A randomised controlled trial of delayed antibiotic prescribing as a strategy for managing uncomplicated respiratory tract infection in primary care

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SUMMARY

Background: *Despite evidence that uncomplicated lower respiratory tract infection (cough) does not respond appreciably to antibiotics and that bacterial resistance is increasing, general practitioners (GPs) still prescribe frequently.*

Aim: *To assess delayed antibiotic prescribing as a strategy for reducing the unnecessary use of antibiotics for cough in primary care.*

Design of study: *Open randomised controlled trial of delayed versus immediate prescribing of antibiotics.*

Setting: *One hundred and ninety-one adult patients with uncomplicated cough in 22 Scottish practices who would have received antibiotics under the GP's usual practice were randomised to receive either an immediate prescription (92 patients) or a delayed prescription (99 patients).*

Method: *Delayed subjects were asked to wait a week before deciding whether to collect their prescription. Outcome measures included symptom duration, prescription uptake, patient satisfaction, patient enablement, and subsequent consultation rates. The 48 GPs who recruited patients were surveyed six months after the trial to see whether they used delayed prescribing as a part of their normal practice.*

Results: *Study and control groups were similar at baseline. Of the subjects in the delayed arm, 55% did not pick up their prescription. Although most patients were satisfied, more patients in the immediate arm were very satisfied with the treatment (P = 0.001) and the consultation (P = 0.03). The patients in the immediate arm were also more enabled (3.3 versus 2.4; P = 0.04), although more of them intended to consult for similar complaints in the future (85% versus 69%, P = 0.02). We were unable to detect any difference in actual consulting behaviour in the follow-up period (mean = 15 months [SD = 5 months]). Subsequently, 68% of GPs used delayed prescribing at least monthly; all gave the prescription to the patient.*

Conclusion: *Delayed prescribing is effective at reducing the use of antibiotics for self-limiting cough; however, patients are less satisfied and enabled as a result. Patients may be deterred from consulting rather than becoming enabled.*

Keywords: *antibiotic prescribing; uncomplicated lower respiratory tract infection; cough; consultation behaviour; patient enablement; patient satisfaction.*

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Introduction

COUGH is a common presenting symptom in primary care with acute conditions relating to the respiratory tract accounting for around 20% of practice consultations.[1] Despite considerable evidence that simple cough does not respond appreciably to antibiotics[2-4] and increasing concern about bacterial resistance,[5] general practitioners (GPs) continue to prescribe antibiotics regularly.[6,7]

Prescribing antibiotics can be an uncomfortable decision[8] which is reflected in the wide variation in prescribing rates for respiratory tract infections. Many GPs feel that antibiotics may be of some help with potential individual benefit outweighing any risk from resistant bacteria.[9] Often the development of resistance or cost to the practice is not considered[10] and the decision to prescribe an antibiotic needs less information than the decision not to prescribe.[11] A strategy that can help this dilemma without detriment to the patient would be of considerable value for practitioners who are unwilling to deny the demand they perceive from patients.

Little *et al*[12] found that delayed prescribing for the management of sore throats reduced the use of antibiotics without affecting symptom resolution. It was acceptable to patients and appeared to reduce future consultations. In this study we tested delayed prescribing in the management of uncomplicated cough.

Method

Subjects

The patients who were targeted were those who would normally have received an antibiotic but had no strong clinical indication for such treatment. Patients aged over 16 years presenting with acute cough as the primary complaint with or without coryza, shortness of breath, sputum, fever, sore throat or chest tightness were eligible for inclusion. Patients to whom the GP would not consider offering antibiotics, and those who expressed a strong preference for antibiotics, were excluded. Toxic patients perceived to require treatment; those with chest signs, immunosuppression, pre-existing lung disease, diabetics or patients for whom a return visit was unusually difficult or who declined the study were excluded.

Intervention

Eligible patients gave written consent within the consultation after reading and discussing a patient information sheet. The trial was introduced as a way of finding out if antibiotics are needed to manage simple cough. Subjects were either
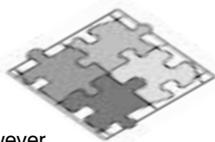
given a prescription for an antibiotic of the GP's choice
immediately or one was lodged at reception and patients
were invited to collect it after one week if required.

Setting

Ethical approval was granted by the Medical Research
Ethics committees in Tayside, Fife and Forth Valley.
Practices were approached between December 1997 and
November 1998. Recruitment was encouraged by maintain-
ing regular contact with surgeries, by producing a study
newsletter, and by reimbursing practitioners for time spent
on the study. In addition, a research nurse was seconded to
six practices for one week.

Sample size estimation

Using the patient as the unit of analysis it was calculated that
180 in each group would give an 80% chance of detecting a
mean difference in cough duration of one day at the 5% sig-
nificance level.

Randomisation

Each of the GPs' patients was randomised in balanced
blocks of four using random number tables. Sealed, num-
bered envelopes were used to ensure that the allocation was
blinded.

Patient data

GPs collected baseline data including symptoms at time of
presentation and the antibiotic prescribed.

Patients received a questionnaire to take home and com-
pleted the first section prior to treatment, including five ques-
tions about worries and satisfaction with the consultation on
a four-point Likert scale ('very', 'moderately', 'slightly', 'not at
all'). Patients were asked to record symptoms until they were
better or for 14 days after consultation (whichever was soon-
est); answered questions about the effectiveness of the
antibiotics, their intention to consult in the future; and com-
pleted Howie's patient enablement index.[13] Within three
days of the consultation each patient was contacted by tele-
phone to ensure that they understood the trial and ques-
tionnaire. If the diaries were not returned three weeks after
entry into the study then the patients were reminded twice,
either by telephone or by letter. Little *et al*[12] had shown pre-
viously that this approach produced reliable results.

The prescriptions of those in the delayed group were kept
at the practice reception and the date on which they were

collected was recorded. The questionnaire asked whether
they had had a prescription and whether the antibiotic was
taken. Uncollected prescriptions were removed after two
weeks.

Note review

At a minimum of six months post-recruitment, patients'
notes were reviewed. Data was collected on consultations
for similar complaints one year before randomisation, 28
days after randomisation, and thereafter. A consultation was
considered to be for a similar complaint if the notes men-
tioned cough, sore throat, shortness of breath, sputum/spit,
runny nose, nasal discharge or congestion, cold, upper or
lower respiratory tract infection, nasopharyngitis, bronchitis,
chest infection, sinusitis, tonsilitis or laryngitis.

A second blinded reviewer extracted the same information
from 40 sets of notes to assess observer bias. Details of the
randomisation episode were covered.

GP use of delayed prescribing

At the end of the trial the 48 practitioners who recruited
patients were surveyed about their subsequent use of the
delayed prescribing strategy.

Data analysis

Data were analysed on an intention-to-treat basis using
SPSS 9.0 for Windows. Data were analysed using non-para-
metric statistics to avoid assumptions of normality. The
kappa statistic was used to test for observer bias. A Poisson
regression with covariates was used to compare consulta-
tion rates after randomisation to allow for variable periods of
follow-up.

Results

Sixty-one practices were approached and 22 agreed to par-
ticipate. Out of 92 GPs, 48 recruited patients into the trial
(range = 1–25 per GP). One hundred and ninety-three
patients were randomised, of whom two were excluded as
they were without cough at baseline. Amoxycillin was the
most widely prescribed antibiotic (148/191 [77.5%]).

Questionnaires were received from 148 (78%) patients
(Table 1). There was no difference in the number of ques-
tionnaires returned between the immediate and delayed
arms or between those patients in the delayed arm who
picked up their prescription and those that did not. The
analysis was not restricted to complete datasets, therefore
denominators vary.

Baseline characteristics

There were no differences in baseline symptoms between
patients returning their questionnaires and those that did
not, or between treatments (Table 1). Within the delayed arm
there was no difference between patients who picked up
their prescription and those that did not.

Symptom duration

Figure 1 shows the probability of recovery from cough over
days 1 to 13 for each arm of the study. Even at the most

Table 1. Characteristics of patients in the immediate and delayed prescribing arms (values are percentages unless indicated otherwise).

Characteristic	Immediate prescription (n = 92)	Delayed prescription (n = 99)	Average (n = 191)	P-value
Males	43	34	39	0.2[a]
Mean age (years)	39.3	43.8	41.6	0.06[b]
Symptoms at baseline (mean number)	3.7	3.4	3.5	0.2[c]
Questionnaires returned	83	73	78	0.1[a]
Cough for ^1 week prior to consultation	60	54	57	0.8[a]
Symptoms at baseline				
Shortness of breath	27	21	24	0.3[a]
Sputum	74	74	74	1.0[a]
Fever	32	28	30	0.6[a]
Sore throat	56	46	51	0.1[a]
Runny nose	47	47	47	0.9[a]
Smoker	31	25	28	0.4[a]
Been in higher education	45	50	48	0.6[a]
Believe antibiotics to be effective for cough	70	63	66	0.4[a]
Taken time off work	31	36	33	0.8[a]
Median duration of cough pre-consultation (days)	4	4	4	0.7[c]

[a]χ^2; [b]z-test; [c]Mann–Whitney U.

divergent point the difference is not significant (global log-rank [Mantel—Haenszel] test, P-value >0.4). There was no difference in the duration of other recorded symptoms. At day 14, one-third of subjects still had cough.

Collection of prescriptions

Of the 95 patients in the delayed arm whose behaviour we could verify, 45% (43/95) collected their prescription. Thirty-five per cent (12/34) waited seven days as asked; however, the mean wait was six days (range = 1–10).

Patient attitudes

Groups had similar opinions on the effectiveness of antibiotics for cough and were worried to a similar extent about their own cough.

There was a high level of satisfaction with all aspects of the consultation and treatment — 132/147 (90%) of subjects overall were very or moderately satisfied. However, there was more dissatisfaction with treatment ('not very' or 'not at all' satisfied) in the delayed arm (9/67 [13%] versus 0%; P = 0.001) and more in the immediate arm were very satisfied with the consultation (P = 0.03). There was no difference in the level of satisfaction with advice or information received (Table 2).

The patients in the immediate arm were more enabled by their experience (patient enablement index: mean, interquartile range 3.3, [1–6] versus 2.4, [0–4]; Mann–Whitney U = 2221; P = 0.04).

The delayed subjects who did not pick up their prescriptions were significantly less worried about their coughs (P = 0.03). There was no difference in the enablement scores (2.2, [0–4] for those that did not pick up, versus 2.6 [0—5.5] for those that did; Mann–Whitney U = 621; P = 0.98).

Effects of GP recruitment rate

The rate at which GPs recruited patients (high = 18–25, low = 1–8) did not affect pick-up rate or enablement; however, more patients of low recruiters were very satisfied with the consultation (P = 0.004), with advice (P = 0.01), and with information (P = 0.04) (Table 2).

Consultation review

A single researcher reviewed 169/191 sets of case notes (88%). The information extracted was compared with a blinded second assessment for 40 sets of notes. There were two discrepancies (out of 40) in the coding for pre-randomisation visits (κ = 0.9), no discrepancies for visits within 28 days of randomisation, and four discrepancies (out of 40) for the post randomisation visits (κ = 0.84).

More in the immediate arm (63/74 [85%] versus 47/68 [69%]; χ^2 = 5.2; P = 0.02) and more of those in the delayed arm who picked up their prescription (23/26 [88%] versus 24/42 [57%]; χ^2 = 7.4; P = 0.007) intended to consult for similar complaints in the future.

Nineteen subjects (nine immediate, 10 delayed) returned within 28 days for persistent symptoms, one with complications (immediate) and one because of a reaction to the antibiotics (delayed). Ten received a prescription for an antibiotic at their return visit (five immediate, five delayed) two of whom received a further prescription within the month (one immediate, one delayed). Similar numbers from the two arms of the study had not reconsulted within the follow-up period (Table 3).

The strongest independent predictor of reconsultation in the next 28 days was the number of surgery visits in the previous two years.[14] Using pre-randomisation consultations, antibiotics prescribed and log (follow-up time) as covariates, no difference could be detected in average post randomisation consultation between the immediate and delayed prescribing arm.

Subsequent GP use of delayed prescribing

Forty-seven out of the 48 GPs (98%) returned the survey. Most GPs found delayed prescribing to be a useful strategy (41/47 [87%]); only three stated that they never used it. It was used when patients either asked for, or clearly wanted, an antibiotic when it was not clinically indicated; for patients

Table 2. Patient satisfaction (percentages) (a) according to when prescription was issued; (b) according to prescription collection (delayed group only); and (c) according to GP recruitment rate.

		Very satisfied		Moderately satisfied		Not very satisfied		Not at all satisfied		P-value (χ^2)
		Immediate (n = 75)	Delayed (n = 73)	Immediate	Delayed	Immediate	Delayed	Immediate	Delayed	
(a)	Consultation	73	54	27	43	0	3	0	0	0.03
	Advice	64	47	33	49	3	4	0	0	0.1
	Information	63	60	36	39	1	1	0	0	0.9
	Treatment	68	42	32	45	0	8	0	6	0.001
		Picked up prescription (n = 29)	Left prescription (n = 43)	Picked up prescription	Left prescription	Picked up prescription	Left prescription	Picked up prescription	Left prescription	
(b)	Consultation	41	63	52	37	7	0	0	0	0.07
	Advice	38	52	55	45	7	2	0	0	0.38
	Information	55	63	41	37	3	0	0	0	0.43
	Treatment	38	45	48	42	3	11	10	3	0.38
		Low recruitment (n = 95)	High recruitment (n = 52)	Low recruitment	High recruitment	Low recruitment	High recruitment	Low recruitment	High recruitment	
(c)	Consultation	74	46	25	52	1	2	0	0	0.004
	Advice	64	40	32	58	4	2	0	0	0.01
	Information	68	50	30	50	2	0	0	0	0.04
	Treatment	58	50	37	40	2	6	2	4	0.54

Table 3. Consultations for similar complaints (percentages).

	Immediate prescription (n = 82)			Delayed prescription (n = 85[a])			P-value (χ^2)
	None	One	More than one	None	One	More than one	
One year pre-randomisation							
Visits	61	22	17	61	26	13	0.22
Antibiotics	71	20	10	69	23	8	0.89
Within 1 month post randomisation							
Visits	88	9	4	88	8	4	0.31
Visits for persistent symptoms	89	7	4	88	8	4	0.2
Visits for complications	99	1	0	100	0	0	0.31
Visits for reaction to antibiotics	100	0	0	99	1	0	0.33
Antibiotics within one month	94	5	1	94	5	1	0.99
Within total follow-up period							
Visits	60	17	23	61	24	15	0.58
Antibiotics	68	21	11	78	12	10	0.23

[a]One patient was randomised at the first visit to the practice so there was no record of pre-randomisation results.

who preferred to avoid antibiotics or if there was a possibility that symptoms might get worse. Thirty-two out of 47 (68%) used delayed prescribing every month or more frequently and all gave the prescription to the patient.

Discussion

This was a pragmatic trial to test a strategy designed to reduce unnecessary antibiotic prescribing for uncomplicated cough. The randomisation was carried out successfully; however, our sample was inadequate for excluding small differences in clinical outcome. We cannot estimate what proportion of appropriate patients were recruited, as GPs did not collect accurate data on all patients presenting with cough. The average GP sees 10 cases of upper respiratory tract infection per week.[15] Data from the Continuous Morbidity Recording Evaluation Project[16] indicates that up to

51% would be excluded from the trial by virtue of age or co-morbidity. We do not know how many of the remaining four or five patients accepted no treatment, declined the trial or received antibiotics. By definition our recruitment process sought patients who were willing but not keen to accept no treatment; this proved to be a difficult assessment to make. Our low recruitment rate could introduce a selection bias, however, this is a common problem in comparable trials. As the two groups had similar characteristics at the start, 78% of patients returned their questionnaire and the randomisation process was successful, the results should be generalisable to those patients who expect but do not need antibiotics. It is hoped that encouraging patients to delay taking antibiotics will eventually break the cycle of expectation and demonstrate that their illness can be managed effectively without antibiotic use.
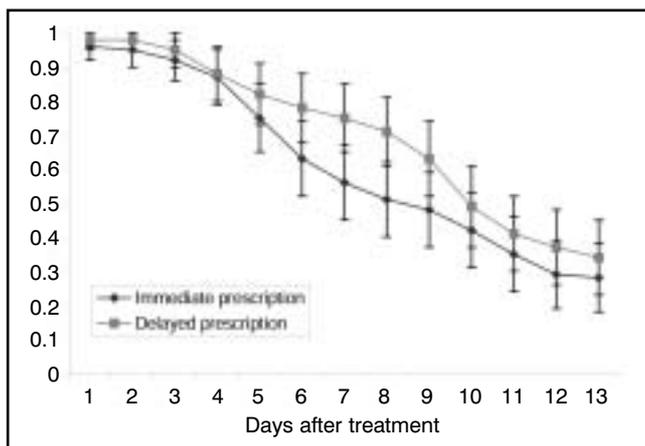
Figure 1. Probability of cough continuing.

Delayed prescribing is effective at reducing the use of antibiotics for self-limiting cough. Fifty-five per cent of patients in the delayed arm did not return to collect their prescription compared with 69% of patients with sore throat in the study by Little et al.[12] The median duration for cough was 9 or 10 days and we asked patients to wait for seven days to reflect the different natural history of the diseases. It would have been helpful to have had a longer period of follow-up as such a high proportion of patients still had cough at 14 days; however, this may have lowered the response rate. More persistent symptoms were consistent with a greater proportion of patients returning for their prescription.

Amoxycillin, a broad-spectrum penicillin, was more widely prescribed than in a recent survey of 115 GPs[6] (77.5% versus 58%) and also more than in Norway[17] where Penicillin V is most frequently prescribed and where antibiotic resistance is still a relatively minor problem. The use of Penicillin V should be encouraged to reduce the danger of debatable antibiotic prescribing.

There was no difference between the two groups in how worried the patients were about their cough; 63.7% of subjects were very or moderately worried about their cough. Patients who consult with cough think that their cough is abnormally severe[18] and that they have an infection that would be helped by antibiotics.[19] Those who picked up their prescriptions were more worried about their cough than those who did not, as might be expected.

Although most of the patients in our study were satisfied, those in the delayed arm were less satisfied with both the treatment and the consultation, a similar finding to Little et al.[12] This is of concern, since there is evidence to suggest that satisfaction with the consultation can predict the duration of illness.[20] Agreement between doctor and patient on the nature of illness is a predictor of symptomatic recovery[21] and dissatisfaction may lead to increased reconsultation for persistent symptoms.[19] Satisfaction with the consultation was greater for those who did not collect their prescription; this group also recovered faster. The greater satisfaction in patients recruited by low-recruiting GPs may indicate that these GPs approached patients who had fewer reservations about the trial.

The mean patient enablement index was 2.8 overall, compared with a mean score of 3.1 in the study by Howie et al.[22]

In their study, patients who wanted, but did not get, a prescription also reported lower enablement. These findings suggest that delayed prescribing may leave patients less satisfied, thus dissuading them from returning to their GP rather than empowering them to manage self-limiting illness with confidence.

Above-average prescribing for acute respiratory illness is associated with higher consultation rates.[23] Little et al[24] demonstrated that an effective way of counteracting increased consultation is for GPs not to prescribe antibiotics so that patients are less likely to reconsult and expect an antibiotic in the future. We were unable to demonstrate a difference in reconsultation rate between the two arms of the study; however, more patients in the immediate group reported an intention to consult for similar complaints in the future.

Delayed prescribing is a useful strategy now used regularly by the GPs who took part in this study. Whether the reduction in the use of antibiotics will be as great as in the trial is debatable, as the prescriptions are given to the patient rather than held for them at the surgery. It is much simpler to suggest a delayed prescription in practice than to explain the rationale for a trial such as this. However, if practitioners give delayed prescriptions to patients they may tend to prescribe more readily, thus avoiding potentially confrontational discussions,[25] and a higher proportion may be encashed. Future studies of delayed antibiotic prescribing should assess this variation as it may affect the subsequent encashment rate or patient satisfaction. The reasons behind any reduction in future consultation also need further investigation.

Acknowledgements

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