P* = 0.698	1.04 (0.89 to 1.21) *P* = 0.631

IQR = interquartile range.

would have been available in the clinical record, because the primary aim of the cohort was to assess risk factors for septic complications. The authors think it unlikely this would introduce any bias in recording of re-consultation. The reported duration of antibiotic consumption in those prescribed 5 days appears longer than that dispensed, but this is an artefact as, each day, antibiotics taken were included and hence the average reflects the final doses being taken on day 6. Those prescribed antibiotics other than penicillin experienced similar symptomatic outcomes, but were at greater risk of re-consultation. This may reflect factors not controlled for in the analysis, which determined the antibiotic choice. In recent years, *Fusobacterium necrophorum* has emerged as a relevant pathogen in recurrent and severe sore throat.[35] Although it may be isolated from 10% of community samples,[36] and may be rarely associated with severe infection, its precise contribution to acute uncomplicated sore throat illness is hard to ascertain. The analysis adjusted for propensity to prescribe, and the negative interaction terms for Centor and FeverPAIN suggest that the adjustment took account of streptococcal infection (that there was no evidence of differential outcomes in those more likely to have streptococcal infection after adjustment). However, these scores will not account for *Fusobacterium necrophorum* and hence the authors cannot rule out residual confounding. This may account for the small difference in re-attendance (5 days 15.3%, 10 days 12.2%). It is of note, however, that the use of broad spectrum antibiotics was not associated with improved outcomes. Although the results fail to show superiority of longer courses of penicillin for symptom relief or re-consultation, this is not the same as equivalence and may reflect a lack of power.

Comparison with existing literature

The most commonly prescribed antibiotic was phenoxymethylpenicillin but there was variation in the duration of the prescription, with the majority receiving 7 days (52%) — an observation that is at odds with the recommendations of current guidelines.[5] Although prescribing rates are similar, broad spectrum antibiotic prescribing is higher in the US (86% antibiotics other than penicillin or erythromycin).[37] The prescription of 5- or 7-day duration antibiotics did not appear to confer any significant increase in re-consultation in the month following the index consultation, nor any worse symptomatic outcomes. A systematic review of studies in children found no difference in clinical outcomes

after shorter courses of antibiotics, but the comparison groups were 10 days of penicillin compared with shorter courses of other antibiotic classes,[15] and so are not directly comparable. There is a paucity of trial data in adults, but one trial identified showed superiority of 7- over 3-days treatment with penicillin.[14]

The authors examined the effect of antibiotics other than penicillin and did not find convincing evidence of differential symptomatic outcome. Non-penicillin antibiotics were associated with higher re-consultation rates. In a Cochrane Review of antibiotic type in acute sore throat, no differences in symptom resolution were observed, but clinical relapse was less likely following cephalosporin treatment.[38]

Implications for practice

When antibiotics are indicated, current guidelines recommend a 10-day course. The authors found that a 10-day course of antibiotics was not associated with greater benefit on either risk of re-consultation or symptom control, compared with 5- or 7-days antibiotic duration. In situations where bacterial eradication is not specifically needed, and where symptomatic cure is the goal, if a decision to prescribe is made then a shorter course of penicillin may be sufficient, and this finding should be confirmed with a randomised controlled trial. These findings should not be generalised to areas with a higher incidence of acute rheumatic fever.

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Provenance

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Competing interests

The authors have declared no competing interests.

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Appendix 1. Baseline characteristics by antibiotic type

	Total cohort (*N* = 7872) [a]	
	Phenoxymethylpenicillin *n* = 5696	**Other *n* = 1857**
Clinical assessment		
Severity of sore throat/difficulty swallowing on a 4-point Likert scale, mean (SD)	3.28 (0.64)	3.13 (0.70)
Severity of all baseline symptoms on a 4-point Likert scale, mean (SD)	2.15 (0.40)	2.14 (0.40)
FeverPAIN score, mean (SD)	2.12 (1.28)	1.57 (1.28)
Centor Score, mean (SD)	2.45 (0.97)	1.97 (1.05)
Prior duration in days, mean (SD)	4.36 (3.60)	514 (4.94)
Age in years, mean (SD)	32.25 (13.60)	3701 (14.95)
Female, *n*/*N* (%)	3835/5696 (67.3)	1265/1857 (68.1)
Smoker, *n*/*N* (%)	1296/5663 (22.9)	384/1850 (20.8)
Fever in last 24 hours, *n*/*N* (%)	3897/5672 (68.7)	1213/1841 (65.9)
Temperature ºC, mean (SD)	36.95 (0.71)	36.87 (0.73)
Pus on tonsils, *n*/*N* (%)	3225/5668 (56.9)	718/1841 (39.0)
Severely inflamed tonsils (%)	1153/5338 (21.6)	234/1736 (13.5)
Prior medical problems, *n* (SD)	0.23 (0.49)	0.31 (0.59)
Return within 4 weeks with new or worsening symptoms, *n*/*N* (%)	725/5624 (12.9)	302/1847 (16.3)
Return within 4 weeks with complications, *n*/*N* (%)	65/5624 (1.2)	28/1847 (1.5)

SD = standard deviation. [a]There were 7872 prescriptions but in 319 it is not know what was prescribed n=*7553.*

Appendix 2. Type and duration of antibiotics issued: comparison of those completing symptom diary with full cohort

	Total cohort[a] *N* = 7474		Patients who completed diaries *N* = 922[b]	
	Given antibiotics (%)	Delayed antibiotics (%)	Given antibiotics (%)	Delayed antibiotics (%)
Antibiotic type				
Phenoxymethylpenicillin	4354/5793 (75.2)	1302/1681 (77.4)	552/725 (76.1)	163/197 (82.7)
Amoxicillin	601/5793 (10.4)	165/1681 (9.8)	78/725 (10.8)	17/197 (8.6)
Erythromycin	542/5793 (9.4)	171/1681 (10.2)	56/725 (7.7)	11/197 (5.6)
Other[c]	296/5793 (5.1)	43/1681 (2.6)	39/725 (5.4)	6/197 (3.0)
Duration of course				
5 days	1125/5651 (19.9)	327/1631 (20.0)	147/709 (20.7)	36/191 (18.8)
7 days	3222/5651 (57.0)	919/1631 (56.3)	427/709 (60.2)	109/191 (57.1)
10 days	1249/5651 (22.1)	371/1631 (22.7)	127/709 (17.9)	42/191 (22.0)
Other duration	56/5651 (1.0)	14/1631 (0.9)	8/709 (1.1)	4/191 (2.1)
Took antibiotics[d]			670/692 (96.8)	115/191 (60.2)
Mean number of days for which antibiotics were taken (SD)			7.07 (2.22)	7.12 (2.92)

*[a] There were 7872 prescriptions but in 319 it is not know what was prescribed and in an additional 79 participants no information is available on whether immediate or delayed (n= 7872 minus 319 minus 79 = 7474). [b] 922/1512 completed diaries and were also prescribed antibiotics. [c] Included cephalexin (*n *= 191), co-amoxiclav (*n *= 40), clarithromycin (*n *= 38), and doxycycline (*n *= 22). [d] There were an additional 105 people out of 554 (18.8%) who were not prescribed antibiotics who reported taking them. SD = standard deviation.*