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# Delayed antibiotic prescription by general practitioners in the UK: a stated-choice study

4 Short title: Delayed prescription by UK general practitioners

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## ABSTRACT

Delayed antibiotic prescription in primary care has been shown to reduce antibiotic consumption, without increasing risk of complications, yet is not widely used in the UK. We sought to quantify the relative importance of factors affecting the decision to give a delayed prescription, using a stated-choice survey among UK general practitioners. Respondents were asked whether they would provide a delayed or immediate prescription in fifteen hypothetical consultations, described by eight attributes. They were also asked if they would prefer not to prescribe antibiotics. The most important determinants of choice between immediate and delayed prescription were symptoms, duration of illness, and the presence of multiple comorbidities. Respondents were more likely to choose a delayed prescription if the patient preferred not to have antibiotics, but consultation length had little effect. When given the option, respondents chose not to prescribe antibiotics in 51% of cases, with delayed prescription chosen in 21%. Clinical features remained important. Patient preference did not affect the decision to give no antibiotics. We suggest that broader dissemination of the clinical evidence supporting use of delayed prescription for specific presentations may help increase appropriate use. Establishing patient preferences regarding antibiotics may help to overcome concerns about patient acceptance. Increasing consultation length appears unlikely to affect use of delayed prescription.

**Keywords:** antibiotic resistance, choice experiment, primary care, general practice, delayed prescription, respiratory tract infection, stewardship, UK

## 1. Introduction

Reducing unnecessary antibiotic consumption is essential to reduce selection pressure on bacteria to develop resistance, and preserve the effectiveness of existing antibiotics [1,2]. In the UK, over 70% of antibiotics are prescribed in primary care [3], with 32 million antibiotic prescriptions dispensed in England in 2019 [4]. Much of this prescribing may be avoidable [5]. Many conditions treated in primary care, such as a substantial proportion of respiratory tract infections, are self-limiting and will resolve without antibiotics [5,6].

Amongst the strategies aimed at reducing antibiotic consumption, one option in primary care is delayed (or 'back-up') prescriptions. With this approach, a prescription is issued, but the patient is advised to wait, and only collect and begin taking the antibiotics if their symptoms worsen or do not resolve within a specified time period. This strategy can be used where the prescriber believes that antibiotics are not needed at the time, but has some clinical uncertainty as to whether the condition could deteriorate without antibiotics [7]. The delayed prescription approach has been shown in randomised trials in primary care to be effective in reducing consumption with little effect on symptom control or risk of complications, in respiratory tract infections [8-11], conjunctivitis [12] and urinary tract infections [13]. In the UK, the National Institute for Health and Care Excellence (NICE) has included the use of delayed prescriptions in its guidelines and Clinical Knowledge Summaries since 2008 [14-18]. The approach has the potential to provide reassurance to both prescribers [19] and patients [20]; it provides easier access to antibiotics should they be needed, but unnecessary consumption may be avoided if the illness follows its expected course. However, despite the supporting evidence, use of delayed prescriptions has been limited, with studies showing that only around 14% of prescriptions for common infections are delayed prescriptions [21,22]. To support more widespread implementation of this strategy for antimicrobial stewardship (in line with NICE guidelines), it is important to understand the barriers to using delayed prescriptions.

Studies to date on primary care physicians' attitudes to delayed prescription have been predominantly qualitative. These studies highlighted concerns over delayed prescriptions giving a potentially ambiguous message to patients, abdication of clinical responsibility, and time taken in the consultation to explain a delayed prescription to the patient [19,23-26]. Our study aimed to develop this evidence base further by providing quantitative information on

86 　the relative importance of factors in the decision to use a delayed prescription as an alternative

87 　to an immediate prescription, with a focus on factors relating to the patient and the

88 　information discussed during the consultation.

89 　Our study setting is primary care in the UK's National Health Service (NHS), where

90 　physicians (known as general practitioners (GPs)) make the majority of antibiotic prescribing

91 　decisions. We focus on respiratory tract infections (RTI), which are among the most common

92 　reasons for GP consultations [14,27], and account for a high proportion of antibiotic prescribing

93 　in primary care [28,29]. A recent analysis indicated that in the years 2013-2015, at least 32% of

94 　primary care antibiotic prescriptions were for RTIs (including ear, nose and throat conditions)

95 　[28]; this represents over 11 million prescriptions in England at the 2018 prescribing level of

96 　625 antibiotic prescriptions per 1000 patients [3]. In particular, we focus on cough and sore

97 　throat symptoms, for which much of the antibiotic prescribing is likely to be unnecessary

98 　[5,30,31]. There is therefore significant potential to reduce prescribing safely in this condition

99 　via broader use of delayed prescriptions where clinically appropriate.

100 　We conducted a stated-choice study, a survey method widely used in health research [32-34].

101 　The method asks respondents to make choices between alternative healthcare options, which

102 　are designed to require trade-offs between the attributes of these options. Our study presented

103 　a sample of UK GPs with fifteen hypothetical consulting scenarios they might encounter when

104 　a patient presents with an RTI, and asked them to choose whether they would give the patient

105 　an immediate or delayed prescription. In each case, respondents were also asked if they would

106 　prefer to give no antibiotic prescription. The scenarios consisted of eight attributes that

107 　described the presenting condition, the patient, and the consultation (Table 1). Respondent

108 　choices were analysed using logistic regression, to determine the relative influence of the

109 　attributes on the prescribing decision.

110

Table 1. Attributes and levels for the choice questions

| Attribute[a] | Levels | Basis |
|---|---|---|
| Symptoms the patient is experiencing [b] | 1: Sore and red throat, and swollen lymph nodes in the neck<br>2: Productive cough and runny nose<br>3: Sore throat, swollen lymph nodes in the neck, pyrexia and purulent tonsils<br>4: Productive cough, pyrexia and pain on breathing | Two upper respiratory tract symptoms, and two lower, to allow exploration of differences in perception of 'throat' and 'chest' infections. Clinical guidelines [14,15], diagnostic criteria (such as FeverPAIN [35]) and practising clinicians were consulted to identify two plausible levels of severity for each, identified as 'minor' (1 and 2) and 'serious' (3 and 4) throughout this paper. |
| How long the person has had the symptoms when they see the primary care physician | 3 days<br>7 days<br>10 days | Durations identified from literature [8], to cover a wide yet realistic range for RTIs. |
| Relevant comorbidities of the patient [b] | 1. None<br>2. One<br>3. Two or more | Reflects clinical guideline CG69 [14], which identifies comorbidities as a risk factor for developing complications, and particularly for acute cough, increasing risk with additional comorbidities or other patient factors. |
| Length of the consultation with the primary care physician | 5 minutes<br>10 minutes<br>15 minutes | Proxy for quality of information exchange between primary care physician and patient. Levels represent plausible consultation durations; the longest consultation is intended to allow for use of tools such as TARGET patient leaflets [36] to explain treatment. |
| Patient opinion on taking antibiotics [b] | 1. Preference to have antibiotics<br>2. No preference expressed<br>3. Preference not to have antibiotics | Patient opinion can influence clinician choices [19,37]. Levels allow for patient preference in either direction, or neutral. |
| Risk of harm from not having antibiotic treatment straight | 1%<br>10% | The GP's judgement of the risk of harm, explained as symptom persistence or recurrence, or complications. Shown as a |

| | | |
|---|---|---|
| away | 20% | percentage, as a graphic, and also described in words ('In 1 case out of every 100 like this, the patient would…'). Levels identified from literature. Rates of complications typically range from <1% to 2% for RTIs in primary care studies without antibiotics [11,38-40]. Symptom persistence at follow-up in the case of acute bronchitis ranges from 18% to 35% in meta-analyses depending on the measure [41], with a reconsultation rate of ~20% for non-resolution for RTIs [10,21], without antibiotics. |
| Risk of an adverse effect from taking antibiotics | 1%<br>10%<br>20% | The GP's judgement of the risk of adverse effect, explained as allergy, side effects, or future resistance. Shown in three formats, as above.<br>Levels identified from literature and public information on rates of side effects and allergy [8,42]. |
| How a delayed prescription would be provided [b] | 1: prescription + advice to delay collection of antibiotics<br>2: post-dated prescription<br>3: collect prescription from the practice reception at a later date | Policy relevance: these formats have been tested in clinical trials [43] and referred to in guidelines [14], but there are no quantitative data on clinician preferences. |

a  Explanations of each attribute and its levels were provided in the survey (see Supplementary Materials S1 section 1).

b  Categorical variable. Other attributes are treated as continuous variables.

## 2. Results

*2.1 Respondent characteristics*

181 GPs completed the survey, with a median completion time of 17 minutes. The sample was consistent with the target distributions for sex, age, country and practice size, reflecting the population of UK GPs (Table 2). One in five respondents reported finding the survey difficult to complete to some degree.

Half of the respondents were partners in their GP practice. The majority considered the practice where they work most often to be of medium level of deprivation, and average level of antibiotic prescribing. On average, respondents reported that 17% of their patients who present with an RTI leave with a delayed antibiotic prescription, but there was wide variation in prescribing patterns between individuals; eight respondents reported never using delayed antibiotic prescriptions for patients with RTIs.

Table 2: Respondent characteristics

| Characteristic | | N (percentage) | Quota (%) [#] |
|---|---|---|---|
| Sex | Male | 98 (54%) | 56 |
| Age (years) | 39 and under | 40 (22%) | 26 |
| | 40-49 | 76 (42%) | 41 |
| | 50-59 | 50 (28%) | 24 |
| | 60 or over | 15 (8%) | 10 |
| | Median age | 46 | |
| Country | England | 152 (84%) | 83 |
| | Scotland | 17 (9%) | 10 |
| | Wales | 9 (5%) | 4.5 |
| | Northern Ireland | 3 (2%) | 2.5 |
| Practice size | 1-2500 patients | 5 (3%) | 4 |
| | 2501 - 5000 | 28 (15%) | 15 |
| | 5001 - 7500 | 40 (22%) | 20 |
| | 7501 - 10000 | 35 (19%) | 20 |
| | 10001 - 12500 | 32 (18%) | |
| | 12501 - 15000 | 14 (8%) | 41 |
| | More than 15000 patients | 27 (15%) | |
| Role in practice | Partner | 96 (53%) | |
| | Salaried GP | 57 (31%) | |
| | Locum | 28 (15%) | |
| Level of local deprivation * | High | 49 (27%) | |
| | Medium | 72 (40%) | |
| | Low | 56 (31%) | |
| Practice's level of antibiotic prescribing compared to similar practices * | Very low/Low | 36 (20%) | |
| | Average | 100 (55%) | |
| | Very high/high | 35 (19%) | |

| | | | |
|---|---|---|---|
| Usual format of delayed prescription* | Standard prescription with recommendation to wait | 145 (80%) | |
| | Post-dated prescription | 23 (13%) | |
| | Electronic post-dated prescription | 7 (4%) | |
| | Prescription available from practice at future date | 4 (2%) | |
| | Other | 2 (1%) | |
| RTI prescribing*: mean percentage of patients who leave with… | An immediate antibiotic prescription (range) | 31% (1 to 90%) | |
| | A delayed antibiotic prescription (range) | 17% (0 to 85%) | |
| | No antibiotic prescription (range) | 52% (0 to 95%) | |
| Found the survey* … | Very easy/easy/quite easy | 90 (50%) | |
| | Neither easy nor difficult | 52 (29%) | |
| | Very difficult/difficult/quite difficult | 39 (21%) | |

\# Based on annual GP omnibus survey, by Medeconnect, the online survey provider

\* Self-reported

1　*2.2 Importance ranking of the attributes*

2　Figure 1 shows the number of respondents who assigned each attribute a given rank, before

3　completing the choice questions. Symptoms were the most important, followed by

4　comorbidities, duration of illness and the risk of harm due to delaying treatment. Respondents

5　ranked length of consultation, the format of the delayed prescription, and patient preference

6　as the least important.

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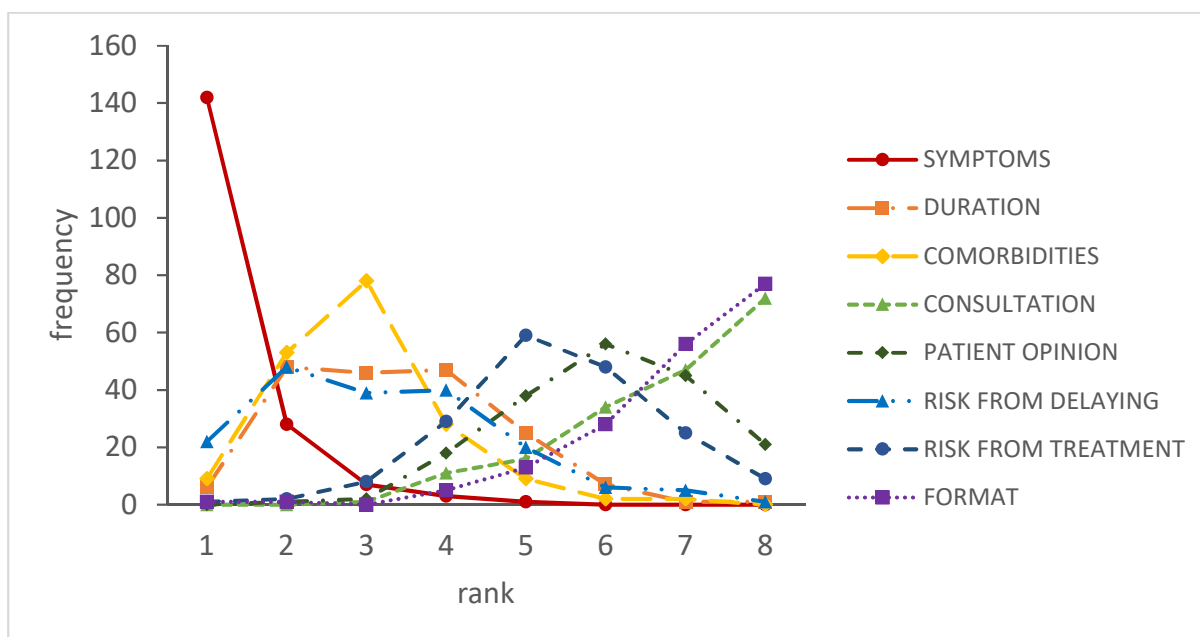


8

9　**Figure 1.** Ranking of attribute importance.

10　Attribute descriptions: DURATION: duration of illness prior to consultation; CONSULTATION: length
11　of consultation; PATIENT OPINION: preferences regarding antibiotics expressed by the patient; RISK
12　FROM DELAYING: risk of harm from not starting antibiotics straight away; RISK FROM TREATMENT:
13　risk of adverse effects from taking antibiotics; FORMAT: how the delayed prescription would be
14　provided.

15　Vertical axis indicates the number of respondents who ranked a given attribute at the rank shown on
16　the horizontal axis (1 = highest rank)

17

18　*2.3 Choice responses*

19　Each of the 181 GPs answered 15 choice questions, resulting in 2715 choice occasions. Initially,

20　68% of choices between delayed and immediate prescription were for a delayed prescription.

21　When the no-prescription alternative was offered, 51% (1393/2715) of choices were for this

22　option, with the vast majority of those choices switching from an initial choice of delayed

23　prescription (1383 of the 1393 no-prescription choices). This left 21% and 28% remaining with

24   their original choice of delayed or immediate prescription respectively. Twenty-six
25   respondents never chose a delayed prescription, with fewer never choosing immediate or no
26   prescription (five and two respondents respectively), and 95% of respondents choosing a
27   delayed prescription six times or fewer. By question, the proportions choosing immediate and
28   no prescription were inversely correlated. The trend in proportion choosing delayed
29   prescription was less clear, but appeared to be higher in the scenarios where there was no
30   strong preference for either immediate or no prescription (Figure 2).
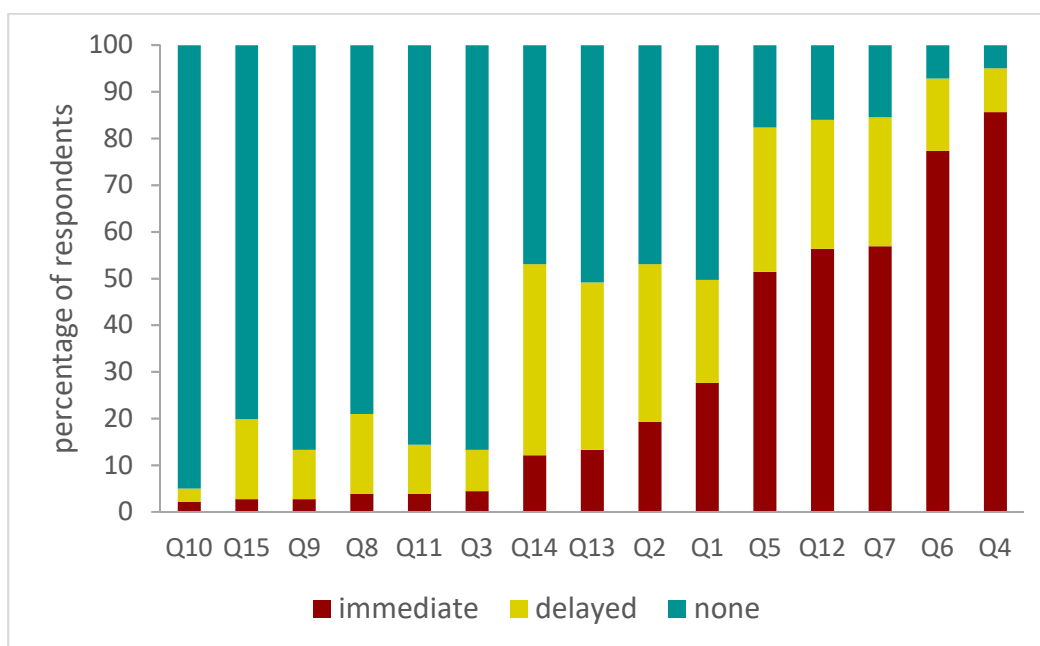


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32   **Figure 2.** Proportions ultimately choosing immediate, delayed and no prescription per choice question.

33   Q: Choice question, numbered by the order in which they were presented to respondents. To illustrate
34   the patterns in proportions choosing immediate, delayed, or no prescription, the graph orders the bars
35   by the proportion ultimately choosing the immediate prescription.

36

37   *2.4 Choice modelling*

38   Table 3 presents a mixed-effect logistic regression model, which estimates the effect of each of
39   the scenario attributes on the likelihood of respondents choosing the delayed prescription
40   option over an immediate prescription. By using a mixed-effect logistic regression, the model
41   allows for differences between respondents in their tendency to choose the delayed
42   prescription. The coefficients are all of the expected sign, giving the model face validity; that
43   is, positive where we would expect an increase in the attribute to increase the likelihood of
44   respondents choosing the delayed prescription, and negative where we would expect the

45    likelihood to decrease. The attributes in the model explain 61% of the variation in responses;

46    this rises to 65% when between-respondent heterogeneity is incorporated.

47

Table 3 Effect of attributes on preferences for delayed prescription

| Attribute/level | | 1. Attributes only | | 2. Respondent characteristics | |
|---|---|---|---|---|---|
| | | Coefficient | 95% CI | Coefficient | 95% CI |
| Symptoms | Sore and red throat, and swollen lymph nodes in the neck ('minor throat') | 3.17 | 2.48 to 3.86 p<0.001 | 3.17 | 2.48 to 3.86 p<0.001 |
| | Productive cough and runny nose ('minor chest') | 3.47 | 2.79 to 4.14 p<0.001 | 3.47 | 2.79 to 4.14 p<0.001 |
| | Sore throat, swollen lymph nodes in the neck, pyrexia and purulent tonsils ('serious throat') | -0.90 | -1.31 to -0.49 p<0.001 | -0.90 | -1.31 to -0.49 p<0.001 |
| | Productive cough, pyrexia and pain on breathing ('serious chest') [a] | 0 | - | 0 | - |
| Symptom duration | Per day longer | -0.33 | -0.43 to -0.23 p<0.001 | -0.33 | -0.43 to -0.23 p<0.001 |
| Relevant comorbidities | None [a] | 0 | - | 0 | - |
| | One | 0.05 | -0.31 to 0.42 p=0.769 | 0.06 | -0.31 to 0.42 p=0.762 |
| | Two or more | -1.18 | -1.64 to -0.72 p<0.001 | -1.18 | -1.64 to -0.72 p<0.001 |
| Consultation length | Per minute longer | 0.05 | 0.02 to 0.09 p=0.003 | 0.05 | 0.02 to 0.09 p=0.003 |
| Patient opinion | Preference to have antibiotics | -0.39 | -0.72 to -0.05 p=0.022 | -0.39 | -0.72 to -0.05 p=0.023 |
| | No preference expressed [a] | 0 | - | 0 | - |
| | Preference not to have antibiotics | 0.33 | 0.05 to 0.60 p=0.020 | 0.33 | 0.05 to 0.60 p=0.020 |
| Risk of harm from not starting antibiotics | Per 1% higher | -0.13 | -0.17 to -0.10 p<0.001 | -0.13 | -0.17 to -0.10 p<0.001 |
| Risk of adverse effect from taking antibiotics | Per 1% higher | 0.03 | 0.01 to 0.05 p=0.001 | 0.03 | 0.01 to 0.05 p=0.001 |

| | | | | | |
|---|---|---|---|---|---|
| Format of the delayed prescription | Advice to delay [a] | 0 | - | 0 | - |
| | Post-dated prescription | -0.03 | -0.37 to 0.31 p=0.872 | -0.03 | -0.37 to 0.31 p=0.872 |
| | Collect from practice | -0.43 | -0.82 to -0.08 p=0.016 | -0.45 | -0.82 to -0.08 p=0.016 |
| Self-reported prescribing behaviour: percent immediate prescriptions for RTI | | | | -0.02 | -0.04 to -0.01 P=0.002 |
| Intercept | | 2.23 | 1.49 to 2.97 p<0.001 | 2.99 | 2.16 to 3.82 p<0.001 |
| Var(intercept) [b] | | 1.57 | 0.96 to 2.57 | 1.41 | 0.88 to 2.28 |
| | | | | | |
| Pseudo $R^2$: attributes only | | 0.61 | | 0.62 | |
| Pseudo $R^2$: attributes and respondent-level effect | | 0.65 | | 0.66 | |
| Akaike Information Criterion | | 1955 | | 1943 | |
| Bayesian Information Criterion | | 2043 | | 2037 | |

a  Reference level for the categorical variables. The coefficient for each level shows the effect of that level on the log odds of choosing delayed prescription, relative to the reference level

b  Variance of the random intercept. This term reflects the unexplained variation between respondents in their tendency to choose the delayed prescription after accounting for explanatory variables listed in the table.

CI  Confidence interval

Respondents were more likely to choose the delayed prescription for the minor versions of both upper and lower respiratory tract symptoms. The probability of choosing the delayed prescription increased by 0.41 for productive cough and runny nose compared to the more serious lower tract symptoms, and by 0.54 for the minor throat symptoms compared to the more serious (for full table of the effects on the marginal probability of choosing delayed prescription including confidence intervals, see Supplementary Material S1 section 2). Respondents were also more likely to choose the delayed prescription if the consultation was longer, or there was a higher risk of adverse events from taking antibiotics, but these effects were small (probability of choosing the delayed prescription increased by 0.005 per additional minute of consultation or 0.003 per 1% increase in risk of adverse effects). They were less likely to choose delayed prescription if the symptoms had been present for longer (probability decreased by 0.03 per day), if the patient had multiple comorbidities (probability decreased by 0.12 compared to no comorbidities), and with increasing risk of harm from delaying treatment (probability decreased by 0.01 per 1% increased risk). A delayed prescription was more likely if the patient expressed a preference not to take antibiotics (probability increased by 0.03), and conversely, less likely if the patient preferred to have antibiotics (probability decreased by 0.04). Compared to the most common format of delayed prescription (giving the patient a prescription with advice to wait), respondents were less likely to choose delayed prescription if the patient would have to return to the surgery to collect it (decrease in probability of choosing the delayed prescription of 0.04).

The relative strength of the attribute effects can be seen by comparing the magnitude of the coefficients. A patient expressing a preference to have antibiotics, for example, had a similar effect to an additional day of illness in reducing the probability of the GP choosing a delayed prescription. Similarly, a patient with a serious chest infection of a given duration, and a patient who had had a minor infection for 10 days longer, would have a similar probability of receiving a delayed prescription. The effect of a 1% difference in the risk from delaying antibiotics was approximately 4-fold greater than the effect of a 1% difference in risks due to antibiotic treatment.

When respondent characteristics were added (Table 3), allowing for self-reported prescribing behaviour improved the fit of the model; respondents who reported a high level of immediate prescribing for RTIs in practice were more likely to choose the immediate prescription in the

32    study. Although the effect per 1% difference in self-reported immediate prescribing was

33    modest, the proportion of self-reported immediate prescriptions for RTI ranged from 1% to

34    90%; at the mean value of 31% immediate prescriptions in practice, the effect was equivalent

35    to 2.3 additional days of illness in reducing the likelihood of a delayed prescription. Other

36    respondent characteristics showed no evidence of an effect on respondents' choices.

37    The model was robust to the exclusion of respondents who chose delayed prescription for the

38    practice question (n=27), chose the same response to all questions (n=6), completed the survey

39    in the fastest 1-5 percentiles (n=9) or who reported that they found the survey 'quite difficult',

40    'difficult' or 'very difficult' (n=39). The coefficients varied slightly, but the conclusions were

41    unchanged.

42    An ordered logistic regression model allows for the additional choice of 'no prescription'

43    (Figure 3). This assumes the three possible outcomes have a natural order (immediate,

44    delayed, and no prescription) and models the probability of respondents choosing each

45    outcome relative to the adjacent one in the hierarchy. Where the two coefficients for a given

46    attribute are not significantly different (p>0.05, Wald test), those coefficients are assumed by

47    the model to be equal (equal bars in Figure 3). Positive coefficients indicate that the attribute

48    increased the likelihood of a reduced prescribing choice (no or delayed prescription), and

49    negative coefficients indicate an increase in the likelihood of any prescription.

50    The direction and relative size of the effect of the attributes was similar to those described

51    above (see Supplementary Material S1 section 3 for a direct comparison). For most attributes,

52    there was no difference between their effect on the decision between an immediate

53    prescription and a reduced prescribing choice, and their effect on the decision to prescribe

54    (delayed or immediate) or not. However, four of the coefficients suggested the attribute had

55    a different effect depending on the type of decision being made. A patient expressing a

56    preference to have antibiotics may influence the type of prescription, but there was no

57    evidence that patient preferences affected the choice to prescribe at all. Similarly, minor

58    symptoms had a stronger effect on the decision not to give an immediate prescription than on

59    whether to prescribe at all. There was a minor difference in the effect of the risk of delaying

60    treatment.

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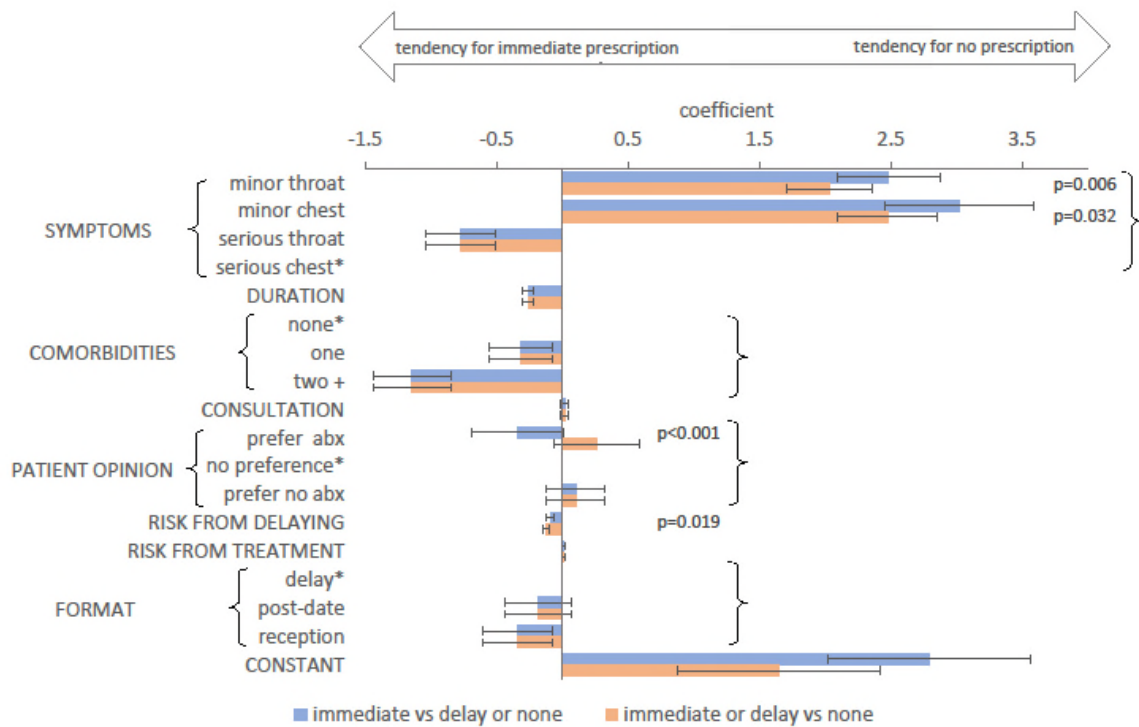
**Figure 3.** Coefficients for the ordered logistic regression model.

Symptoms descriptions: minor throat - sore throat and swollen glands; minor chest – chesty cough and runny nose; serious throat – sore throat, swollen glands and fever; serious chest – chesty cough, fever and pain on breathing

* Reference level for categorical variables. p-values are shown where the coefficients differed ($p<0.05$) between the choice to give an immediate prescription, and the choice to prescribe at all. For all other attributes and levels, the p-value for this difference was greater than 0.05, and the coefficients were constrained to be equal in the model. Bars indicate 95% confidence intervals.

Abbreviations: abx - antibiotics

Figure 4 shows the probability of choosing each prescription type for each of the four types of symptoms presented in the survey, as predicted by the ordered logistic regression model. No prescription was the most likely choice for the minor symptoms, whilst an immediate prescription was most likely for the more serious symptoms. The proportion of delayed prescriptions remained almost constant across the four symptom levels. A similar pattern was seen for the other categorical attributes (see Supplementary Material S1 section 4).
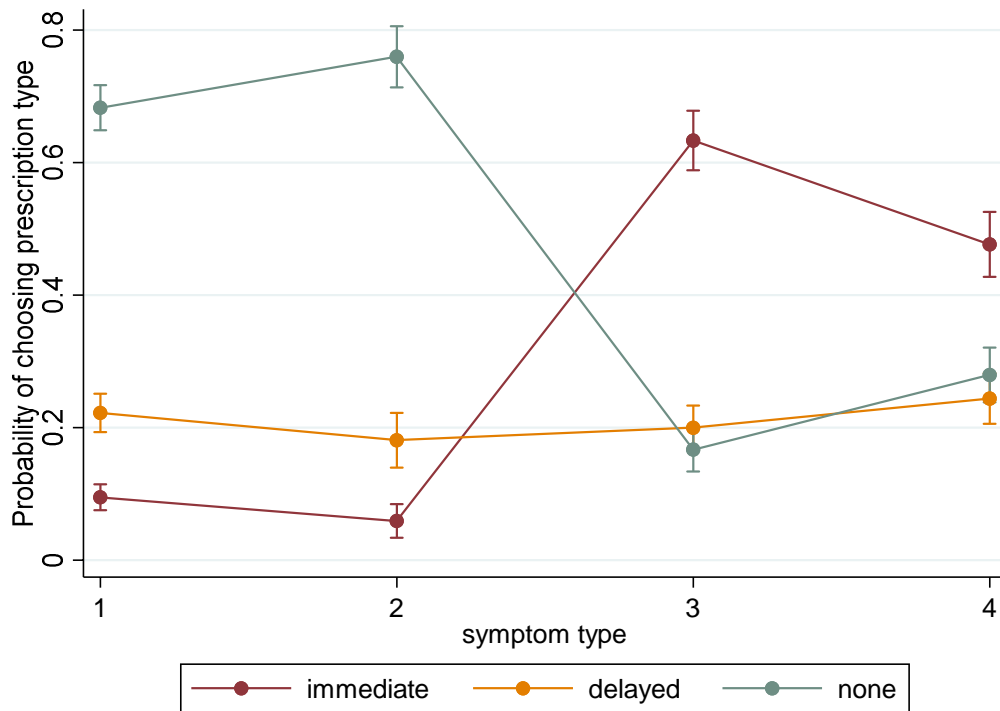
**Figure 4.** Probability of choosing immediate, delayed or no prescription, for each symptom type.

**Symptom descriptions:** 1 minor throat – sore throat and swollen glands; 2 minor chest – chesty cough and runny nose; 3 serious throat – sore throat, swollen glands and fever; 4 serious chest – chesty cough, fever and pain on breathing. Bars indicate 95% confidence intervals

## 3. Discussion

Our study suggests that clinical indicators – presenting symptoms, duration of illness, and patient comorbidities – are important factors in the decision to use delayed prescription. Patient preferences have some influence on the decision between immediate and delayed prescription, and GPs are less likely to use delayed prescription if the patient would have to come back to the practice to collect the prescription. The risk from delaying antibiotic treatment has a greater effect on the decision than the risk due to antibiotic treatment, demonstrating greater risk adversity regarding adverse outcomes than side effects. There is little effect of consultation length on prescription choice.

To our knowledge this is the first large-scale study to quantify the trade-offs made by UK GPs in considering delayed prescription. A smaller (n=23) choice study of prescribing decisions among Australian GPs examined factors affecting antibiotic prescribing overall. Two attributes shared with our study (patient preferences and duration of illness) had significant effects in both studies; the effect of patient preferences was less in our study, possibly due to

101    the strong effect of symptoms in our study, which were held constant in the Australian work

102    [26]. Our findings are consistent with qualitative observations on the importance of perceived

103    patient expectations in different countries [19,24-26,44,45]. These similarities suggest our results

104    may be generalisable to other settings with similar primary healthcare systems.

105    The relative importance of the attributes from the regression models is broadly consistent with

106    respondents' importance rankings. Both indicate that concerns about the potential for harm

107    due to delaying antibiotics is more important in the prescribing decision than the risk of

108    adverse effects due to taking antibiotics. This may reflect the doctor's role to treat patients, so

109    the risk of a negative outcome from 'doing nothing' may be seen as worse than the risk of a

110    negative outcome from giving treatment. Alternatively, it may be an acknowledgement that

111    in a situation where antibiotics are indicated, the benefit from prescribing is accepted to

112    outweigh the risk of harm from doing so. The length of the consultation was ranked low,

113    consistent with its modest effect in the choice questions, despite concerns raised in qualitative

114    studies over the time taken to explain the delayed prescription [19]. Our findings suggest that

115    increasing the length of consultations to allow for the explanation required would not

116    necessarily increase the uptake of delayed prescription.

117    Given the similarity of the coefficients in the two types of model, and the observation that the

118    majority of 'no prescription' choices were originally for delayed prescription, we have not

119    found a unique model for delayed prescription. Rather, our results appear to reflect a

120    spectrum from immediate to no need for antibiotics, and our models indicate factors that

121    move a GP's prescribing decision towards reduced prescribing – that is, to delayed or no

122    prescription. This is perhaps consistent with findings in observational studies of delayed

123    prescription, that the population of patients given a delayed prescription show a symptom

124    distribution that is intermediate between those offered immediate or no prescription [10,21]. It

125    may be that this rather loosely-defined intermediate position contributes to the uncertainty in

126    using delayed prescription noted by some GPs in qualitative work [19,26], thus reducing its

127    use.

128    The serious sore throat symptoms (sore throat, swollen glands and fever) had a greater

129    negative effect on the likelihood of GPs using delayed or no prescription than serious chest

130    symptoms (chesty cough, fever and pain on breathing). This is perhaps counter-intuitive

131  given the potential seriousness of bacterial pneumonia, and may be due to variation in the
132  way respondents interpreted the descriptions, for example assuming pneumonia had been
133  excluded, or that the pain on breathing was due to coughing. Alternatively, respondents with
134  recent experience with streptococcal pharyngitis or rising incidence of scarlet fever [46,47],
135  may have been sensitised to be more concerned about throat symptoms.

136  Based on our results, we suggest two possible approaches for continued reduction of
137  antibiotic prescribing. First, our findings concur with other work recommending support for
138  GPs in handling perceived patient pressure to prescribe [23,26,48]. In addition, we recommend
139  patients are encouraged to express any preference not to have antibiotics (or a neutral
140  opinion), and GPs to ask questions to establish that preference during the consultation.
141  Although patients preferring not to have antibiotics was not consistently a strong factor in
142  determining the prescribing decision in our models, we note that GPs' perceptions of patients'
143  preferences are not necessarily accurate [49-52]. Hearing the patient's actual preference would
144  avoid assumption that the patient expects antibiotics; this would also reduce concerns about
145  delayed prescription giving an ambiguous message to the patient if it is clearly in line with
146  the patient's preference.

147  Second, whilst symptoms and their duration are a key driver of prescribing behaviour, some
148  GPs appear to be more averse to delayed or no antibiotic prescribing than would be expected
149  from clinical evidence and guidelines. Reasons for this variation could include an individual's
150  previous negative experience, tolerance of risk or ambiguity, or the mechanisms available for
151  keeping up to date with data and guidelines. Raising awareness and understanding of the
152  trial data supporting the use of delayed prescription may be helpful in reducing prescribing
153  overall, including use of delayed prescription. A 'one-stop' website containing the key
154  evidence for specific presentations, and current guidance, along with peer suggestions for
155  explaining prescribing decisions to patients, may be helpful.

156  Some practitioners oppose the use of delayed prescription [53]. Two subgroups identified in
157  our study could reflect views of this type: respondents who never chose the delayed
158  prescription option in the study, and respondents who reported never using delayed
159  antibiotic prescription in practice. There was minimal overlap between these two groups, and
160  the groups were too small to draw any conclusions from our data. Further work to understand

161 these polarised opinions would be helpful – particularly if they tend to be high prescribers –

162 to identify alternative routes to support them in reducing antibiotic use.

163 *3.1 Limitations*

164 The study is limited by its hypothetical nature, meaning the responses may be idealised and

165 not reflect actual practice. We suggest this may be particularly true of studies such as this

166 where experts respond in their professional capacity, in contrast to general population or

167 patient studies where we are seeking opinions; here, there may be consistency stemming from

168 professional training or best practice guidance, and respondents might wish to reflect that in

169 their responses. This may explain the relatively low heterogeneity of responses seen in this

170 study. However, concerns that responses do not reflect actual practice are somewhat allayed

171 by the observation that reported prescribing behaviour in practice not only varied widely, but

172 was a significant predictor of responses to the choice questions.

173 Further, in constructing the scenarios, the number of attributes was inevitably constrained in

174 order to manage respondent burden, and the scenarios may have omitted important features

175 (for example, additional information about the patient, social factors, or clinical findings) that

176 would affect the results. Our study included eight attributes; this is relatively high compared

177 to studies among members of the public, which mostly use six or fewer [32,33,54], and a fifth

178 of respondents reported finding the choices difficult. However, GPs are used to making

179 complex decisions in their clinical practice; further, free-text comments on the survey did not

180 raise complexity as an issue, and the relatively low heterogeneity of responses suggests that

181 even if the choices were difficult, respondents were able to make consistent choices.

182 Nonetheless, respondents may have used simplifying heuristics, such as ignoring certain

183 attributes; for example, it is possible that respondents assessed the risk of recurrence or

184 progression from the clinical features, and paid reduced attention to the attribute that

185 quantified that risk.

186 Our choice question was presented in two parts, with the second allowing the option of no

187 antibiotic prescription. This was to allow us to capture data on the choice between immediate

188 and delayed prescription, our primary interest. However, it may not reflect the actual decision

189 process in practice, which may have introduced bias to the choices. It may be that, having

190 made a decision, respondents were more reluctant to change their mind and switch to 'no

191 prescription', so overestimating the likelihood of prescribing an antibiotic and reducing the
192 estimated impact of the attributes. However, the results show that 51% of choices switched in
193 this way, suggesting it did not have a major impact.

194 The study design was optimised to quantify the main effects of the attributes, but did not
195 allow for evaluation of interactions between the attributes. Some exploratory analyses were
196 attempted, but the findings were difficult to interpret due to collinearity between the
197 attributes. To explore interactions effectively, future studies could use a blocked design,
198 where a larger number of choice questions is generated, of which each respondent sees a
199 randomly allocated subset [55].

200 Respondents were recruited by broad invitation to GP's who had signed up to be part of a
201 panel. It is possible that those who chose to participate in this study had a particular interest
202 in infectious disease, or antibiotic and resistance. Their level of knowledge may therefore not
203 be representative of the broader population of GPs. Similarly, the offer of an incentive to
204 participate (although this is normal) may have appealed to a particular population among
205 GPs, although it is not obvious that the presence of an incentive would have affected
206 respondents' answers in any particular direction in this study.Finally, the study was run
207 before the COVID-19 pandemic, which led to a rapid shift to remote consultations; this change
208 in practice may persist beyond the immediate lockdown restrictions. The effect of this may be
209 reduced certainty of prescribing in the absence of some physical examinations and face-to-
210 face cues [56]. This could lead either to an increase in use of delayed prescription in response
211 to that uncertainty, or to an increase in immediate prescriptions which could have important
212 consequences for antimicrobial resistance. Future work is needed to identify any such changes
213 in practice, and determine their effect on antibiotic consumption.

214

215 **4. Methods**

216 Study design, data collection and analysis followed good practice guidance for similar choice-
217 based studies [57]. Ethical approval was granted by the University of Oxford Medical Sciences
218 Interdivisional Research Ethics Committee (R58586/RE002). All respondents gave their
219 informed consent before participating.

220 *4.1 Defining survey attributes and levels*

221 Factors expected to influence GPs' use of delayed prescription (termed 'attributes') were
222 identified from a literature search (summarised in the Supplementary Material S1 section 5).
223 Eight attributes were selected from this long-list based on: a) importance rankings from a
224 convenience sample of practicing GPs (n=4); b) face validity based on the clinical experience
225 within the project team; and c) policy relevance.

226 Levels for each attribute were determined from clinical guidelines [14,15], Cochrane reviews
227 [8,41,58,59] and primary care studies [11,21,38-40], current NHS prescribing tools and support
228 materials [36,60,61], and clinical expertise within the project team. Attributes, their levels, and
229 rationale are shown in Table 1.

230 *4.2 Choice questions*

231 Respondents (GPs) were asked to consider a consultation in which an adult patient presents
232 with an RTI. In each choice question, they were presented with a profile describing the
233 patient's condition, and asked to choose between immediate or delayed prescription. To allow
234 for the possibility that some respondents would have chosen not to prescribe antibiotics at all
235 in some of the scenarios described, they were then offered the choice to prescribe no
236 antibiotics, or remain with their original choice. The 'no prescription' option was not
237 presented initially, to avoid losing information on our primary question regarding preferences
238 for delayed prescription as an alternative to immediate prescription.

239 *4.3 Survey and experimental design*

240 The survey was presented on-line, in English (full survey text provided in Supplementary
241 Material S1 section 1). Respondents were provided with information about the survey and
242 gave their informed consent to participate. They were given instructions on how to complete
243 the survey, and an explanation of each of the attributes. The next section asked respondents
244 to rank the attributes in order of importance to the prescribing context (with the attributes
245 presented in randomised order), and to complete a practice choice question, which consisted
246 of the attribute levels most likely to lead to an 'immediate' prescription.

247 Respondents then completed 15 choice questions; this is generally considered an acceptable
248 number of questions in this type of survey [32,33,54,62,63]. All respondents saw the same 15
249 questions. Finally, respondents answered questions about themselves, their practice, and their

250    antibiotic prescribing. The survey was reviewed with GPs on the project team at all stages of

251    its construction, to ensure clarity and medical accuracy.

252    The choice questions were produced using experimental design software, Ngene [64], to create

253    an efficient design (that is, one that maximises the information available from respondents'

254    choices). Constraints were applied to avoid implausible scenarios (see Supplementary

255    Material S1 section 6). In line with recommended practice, an initial design was created, and

256    used in a pilot sample (23 GPs recruited in the same way as for the main study). The choices

257    from this pilot were used to optimise the design for the main study, but were not included in

258    the final analysis. The most efficient design generated by the software was selected, following

259    checks by clinical experts that none of the scenarios were implausible, nor were expected to

260    lead to the same decision by all respondents.

261    A sample size estimate based on the standard errors predicted from the experimental design

262    (52) indicated that at the target sample size of 180, the study would be able to detect

263    coefficients of value 0.24 for the levels of the symptoms attribute, and 0.01 for the other

264    attributes, at a two-sided significance level of 0.05 and with power of 80%.

265    *4.4 Data collection*

266    Respondents were recruited from an existing panel of UK GPs curated by Medeconnect, a

267    market research provider specialising in healthcare professionals. Quotas based on

268    Medeconnect's annual GP Omnibus study were used to recruit a study sample representative

269    of UK GPs in terms of gender, age, country within the UK, and practice size. Respondents

270    who completed the survey received reward points equivalent to £20 in the form of vouchers,

271    which is in line with standard practice of this provider for this type and length of survey. The

272    data were collected in February and March 2019. No response rate could be calculated, as it

273    was not known how many people would have seen the invitation to participate on the

274    provider's website.

275    *4.5 Analysis*

276    Data analysis was performed in Stata (v.15SE) [65]. Choices between delayed and immediate

277    prescription were analysed using a mixed-effects logistic regression model, which models the

278    log-odds of choosing delayed prescription as a linear combination of the attribute levels. This

model was chosen because it allows for heterogeneity between respondents in their tendency to choose the delayed prescription (that is, it includes a random intercept per respondent), and can incorporate respondent characteristics directly as predictors. The coefficients represent the effect of one unit of the attribute on the log-odds of respondents choosing the delayed prescription. Cluster-robust standard errors were used throughout, to allow for the fact that each respondent contributes 15 responses. To assess whether the time and risk attributes could be appropriately represented as continuous variables with a linear relationship with the outcome, these attributes were also modelled as categorical variables (see Supplementary Material S1 section 7).

For the second part of the question (including the no-prescription alternative) choices were modelled using a partial proportional ordered logit model (gologit2 command in Stata). This assumes the three possible outcomes have a natural order (immediate, delayed, and no prescription) and models the probability of respondents choosing each outcome relative to the adjacent one in the hierarchy. The partial proportional model was chosen because it relaxes the assumption that each attribute has a consistent effect on the probability of choosing each category. The model generates two coefficients for each attribute: one for its effect on the probability of choosing an immediate prescription rather than delayed or no prescription, and one for its effect on the probability of choosing a prescription (either type) rather than no prescription. The two coefficients are tested to determine if they are statistically significantly different (Wald test, $p<0.05$) and if so, they are retained as different coefficients.

To help interpret model coefficients, the average predicted probability of choosing each type of prescription for each level (the marginal predicted mean) was calculated, using the 'margins' command in Stata. This method sets the attribute to that level for all observations, keeping the other variables at their observed levels. The probability of choosing delayed prescription is then predicted for each observation using the regression model, and the mean probability calculated. This can also be expressed as the effect of one unit of the attribute on the probability of choosing the delayed prescription.

Models were compared using a measure of how much of the variability in responses was explained by the model (McKelvey and Zavoina Pseudo-$R^2$ [66]) and measures of goodness-of-fit (the Akaike and Bayesian Information Criteria).

309     The dataset is available from the corresponding author on reasonable request.

310

**5. Conclusion**

312     Clinical features (symptoms, duration and comorbidities) are appropriately the most
313     important factors for GPs in deciding between immediate, delayed, and no antibiotic
314     prescription. However, broader dissemination of the relevant clinical evidence for specific
315     presentations may be helpful in supporting GPs to make greater use of delayed prescription.
316     With patient opinion playing a role in the choice of prescription type, establishing a patient's
317     actual preference during the consultation may also help to reduce the number of immediate
318     prescriptions. Extending consultation duration appears unlikely to increase use of delayed
319     prescription.

320

**List of abbreviations**

322     abx         antibiotics
323     GP          general practitioner
324     NHS         National Health Service
325     NICE        National Institute for Health and Care Excellence
326     RTI         respiratory tract infection

327

328     **Supplementary Materials:** Supplementary materials S1 (word document) are available
329     online at www.mdpi.com/xxx/s1

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357

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**SUPPLEMENTARY MATERIAL**


**Delayed antibiotic prescription by general practitioners in the UK: a stated-choice study**


Morrell, L et al, on behalf of the STEP-UP team



**Contents**

**SECTION 1. Survey instrument**

A survey on attitudes to antibiotic prescribing in general practice

Doctors.net.uk invites you to take part in a short survey commissioned by an academic researcher to investigate your attitude to antibiotic prescribing decisions in general practice.

The aim of this study is to learn more about the factors that are important to GPs when deciding how to treat patients who they think might need an antibiotic. The results will help to inform antibiotic prescribing policies for the NHS in the future. We would like to invite you as a GP to participate in our online survey.

In this survey, we will show you a series of hypothetical situations. We will ask you to make a decision about antibiotic treatment for the patient described in each situation.

The survey should take up to 20 minutes to complete and all members completing the survey in full will receive 4000 eSR points. We would like you to answer all of the questions. To help you to answer the questions we have provided some background information for you to read at the start of the survey.

Please note that your participation is voluntary. You may withdraw at any point during the questionnaire for any reason, before submitting your answers, simply by closing your computer's browser window. However, we are only able to award points to participants who complete the full survey.

The survey is being run by the Nuffield Department of Population Health at the University of Oxford. The lead researcher is Dr. Liz Morrell. This project has been reviewed by, and received ethics clearance through, the University of Oxford Central University Research Ethics Committee [R58586/RE002].

Please read the following text, which further explains the key aspects of this research:
- I understand that this research is commissioned by an academic researcher and is being carried out within the code of conduct of the Market Research Society and the British Healthcare Business Intelligence Association
- Doctors.net.uk will comply with all UK laws protecting your personal data and the British Healthcare Business Intelligence Association and Market Research Society guidelines
- The research is not intended to be promotional and any information presented is done so solely to explore reactions to such information
- Your responses will be totally anonymous and confidential
- The aggregated findings of this research may be published in academic publications, however at no stage will it be possible to identify any participants

Doctors.net.uk is the data controller with respect to your personal data and, as such, will determine how your personal data is used. Please see Doctors.net.uk's privacy notice here. Doctors.net.uk will share only fully anonymised data with the University of Oxford, for the purposes of research.

All results will be anonymised in accordance with Doctors.net.uk's zero-tolerance privacy policy and the Market Research Society Code of Conduct. The anonymised data will be stored on secure networks at the University of Oxford, and archived securely at the end of the project.

What if there is a problem?
If you wish to contact us about this survey, here are our contact details.
    Researcher: Peter Constable    Email: [SurveyHelp@mess.doctors.org.uk](mailto:SurveyHelp@mess.doctors.org.uk)
    Contact reference for inclusion in the email subject: Survey 01206970

If we cannot resolve your question, we will contact the lead researcher and work with her to deal with your concern. If you remain unhappy or wish to make a formal complaint, we will provide you with contact details for the Chair of the Research Ethics Committee at the University of Oxford.

Please confirm that you have read and understood this information, and agree to take part in the survey
    Yes
    No              **THANK AND CLOSE**

[screener questions for quotas]

1. How old are you?
   [write in number]

2. What is your gender?
   Male            Female            Other            Prefer not to say

3. In which part of the UK do you currently practice?

4. Thinking about the number of registered patients, how big is the practice where you work most often?
   Less than 5000        5001-10000        10001-15000    greater than 15000

Thank you for providing that information.

This survey is about the management of respiratory tract infections (RTIs) in general practice.

Current guidelines for antibiotic use in RTIs (for example, [NICE clinical guideline 69](#)) allow for the use of one of three antibiotic prescribing strategies: immediate prescribing, delayed or 'back-up' prescribing, or no prescribing. We want to understand how GPs decide whether to give an immediate or a delayed prescription to a patient with an RTI who they believe might need antibiotics.

We are interested in your views about what factors are important when deciding on the treatment approach for a patient with an RTI. Our results will help inform future antimicrobial stewardship practices and clinical guidelines.

The next page provides some information on the survey, and how to complete it.

**HOW TO COMPLETE THIS SURVEY**

For this survey, we would like you to consider the following hypothetical scenario:

> *An adult patient has presented with a respiratory tract infection. You think that the patient might need antibiotics, and you now need to decide whether to prescribe immediate antibiotics, or provide a delayed prescription for antibiotics that the patient can take later if necessary.*

In the survey, we will show you a series of situations and ask you two questions about each. First, we will ask you to decide whether to give the patient an immediate or delayed prescription for antibiotics. We appreciate that prescribing preferences vary, and in some situations you might prefer not to prescribe antibiotics. We will ask if that is the case in the second question. Regardless of whether you would prefer not to prescribe antibiotics, we would still like you to answer the first question, and decide between an immediate or delayed prescription in each situation.

Each situation is made up of eight features, describing the patient's condition, and the discussion during your consultation. There are three or four possible options for each feature, and the options that are presented to you will vary in each situation. Detailed descriptions of each feature and the possible options are provided on the following pages. Please read these descriptions carefully, then answer all of the questions that follow.

**THANK YOU FOR YOUR HELP**

**Feature 1**

**Patient's symptoms and physical signs**

In each situation, the symptoms will be one of the following four options:

- Sore and red throat, and swollen lymph nodes in the neck
- Sore throat, swollen lymph nodes in the neck, pyrexia, and purulent tonsils
- Productive cough and runny nose
- Productive cough, pyrexia, and pain on breathing


**Feature 2**

**Duration of the patient's symptoms**

This describes how long the patient has had their current symptoms, before their consultation with you. In each situation, this will be one of the following three periods:

- 3 days
- 7 days
- 10 days


**Feature 3**

**Relevant comorbidities or complicating factors**

Relevant comorbidities could include, for example, heart or lung conditions, another chronic disease, a recent hospitalisation, or the patient being aged over 65.

In each situation, the patient will have:

- No relevant comorbidities
- One relevant comorbidity
- Two or more relevant comorbidities


**Feature 4**

**Length of time you have available to spend with this patient**

In each situation, the length of time spent with the patient will be one of the following three options:

- 5 minutes
- 10 minutes
- 15 minutes

**Feature 5**

**Opinions expressed by the patient about antibiotic treatment**

In each situation, the opinions expressed by the patient will be one of the following:

- Patient has expressed a preference <u>to have</u> antibiotics
- Patient has not expressed any preference relating to antibiotics
- Patient has expressed a preference <u>not to have</u> antibiotics

**Feature 6:**

**Likelihood of harm from <u>not having</u> immediate antibiotic treatment**

This harm might be persistence or recurrence of presenting symptoms, or complications, all of which may lead to a re-consultation.
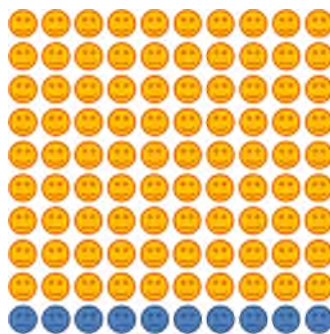
You should assume that your judgement of this probability is based on your clinical experience, local or national guidelines, and evidence from clinical studies. Your judgement will include patient factors not reflected in the profile so you should accept the risk figures given as accurate.

In each situation, the likelihood that the patient will experience harm from not having antibiotics will be one of three options, which are illustrated in the diagrams below:

- <u>Unlikely</u>: in 1 case out of every 100 like this, the patient will experience persistent or recurrent symptoms, or complications
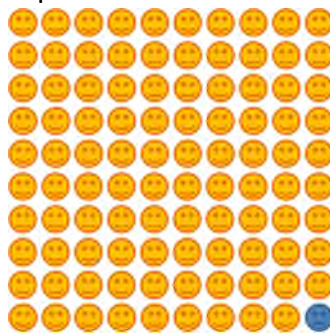


- <u>Somewhat likely</u>: in 10 cases out of every 100 like this, the patient will experience persistent or recurrent symptoms, or complications



- <u>Likely</u>: in 20 cases out of every 100 like this, the patient will experience persistent or recurrent symptoms, or complications
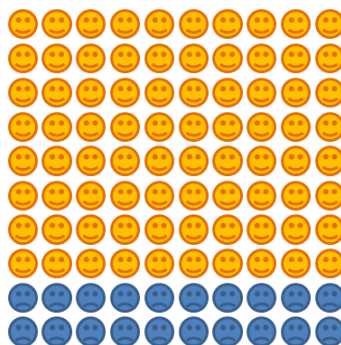
**Feature 7**

**Likelihood of an adverse effect from <u>having</u> antibiotic treatment**

An adverse effect might be a gastro-intestinal side effect, an allergic reaction, or a future antibiotic-resistant infection. You should assume that your judgement of this probability is based on clinical experience, local or national guidelines, and evidence from clinical trials for the antibiotic(s) you are considering prescribing.

In each situation, the likelihood that the patient will experience an adverse event from taking antibiotics will be one of three options, which are illustrated in the diagrams below:

- <u>Unlikely</u>: in 1 case out of every 100 like this, the patient will experience an adverse effect from antibiotic treatment
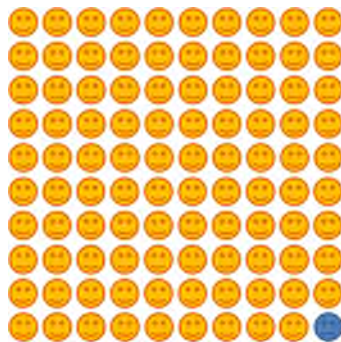
- <u>Somewhat likely</u>: in 10 cases out of every 100 like this, the patient will experience an adverse effect from antibiotic treatment
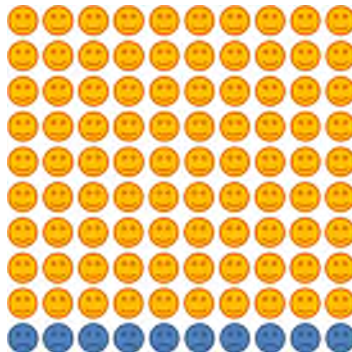
- <u>Likely</u>: in 20 cases out of every 100 like this, the patient will experience an adverse effect from antibiotic treatment

**Feature 8**

**How your practice would issue a delayed prescription**

Practices may have different ways of issuing delayed prescriptions. They differ in how much control you have over when the patient collects the medication, and convenience for the patient. In each situation, please assume you have one of the following three mechanisms available to you:
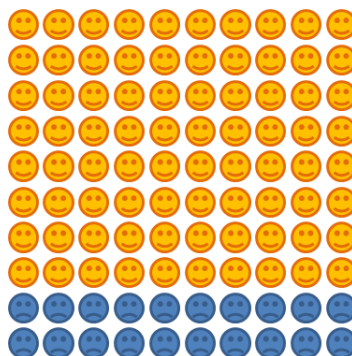
- Give a prescription with recommendation to delay collection. You would hand the patient a prescription, but advise them only to collect the antibiotics if their symptoms do not start to resolve after a specified number of days.
- Give a post-dated prescription. You would hand the patient a prescription showing a date several days in the future. The pharmacy would only be able to dispense the antibiotics on or after that date.
- Prescription available from the practice at a future date. You would not hand the patient a prescription during the consultation. You would explain that if their symptoms do not start to resolve after a specified number of days, they can return to the practice and collect the prescription from the receptionist.

**[SUMMARY TABLE]**

The table below summarises the eight features and the different options that may be presented to you in each situation.

| FEATURE | POSSIBLE OPTIONS |
|---|---|
| Patient's symptoms and signs | • Sore and red throat, and swollen lymph nodes in the neck<br>• Sore throat, swollen lymph nodes in the neck, pyrexia, and purulent tonsils<br>• Productive cough and runny nose<br>• Productive cough, pyrexia, and pain on breathing |
| Duration of symptoms | • 3 days<br>• 7 days<br>• 10 days |
| Patient's comorbidities | • No relevant comorbidities<br>• One relevant comorbidity<br>• Two or more relevant comorbidities |
| Length of time to spend with the patient | • 5 minutes<br>• 10 minutes<br>• 15 minutes |
| Patient's opinions | • Patient has expressed a preference <u>to have</u> antibiotics<br>• Patient has not expressed any preference relating to antibiotics<br>• Patient has expressed a preference <u>not to have</u> antibiotics |
| Likelihood of harm from not having immediate antibiotics | • Unlikely: in 1 case out of every 100 like this, the patient will experience persistent or recurrent symptoms, or complications<br>• Somewhat likely: in 10 cases out of every 100 like this, the patient will experience persistent or recurrent symptoms, or complications<br>• Likely: in 20 cases out of every 100 like this, the patient will experience persistent or recurrent symptoms, or complications |
| Likelihood of an adverse effect from having antibiotics | • Unlikely: in 1 case out of every 100 like this, the patient will experience an adverse effect<br>• Somewhat likely: in 10 cases out of every 100 like this, the patient will experience an adverse effect<br>• Likely: in 20 cases out of every 100 like this, the patient will experience an adverse effect |
| How your practice would issue a delayed prescription | • Give a prescription with recommendation to delay collection<br>• Give a post-dated prescription<br>• Prescription available from the practice at a future date |

**[RANKING EXERCISE]**

We would now like to know which of these features are most important to you, when you are making antibiotic prescribing decisions for RTIs.

Please consider all eight features and then rank them below. Rank the most important feature as 1, down to the least important as 8.

*Drag and drop the items in order of importance, placing the most important at the top and the least important at the bottom*

[Randomised presentation order]

> Patient's symptoms and signs
> Duration of symptoms
> Patient's comorbidities
> Length of time to spend with the patient
> Patient's opinions
> Likelihood of harm arising from not having immediate antibiotics
> Likelihood of an adverse effect from having antibiotics
> How your practice would issue a delayed prescription

**[PRACTICE QUESTION]**

Now we would like you to complete a practice choice question, as an example of the questions you will see in the main survey.

Please consider the following scenario:

> *An adult patient has presented with a respiratory tract infection. You think that the patient might need antibiotics, and you now need to decide whether to prescribe immediate antibiotics, or provide a delayed prescription for antibiotics that the patient can take later if necessary.*

The situation is described below.

| | |
|---|---|
| Patient's symptoms and signs | Productive cough, pyrexia, and pain on breathing |
| Duration of symptoms | 3 days |
| Patient's comorbidities | 2 or more relevant comorbidities |
| Length of time to spend with patient | 5 minutes |
| Patient's opinions | Preference to have antibiotics |
| Likelihood of harm arising from not having immediate antibiotics | Likely (20/100) |
| Likelihood of an adverse effect from having antibiotics | Unlikely (1/100) |
| How your practice would issue a delayed prescription | Prescription available from the practice at a future date |

In this situation which would you give the patient:

An immediate antibiotic prescription ☐
OR
A delayed antibiotic prescription ☐

If we had offered the option of not prescribing antibiotics for this patient, would you have selected:

An antibiotic prescription, as chosen above ☐
OR
No antibiotic prescription ☐

**[MAIN QUESTIONS]**

Thank you for completing the ranking exercise and practice question.

Now we would like you to complete the main part of the survey.

We are going to describe 15 situations.

In all of them, we will ask you to consider the same scenario, of an adult patient with an RTI, as in the practice question. However, the characteristics of the patient and the consultation will be different each time.

Please indicate for each situation, whether you would give the patient an **immediate prescription** or a **delayed prescription** for antibiotics.

QUESTION 1

Please consider the following scenario:

> *An adult patient has presented with a respiratory tract infection. You think that the patient might need antibiotics, and you now need to decide whether to prescribe immediate antibiotics, or provide a delayed prescription for antibiotics that the patient can take later if necessary.*

The situation is described below.

| Patient's symptoms and signs | Sore and red throat, and swollen lymph nodes in the neck |
|---|---|
| Duration of symptoms | 10 days |
| Patient's comorbidities | Two or more relevant comorbidities |
| Length of time to spend with patient | 10 minutes |
| Patient's opinions | Preference to have antibiotics |
| Likelihood of harm arising from not having immediate antibiotics | Unlikely (1/100) |
| Likelihood of an adverse effect from having antibiotics | Somewhat likely (10/100) |
| How your practice would issue a delayed prescription | Prescription available from the practice at a future date |

In this situation which would you give the patient:

An immediate antibiotic prescription ☐
OR
A delayed antibiotic prescription ☐

If we had offered the option of not prescribing antibiotics for this patient, would you have selected:
An antibiotic prescription, as chosen above ☐
OR
No antibiotic prescription ☐

(similarly for questions 2-15)

**[RANKING EXERCISE – PART TWO]**

Thank you for completing the main part of the survey.

Now we would like you to complete the ranking exercise again to see if your opinions have changed after answering these questions.

Please consider how important the eight features are to you, and then rank them below. Rank the most important feature as 1, down to the least important as 8.

*Drag and drop the items in order of importance, placing the most important at the top and the least important at the bottom*

> Patient's symptoms and signs
> Duration of symptoms
> Patient's comorbidities
> Length of time to spend with the patient
> Patient's opinions
> Likelihood of harm arising from not having immediate antibiotics
> Likelihood of an adverse effect from having antibiotics
> How your practice would issue a delayed prescription

**[RESPONDENT CHARACTERISTICS]**

Now we would like to ask some questions about you.

All of the information that you provide will help us in our analysis, and all of your details will remain confidential. If you do not wish to answer some of these questions you do not have to – you can just skip the question.

The first questions are about your responses to the scenarios.

1.  When you were answering the choice questions, what 'adverse effect(s)' from having antibiotics were you predominantly considering?
    [free text]

2.  The survey questions assumed that you could judge the likelihood of patients experiencing adverse effects from antibiotic treatment. How easy or difficult was it to imagine you could judge this for:
    side effects
    allergic reactions
    future antibiotic resistance

    [5-point scale for each: Very easy – Easy – Neither easy nor difficult – Difficult – Very Difficult]

    Are there any further comments you would like to make regarding judgement of the likelihood of adverse effects from antibiotic treatment?
    [free text]

Now we would like to ask some questions about your practice.

3.  Which of the following options best describes your role in the practice where you work most often?
    Partner        Salaried GP        Locum        GP trainee        Other (please write in [text])

4.  Relative to other areas in the UK, how would you describe the level of deprivation in the area where you work most often?
    High                    Medium                    Low                    I don't know

5.  Compared to similar practices, how would you describe the level of antibiotic prescribing in the practice where you work most often?
    Very low                        Low                        Average
    High                            Very high                  I don't know

6.  What guidelines, if any, do you follow for antibiotic prescribing in RTIs? (please select all that apply)
    NICE                                        Public Health England
    Department of Health and Social Care        Health Protection Scotland
    Royal College of GPs                        Public Health Agency Northern Ireland
    CCG                                         Public Health Wales
    Practice's own                              Other (please write in: [text])

7. Please estimate what percentage of your patients with an RTI leave the consultation with:
   An immediate antibiotic prescription         [write in 1-100]
   A delayed antibiotic prescription            [write in 1-100]
   No antibiotic prescription                   [write in 1-100]

8. In the practice where you most often work, how are delayed antibiotic prescriptions usually issued? [select one]
   Standard prescription with recommendation to delay collection
   Post-dated prescription
   Electronic prescription with delayed collection date
   Prescription available from the practice at a future date
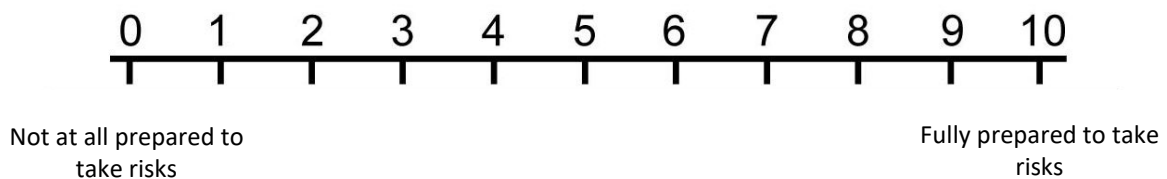   Other (please specify) [free text]

9. We would like to end this survey by asking about how you see yourself. There are 10 statements below. Please indicate how well each of these statements describes your personality.
   [This question is not mandatory]

   "I see myself as someone who is reserved."
   "I see myself as someone who is generally trusting."
   "I see myself as someone who tends to be lazy."
   "I see myself as someone who is relaxed, handles stress well."
   "I see myself as someone who has few artistic interests."
   "I see myself as someone who is outgoing, sociable."
   "I see myself as someone who tends to find fault with others."
   "I see myself as someone who does a thorough job."
   "I see myself as someone who gets nervous easily."
   "I see myself as someone who has an active imagination."

   [Response options]

   Agree strongly | Agree a little | Neither agree nor disagree | Disagree a little | Disagree strongly

10. Finally, are you generally a person who is fully willing to take risks or do you try to avoid taking risks? Please indicate on the scale below, where 0 means "not at all prepared to take risks" and 10 means "fully prepared to take risks". [This question is not mandatory.]

   0   1   2   3   4   5   6   7   8   9   10

   Not at all prepared to                          Fully prepared to take
   take risks                                             risks

11. How easy or difficult did you find the questions in this survey?
    [Likert scale 1-7, 1 = very easy, 7 = very difficult]

12. Are there any further comments that you would like to make regarding this survey?
    [free text]
    [not mandatory]

**You have reached the end of the survey. Thank you for taking the time to participate.**

## SECTION 2

Effect of attributes on the probability of respondents choosing the delayed prescription

| Attribute/level | | Coefficient | 95% CI | Effect on probability [a] | 95% CI |
|---|---|---|---|---|---|
| Symptoms | Sore and red throat, and swollen lymph nodes in the neck ('minor throat') | 3.17 | 2.48 to 3.86 p<0.001 | 0.39 | 0.32 to 0.46 |
| | Productive cough and runny nose ('minor chest') | 3.47 | 2.79 to 4.14 p<0.001 | 0.41 | 0.35 to 0.47 |
| | Sore throat, swollen lymph nodes in the neck, pyrexia and purulent tonsils ('serious throat') | -0.90 | -1.31 to -0.49 p<0.001 | -0.14 | -0.21 to -0.08 |
| | Productive cough, pyrexia and pain on breathing ('serious chest') [b] | 0 | - | - | - |
| Symptom duration | Per day longer | -0.33 | -0.43 to -0.23 p<0.001 | -0.03 | -0.04 to -0.02 |
| Relevant comorbidities | None [b] | 0 | - | - | - |
| | One | 0.05 | -0.31 to 0.42 p=0.769 | 0.01 | -0.03 to 0.04 |
| | Two or more | -1.18 | -1.64 to -0.72 p<0.001 | -0.12 | -0.16 to -0.07 |
| Consultation length | Per minute longer | 0.05 | 0.02 to 0.09 p=0.003 | 0.005 | 0.002 to 0.008 |
| Patient opinion | Preference to have antibiotics | -0.39 | -0.72 to -0.05 p=0.022 | -0.04 | -0.08 to -0.01 |
| | No preference expressed [b] | 0 | - | - | - |
| | Preference not to have antibiotics | 0.33 | 0.05 to 0.60 p=0.020 | 0.03 | 0.01 to 0.06 |
| Risk of harm from not starting abx | Per 1% higher | -0.13 | -0.17 to -0.10 p<0.001 | -0.01 | -0.02 to -0.01 |
| Risk of adverse effect from taking abx | Per 1% higher | 0.03 | 0.01 to 0.05 | 0.003 | 0.001 to 0.005 |

| | | | p=0.001 | | |
|---|---|---|---|---|---|
| Format of the delayed prescription | Advice to delay [b] | 0 | - | - | - |
| | Post-dated prescription | -0.03 | -0.37 to 0.31 p=0.872 | -0.003 | -0.03 to 0.03 |
| | Collect from practice | -0.43 | -0.82 to -0.08 p=0.016 | -0.04 | -0.08 to -0.01 |

a  The effect of the attribute on the probability of respondents choosing the delayed prescription. For categorical attributes, this is the change in probability when the attribute was set at this level, compared to the reference level. For continuous attributes, this is the change in probability for a one-unit increase in the attribute.

b  Reference level for the categorical variables. The coefficient for each level shows the effect of that level on the likelihood of choosing delayed prescription, relative to the reference level

abx   antibiotics

**SECTION 3**

Table showing coefficients from mixed logit and generalised ordered logit side-by-side for ease of comparison (coefficient and 95% confidence interval)

| | | Mixed logit | Generalised ordered logit | |
|---|---|---|---|---|
| Attribute/level | | Delayed vs Immediate | None or delayed vs Immediate | None vs Delayed or Immediate |
| Symptoms | Sore and red throat, and swollen lymph nodes in the neck ('minor throat') | 3.17 (2.48 to 3.86) | 2.48 (2.09 to 2.87) | 2.04 (1.71 to 2.36) |
| | Productive cough and runny nose ('minor chest') | 3.47 (2.79 to 4.14) | 3.02 (2.46 to 3.58) | 2.48 (2.10 to 2.85) |
| | Sore throat, swollen lymph nodes in the neck, pyrexia and purulent tonsils ('serious throat') | -0.90 (-1.31 to -0.49) | -0.77 (-1.03 to -0.50) | -0.77 (-1.03 to -0.50) |
| | Productive cough, pyrexia and pain on breathing ('serious chest') [a] | 0 | 0 | 0 |
| Symptom duration | Per day longer | -0.33 (-0.43 to -0.23) | -0.26 (-0.31 to -0.21) | -0.26 (-0.31 to -0.21) |
| Relevant comorbidities | None [a] | 0 | 0 | 0 |
| | One | 0.05 (-0.31 to 0.42) | -0.32 (-0.56 to -0.07) | -0.32 (-0.56 to -0.07) |
| | Two or more | -1.18 (-1.64 to -0.72) | -1.14 (-1.43 to -0.85) | -1.14 (-1.43 to -0.85) |
| Consultation length | Per minute longer | 0.05 (0.02 to 0.09) | 0.02 (-0.01 to 0.05) | 0.02 (-0.01 to 0.05) |
| Patient opinion | Preference to have antibiotics | -0.39 (-0.72 to -0.05) | -0.34 (-0.69 to 0.01) | 0.26 (-0.06 to 0.59) |
| | No preference expressed [a] | 0 | 0 | 0 |
| | Preference not to have antibiotics | 0.33 (0.05 to 0.60) | 0.11 (-0.12 to 0.33) | 0.11 (-0.12 to 0.33) |
| Risk of harm from not starting abx | Per 1% higher | -0.13 (-0.17 to -0.10) | -0.09 (-0.12 to -0.06) | -0.12 (-0.15 to -0.10) |
| Risk of adverse effect from taking abx | Per 1% higher | 0.03 (0.01 to 0.05) | 0.01 (0.00 to 0.02) | 0.01 (0.00 to 0.02) |
| Format of the delayed prescription | Advice to delay [a] | 0 | 0 | 0 |
| | Post-dated prescription | -0.03 (-0.37 to 0.31) | -0.18 (-0.43 to 0.08) | -0.18 (-0.43 to 0.08) |
| | Collect from practice | -0.43 (-0.82 to -0.08) | -0.34 (-0.60 to -0.07) | -0.34 (-0.60 to -0.07) |
| | | | | |
| Intercept | | 2.23 (1.49 to 2.97) | 2.79 (2.02 to 3.56) | 1.65 (0.88 to 2.42) |

a  Reference level for the categorical variables. The coefficient for each level shows the effect of that level on the likelihood of choosing delayed prescription, relative to the reference level

abx   antibiotics

**SECTION 4**

Graphs showing the predicted probability of choosing immediate, delayed or no prescription, for each level of each of the categorical variables. Predictions are based on the ordered logit model.
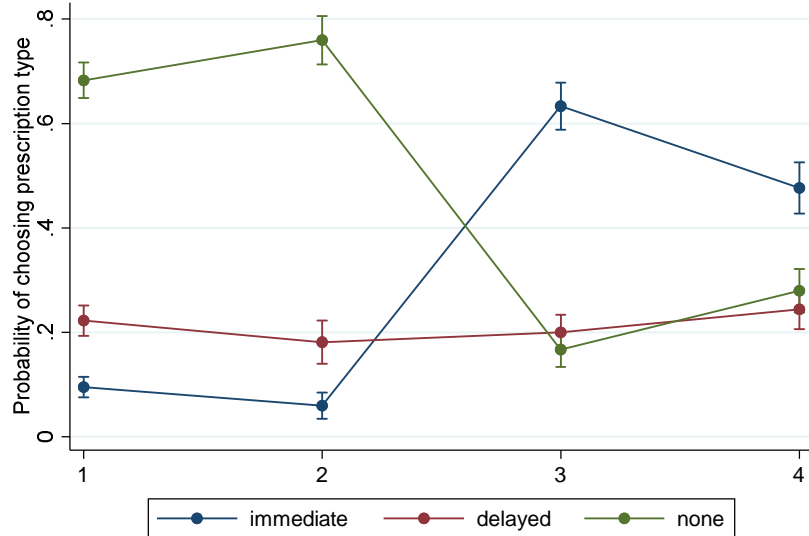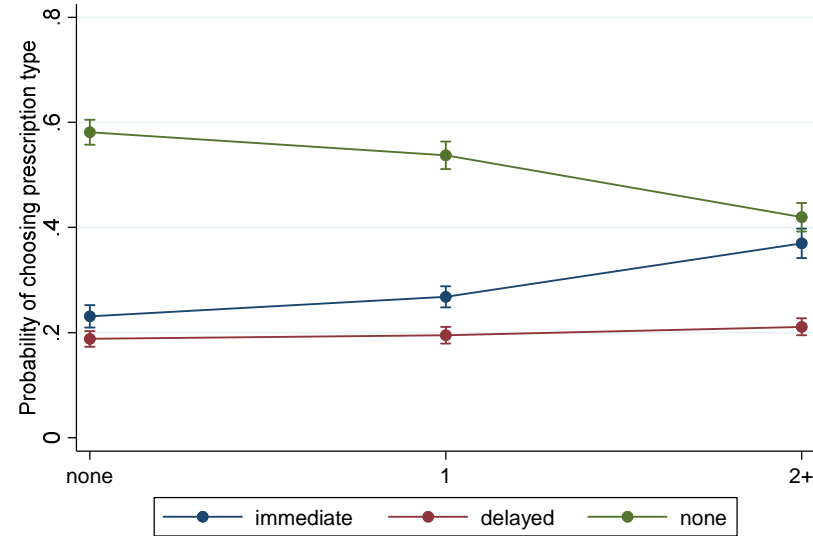


1 minor throat: sore and red throat, and swollen lymph nodes in the neck

2 minor chest: productive cough and runny nose

3 serious throat: sore throat, swollen lymph nodes in the neck, pyrexia and purulent tonsils

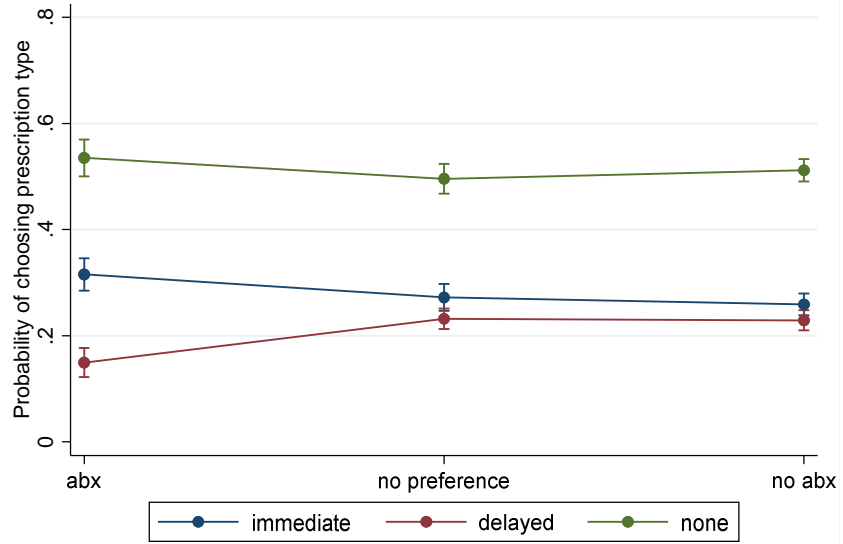4 serious chest: productive cough, pyrexia and pain on breathing

none: no relevant comorbidities

1: one relevant comorbidity

2+: two or more relevant comorbidities

## 3. Patient opinion

*Probability of choosing prescription type* (y-axis: 0, .2, .4, .6, .8)

x-axis: abx, no preference, no abx

Legend: immediate, delayed, none

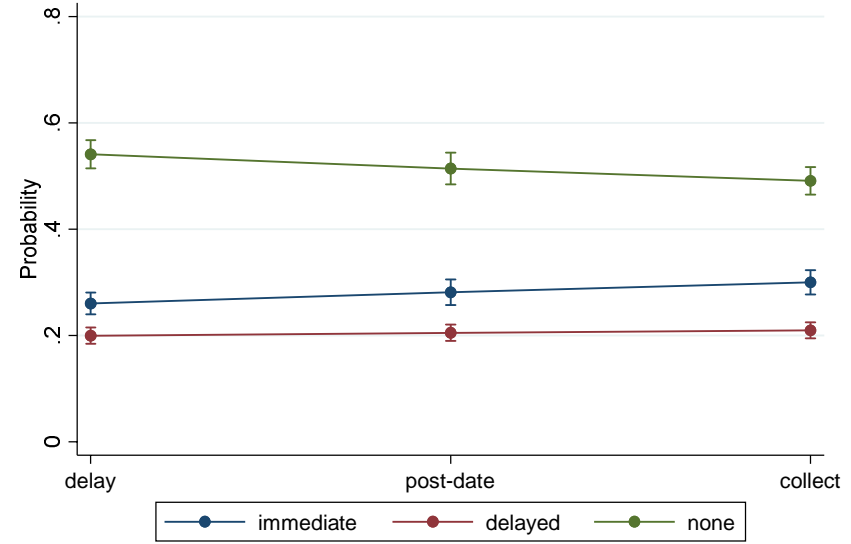abx: expressed a preference to have antibiotics

no abx: expressed a preference not to have antibiotics

## 4. Format of delayed prescription

*Probability* (y-axis: 0, .2, .4, .6, .8)

x-axis: delay, post-date, collect

Legend: immediate, delayed, none

delay: advice to delay starting antibiotics

post-date: prescription has a date in the future

collect: collect prescription from practice reception

**SECTION 5. Literature search and rationale for attribute selection**

The attribute long-list was developed from a structured literature review, conducted to inform a series of choice studies in different contexts, one of which was this choice study. The overall aim was to generate a long-list of attributes that could potentially influence clinicians, patients, or members of the public, in giving, seeking or stopping antibiotic treatment for any condition.

Searches were restricted to studies in humans, and used the search syntax:

> (antibacterial OR anti-bacterial OR antibiotic* OR anti-infective OR antimicrobial* OR anti-microbial* OR AMR) AND (preference* OR DCE OR conjoint* OR best-worst* OR BWS OR discrete choice*)

Databases searched:

|  | **PubMed** | **Embase** | **Econlit** | **PsychInfo** |
|---|---|---|---|---|
| **Date range searched** | 01/01/2005-12/02/2017 | 01/01/2005-12/02/2017 | 01/01/2005-12/02/2017 | 01/01/2005-13/07/2017 |

The literature search was undertaken in July 2017, and identified 3,066 papers. After removing duplicates, screening titles and abstracts, and then assessing full-text papers for eligibility, 89 papers met the inclusion criteria. In addition, 23 papers were identified from other sources (for example, papers that were already known to the study team). Overall, 112 papers were included.

116 potential attributes were identified in these papers. Attributes that might be important to general practitioners (GPs) in the context of this choice study were identified through discussion within the study team, which included 4 practicing GPs and a pharmacist. Related ideas were collapsed into single attributes where necessary (for example, the 'symptoms' attribute resulted from collapsing an attribute 'severity of symptoms' with specific symptoms such as 'colour of nasal discharge' and 'abnormal lung sounds'). 17 such attributes were then scored for importance by a convenience sample.

Table S1: Summary of attributes as scored by convenience sample of GPs

|  | Attributes | GPs (N=4) | |
|---|---|---|---|
|  |  | **Mean score** | **Rank** |
| 1. | Symptoms | 7.8 | 1= |
| 2. | Premorbid condition of patient | 7.8 | 1= |
| 3. | Risk of significant harm from not giving antibiotic treatment | 7.5 | 3= |
| 4. | Recommendation from guidelines, literature or local protocol | 7.5 | 3= |
| 5. | Degree of benefit from antibiotics | 7.3 | 5 |
| 6. | Length of illness | 6.5 | 6= |
| 7. | Risk of antibiotic resistance developing | 6.5 | 6= |
| 8. | Whether antibiotics are indicated by a diagnostic test | 6.3 | 8 |
| 9. | Patient's age | 6.0 | 9 |
| 10. | Length of consultation time available | 5.5 | 10= |
| 11. | Information on resistance patterns/rates (e.g. from antibiogram) | 5.5 | 10= |
| 12. | Risk of significant harm from giving antibiotic treatment | 5.3 | 12 |
| 13. | Number of days off work due to sickness | 4.8 | 13 |
| 14. | Pressure from patient or family to prescribe antibiotics | 4.0 | 14= |

| 15. | Probability that patient might acquire a bacterial infection, or that infection may recur | 4.0 | 14= |
|-----|-----|-----|-----|
| 16. | Financial incentives | 3.0 | 16 |
| 17. | Cost of antibiotics | 2.0 | 17 |

We aimed to describe the choice situations using 6-8 attributes, to be acceptable to respondents without making choices excessively complex. Further, we aimed to maximise overlap between this work and a related study among the general public, for comparability and to identify potential differences between patients and clinicians. This meant it was possible for some attributes to be excluded from this study, despite a high importance ranking, if they were less important to the public.

The four highest ranked attributes were initially selected for inclusion. However, on further review of the guidelines, we noted that these already incorporate symptoms and comorbidities as part of the decision process. An attribute indicating consistency with guidelines would therefore need to be aligned with the clinical features described, and as such would add limited additional information to the study (that is, it could not be independent of the symptoms and comorbidities). We therefore did not select this attribute.

'Degree of benefit from taking antibiotics' was important to GPs, and to the general public. However, capturing this as an attribute appeared problematic, as GPs will have their own views on likely benefit. Telling respondents what the degree of benefit is in an attribute-level did not therefore seem feasible. The attribute 'Risk of harm from not giving antibiotics' captures a similar concept (the degree of benefit is in avoiding the harms from not taking antibiotics), which was more readily captured in a numerical attribute derived from trial data. Hence we chose to use the attribute framed in terms of the risk of harm.

Length of illness was ranked sixth, was also important to members of the public, and is used in some diagnostic algorithms (e.g. FeverPAIN criteria for sore throat), and so was included.

Risk of antibiotic resistance developing had the same rank as length of illness. However, comments from respondents suggested this would should be couched at a personal rather than societal level (that is, the risk of this patient developing a resistant infection in the future), which realistically is not known. We therefore chose to incorporate this feature within 'risk of harm from giving antibiotic treatment', with 'harm' described as the risk of side effects, allergy, and resistance.

Diagnostic testing was important to both groups; however, there is no good test for RTIs in common use in primary care in the UK, so it was felt this attribute was unrealistic and it was not selected.

Although 'Length of consultation time' only got a moderately high rank, we felt it was important to include this for face validity. It takes time to explain what a delayed prescription is and why it is being given.

Attributes relating to patient characteristics (such as age, socioeconomic status) were potentially of interest – for example, one respondent commented that time taken off work could be a factor if their patient was of low socio-economic status and missing work could have important consequences. However, there are multiple possible variables we could have considered, and somewhat arbitrary choices would be needed to describe relevant patient profiles in a single attribute. We therefore chose to keep patient characteristics constant across scenarios, and acknowledge that further work may be needed on this question.

The format of delivering the delayed prescription was not part of this preliminary survey. It was included for policy relevance; the formats have been tested in clinical trials and referred to in guidelines, but there are no quantitative data on patient preferences.

Reference: FeverPAIN clinical score

Little P, Stuart B, Hobbs FDR, Butler CC, Hay AD, Campbell J, et al. Predictors of suppurative complications for acute sore throat in primary care: prospective clinical cohort study. BMJ : British Medical Journal. 2013;347:f6867. Scoring tool available at https://ctu1.phc.ox.ac.uk/feverpain/index.php

**SECTION 6. Design constraints**

Constraints on which levels of specific attributes could not appear together were suggested by reviewing designs run without any constraints, and checking for implausible combinations of levels.

1. If the level for Symptoms was 'Sore throat, swollen lymph nodes in the neck, pyrexia, and purulent tonsils' or 'Productive cough, pyrexia, and pain on breathing' then the following attribute levels were **not** permitted:

   - Duration: 10 days. It is unlikely that a patient would have been suffering a fever for such an extended period without seeking medical advice – or in fact would have had a fever for such a length of time without the condition either resolving or progressing.
   - Appointment: 5 minutes. It is implausible that even the busiest GP would spend only 5 minutes with a patient with a fever.
   - RiskNot: Negligible (1%). These symptoms are suggestive of bacterial tonsillitis, so the risk of illness continuing or worsening without antibiotics is higher than 1%.

2. If the level for Symptoms was 'Sore and red throat, and swollen lymph nodes in the neck' or 'Productive cough and runny nose' then the following attribute level was **not** permitted:

   - RiskNot: Likely (20%). These symptoms are likely to be a viral sore throat or a cold. NICE Clinical Guidance CG69 states: "*These conditions are largely self-limiting and complications are likely to be rare if antibiotics are withheld*". Hence we avoided scenarios that presented the risk of relapse or progression with no antibiotics as 'Likely'.

Reference:

NICE Clinical Guidance CG69. Respiratory tract infections (self-limiting): prescribing antibiotics (2008). https://www.nice.org.uk/guidance/cg69, accessed 5/12/19

## SECTION 7. Modelling the continuous variables as categorical

The models assume that the time and risk attributes can be represented as continuous variables, with a linear relationship with the outcome on the log-odds scale. In an exploratory analysis, these attributes were modelled and plotted as categorical variables.

The plot for risk due to delaying treatment suggested a threshold effect, with similar coefficients for the lower two attributes and a greater effect for the highest level. Conversely, the plot for duration of treatment showed a plateau, with the coefficient increasing with the attribute level then levelling off. Alternative models with these attributes as dichotomised variables showed marginally improved model fit though the results were qualitatively very similar. However, the models exhibited collinearity due to the restructuring of the variables, and there was insufficient information to determine exactly where the cut-off should be. As a result the linear approximation was retained in the models.