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Antibiotics for acute cough:

an international observational study of patient adherence in primary care

Abstract

Background
Non-adherence to acute antibiotic prescriptions is poorly described and may impact on clinical outcomes, healthcare costs, and interpretation of research. It also results in leftover antibiotics that could be used inappropriately.

Aim
To describe adherence to antibiotics prescribed for adults presenting with acute cough in primary care, factors associated with non-adherence, and associated recovery.

Design and setting
Prospective observational cohort study in general practices in 14 European primary care networks.

Method
GPs recorded patient characteristics and prescribing decisions for adults with acute cough or clinical presentation suggestive of lower respiratory tract infection. Patients recorded antibiotic consumption and daily symptoms over 28 days. Rates of adherence to prescribed antibiotics were assessed, and factors associated with non-adherence were identified using logistic regression. Recovery was compared using a Cox proportional hazards model.

Results
Of 2520 patients prescribed immediate or no antibiotics at the index consultation, 282 (11.2%) took an antibiotic during the follow-up period that was not prescribed for them at the index consultation. Of these, 38.1% had no reconsultations during this period. Prior duration of symptoms, antibiotic treatment duration, antibiotic choice, and primary care network were all associated with adherence. There was no difference in time to recovery between those who were prescribed antibiotics at the index consultation and were fully adherent, partially adherent, and non-adherent.

Conclusion
Non-adherence to antibiotics for acute cough or lower respiratory tract infection is common. Duration of treatment, choice of antibiotic, and setting were associated with adherence but adherence to treatment was not associated with differences in recovery.

Keywords
anti-bacterial agents; cough; general practice; medication adherence; respiratory tract infections.

INTRODUCTION

Poor adherence to prescribed medication is common and compared to high levels of adherence, it can result in worse health outcomes and increased costs.[1] Although adherence to medication for long-term conditions has been frequently studied,[2] adherence to short-term prescriptions, such as antibiotic courses, is less well described. Incomplete adherence to antibiotics wastes healthcare resources and may impact on clinical outcomes (if the prescription was targeted at an individual likely to benefit). Non-adherence, or incomplete adherence, results in leftover antibiotics, which are often kept and used at a later date or given to others.[3,4] Such use could also impact negatively on recovery and increase the selective pressures for antibiotic resistance. Clinical studies of antibiotic use — such as studies of interventions designed to modify antibiotic use, studies exploring the relationship between antibiotic use and the development of antibiotic resistance, and studies looking at the effectiveness of antibiotics in preventing severe infections or complications — usually equate antibiotic prescribing with antibiotic use. If non-adherence and incomplete adherence are common however, this assumption is not valid and the results of such studies have to be called into question.

Approximately 80% of all courses of antibiotics are prescribed in primary care, with respiratory tract infections being the most common indication[5] — over 50% of patients with acute cough/lower respiratory tract infection are prescribed antibiotics in primary care.[6] However, the relationship between prescribing and consumption is not clearly understood. Studies of antibiotic adherence in secondary care[7] or in clinical trial settings[8–10] are unlikely to provide a reliable indication of adherence in routine primary care practice. Furthermore, measuring only the consumption of the antibiotic prescribed at an individual consultation will not provide a true picture of overall antibiotic use, including use of leftover antibiotics, shared antibiotics, over-the-counter antibiotics, and antibiotics prescribed during subsequent consultations

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Submitted: 6 September 2011; **Editor's response:** 9 November 2011; **final acceptance:** 9 January 2012.

How this fits in

Adherence to antibiotics for acute cough using observational studies of routine clinical care is not well described. The study found that non-adherence to antibiotics for acute cough or lower respiratory tract infection is common, with over half of patients who were prescribed antibiotics not adhering to the full course, and over 40% not taking any of the prescribed course. Around 10% took antibiotics that were not prescribed at the index consultation. Having symptoms for 28 days or more prior to consulting was associated with greater adherence and antibiotic courses longer than 5 days were associated with worse adherence. Choice of antibiotic, and research network, were also associated with differences in adherence. Adherence to treatment was not associated with differences in recovery. These data should inform physician patient communication about antibiotic treatment, as well as interpretation of research relating antibiotic prescribing to antibiotic consumption, clinical outcomes and antibiotic resistance.

for that illness episode.

Adherence to medication should not be an end point in itself;[2] it is important to also assess the association between adherence and outcomes. Therefore, the study set out to describe:

- antibiotic consumption for adults presenting in primary care with acute cough/lower respiratory tract infection who were, and were not, prescribed antibiotics;
- adherence to the prescribed treatment course in those who were prescribed antibiotics;
- factors associated with non-adherence; and
- the association between antibiotic treatment, adherence, and recovery.

METHOD

Study design

This was a prospective observational study in 14 primary care research networks in 13 European countries. The overall aim was to describe the presentation, management, and outcome of acute cough/lower respiratory tract infection in primary care, and the variation between contrasting European settings. More details, including recruitment methods and time periods, on this observational GRACE (Genomics to combat Resistance against Antibiotics in Community-acquired lower respiratory tract infection in Europe; www.grace-lrti.org) study of acute cough/lower respiratory tract infection can be found elsewhere.[6,11–14]

Participants

Participating clinicians were asked to identify, during routine consultations, consecutive patients who were eligible and invite them to participate in the study. Those who were eligible were aged ≥18 years, consulting with an illness where an acute or worsened cough was the main or dominant symptom, or had a clinical presentation that suggested a lower respiratory tract infection that had been present for ≥28 days.

Data collection

Clinicians recorded aspects of patients' history, symptoms, comorbidities (diabetes; chronic lung disease, including chronic obstructive pulmonary disease (COPD); and cardiovascular disease), clinical findings, and their management on a case report form at the time of first presenting in primary care. Clinicians recorded whether or not they prescribed antibiotics and, if they did, the name, dose, and duration of that antibiotic.

Patients completed a daily diary for 28 days, which included the day they felt better, their satisfaction with the consultation, and weekly details on antibiotic consumption, including antibiotic name, dose, and days taken.

A formal power calculation for the current analyses was not conducted as all available data from the original study were used. The original sample size calculation was based on giving 95% confidence intervals (CIs) of 44 to 56 around an estimated antibiotic prescribing rate within each network of 50%.[6]

Analysis

Descriptives. Patient-reported weekly medication use was categorised as an antibiotic or not by manually inspecting and coding free text in the patient-completed diaries. Antibiotics were categorised as one of the following: amoxicillin, co-amoxiclav, doxycycline, clarithromycin, azithromycin, cephalosporins, quinolones, phenoxymethylpenicillin, spiramycin, erythromycin, and other (which included other tetracyclines, other macrolides, sulfonamides/trimethoprim, and fusafungine). Ambiguous responses were discussed by the study team and classified, or recorded as missing, depending on

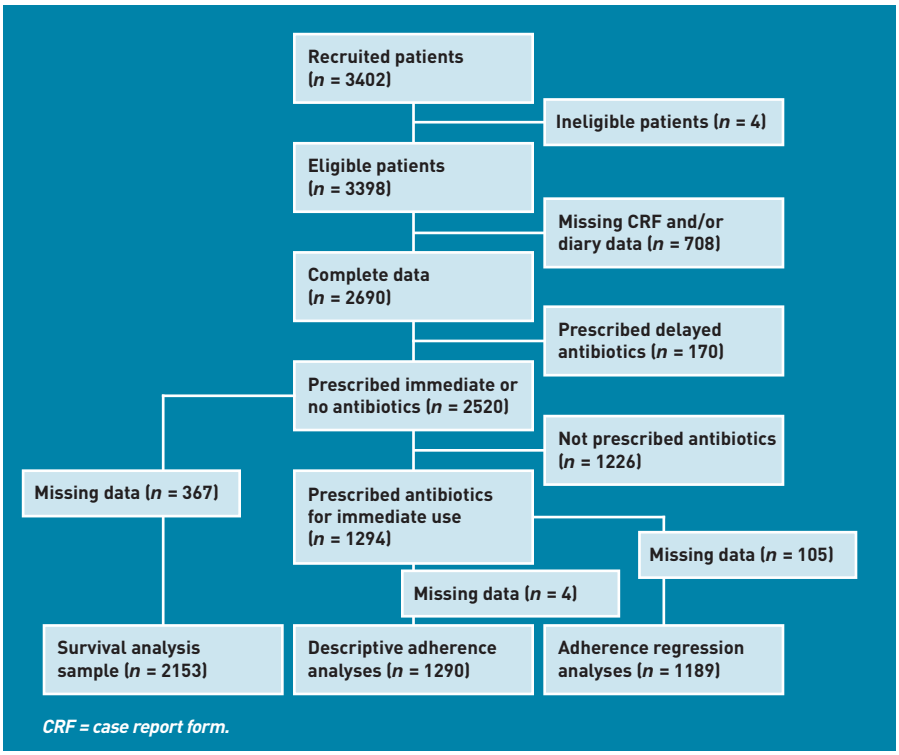


Figure 1. Patient flow diagram.

group consensus. Patients who had been prescribed antibiotics, but for whom the prescribing clinician had indicated that those antibiotics were intended for delayed use, were excluded as consumption in this group has different implications. Calculations were done to ascertain the proportion of patients who reported taking:

- the antibiotic prescribed at the index consultation for the full prescribed course;
- the antibiotic prescribed at the index consultation for only part of the prescribed course;
- none of the prescribed course, but antibiotics from another source during the 28-day follow-up period; and
- no antibiotics during the follow-up period.

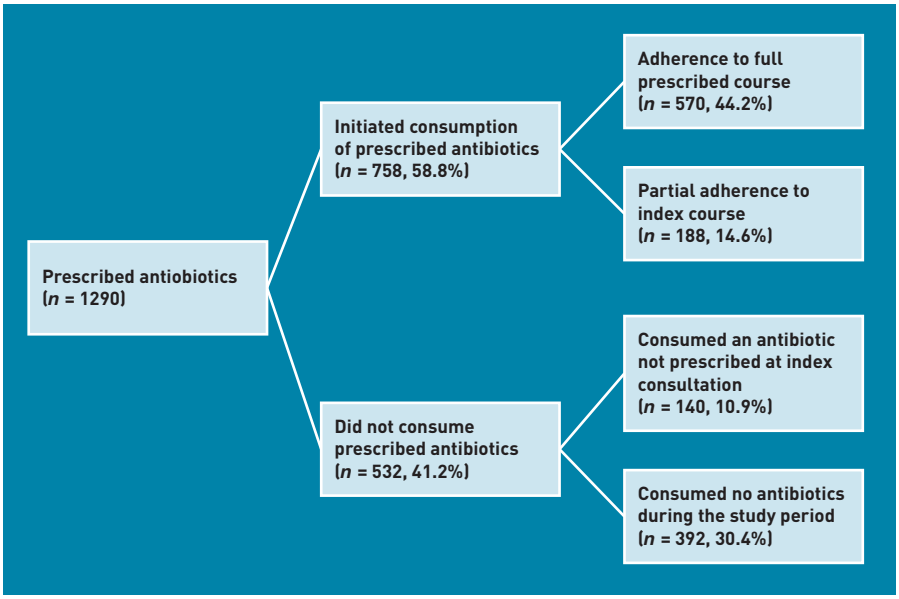


Figure 2. Antibiotic consumption among those prescribed antibiotics for immediate use.

Modelling

Adherence/non-adherence. The study was unable to identify a standard definition of adherence to antibiotic therapy in the literature; therefore, adherence was defined as consuming the complete prescribed antibiotic course.[7] A two-level hierarchical logistic regression model, with patients nested within clinicians, was fitted using MLwiN (version 2.2) to patients who were prescribed immediate antibiotics to investigate factors associated with adherence. Variables in the model included:

- patient characteristics (age, sex, and comorbidities);
- the number of days the patient had the illness before consulting their clinician;
- clinician-rated symptom severity at consultation;[6]
- the clinician's working diagnosis.
- antibiotic class;
- frequency of antibiotic dose;
- patient's hope for antibiotics to be prescribed;
- clinicians' perception of patient expectations for antibiotics;
- the prescribing rate of each clinician in the model; and
- the network in which a patient presented.

Time until patient reported recovery. A two-level hierachical (patients nested within clinicians) Cox proportional hazards model was fitted using Stata (version 10; StataCorp LP) to investigate whether time to reported recovery varied between patients who were:

- prescribed an antibiotic at the index consultation and fully adherent to the course;
- prescribed an antibiotic at the index consultation, not fully adherent to index antibiotics but who did consume some of the index antibiotics or an alternative antibiotic;
- prescribed an antibiotic at the index consultation and consumed no antibiotics during the next 28 days;
- not prescribed an antibiotic at the index consultation but consumed an antibiotic

Table 1. Consumption of an antibiotic prescribed at index consultation, and any antibiotic consumption during the subsequent 28 days, by primary care network

Network	Number of participants	Number prescribed antibiotics (for immediate use)	Of those prescribed antibiotics at the index consultation, *n* (%)			
			Initiated antibiotics (consumed at least 1 day)	Adhered to at least a 3-day course of antibiotics	Adhered to full prescribed antibiotic course	Consumed an antibiotic at any point during the study follow-up period
Antwerp (Belgium)	164	38 (23.2)	26 (68.4)	25 (65.8)	12 (31.6)	29/38 (76.3)
Balatonfüred (Hungary)	320	208 (65.0)	165 (79.3)	164 (78.8)	139 (66.8)	190/208 (91.3)
Barcelona (Spain)	169	29 (17.2)	18 (62.1)	18 (62.1)	10 (34.5)	26/29 (89.7)
Bratislava (Slovakia)	299	249 (83.3)	75 (30.1)	73 (29.3)	57 (22.9)	85/249 (34.1)
Cardiff (Wales)	181	124 (68.5)	57 (46.0)	54 (43.5)	47 (37.9)	67/124 (54.0)
Helsinki (Finland)	90	34 (37.8)	30 (88.2)	30 (88.2)	23 (67.6)	30/34 (88.2)
Jönköping (Sweden)	222	75 (33.8)	59 (78.7)	58 (77.3)	41 (54.7)	63/75 (84.0)
Lodz (Poland)	221	142 (64.3)	98 (69.0)	98 (69.0)	77 (54.2)	113/142 (79.6)
Mataró (Spain)	179	57 (31.8)	24 (42.1)	24 (42.1)	18 (31.6)	47/57 (82.5)
Milan (Italy)	153	102 (66.7)	64 (62.7)	62 (60.8)	43 (42.2)	80/102 (78.4)
Rotenburg (Germany)	181	58 (32.0)	32 (55.2)	32 (55.2)	23 (39.7)	41/58 (70.7)
Southampton (England)	168	52 (31.0)	24 (46.2)	22 (42.3)	20 (38.5)	29/52 (55.8)
Tromsø (Norway)	148	42 (28.4)	36 (85.7)	36 (85.7)	21 (50.0)	40/42 (95.2)
Utrecht (Netherlands)	195	80 (41.0)	50 (62.5)	50 (62.5)	39 (48.8)	58/80 (72.5)
Overall	2690	1290/2690 (48.0)	758/1290 (58.8)	746/1290 (57.8)	570/1290 (44.2)	898/1290 (69.6)

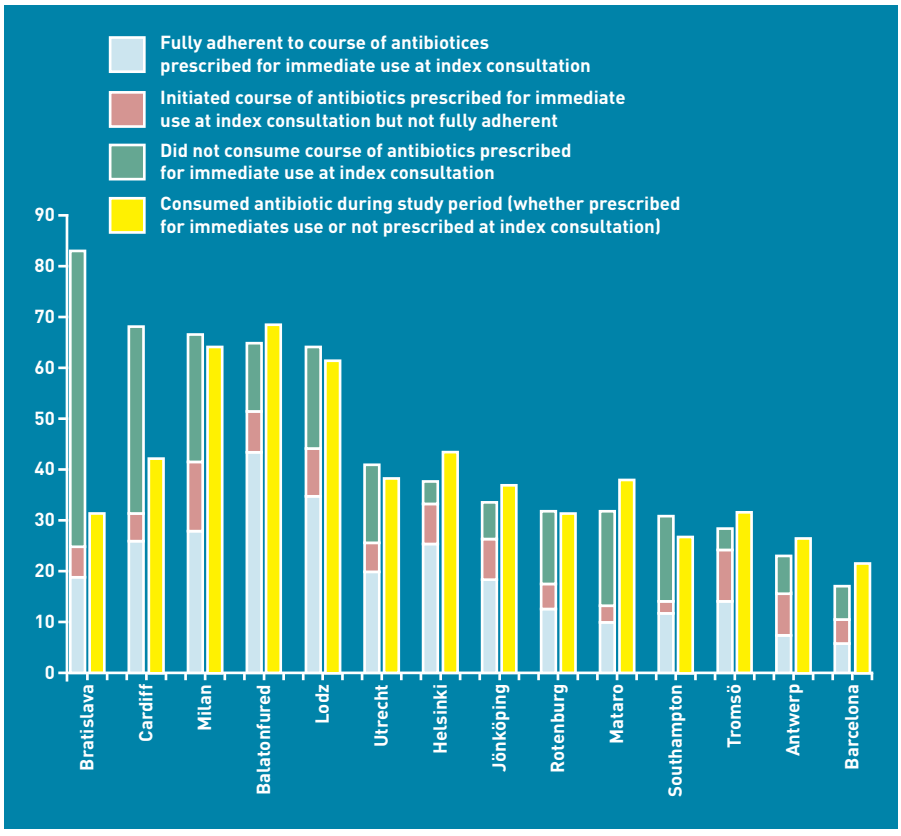
during the next 28 days; and

- not prescribed an antibiotic at the index consultation and consumed no antibiotics during the next 28 days.

Clinical presentation was controlled for:

- 13 of the 14 clinician-recorded symptoms at index consultation (cough was excluded as it was an inclusion criterion);
- temperature;
- age;
- comorbidities;
- smoking status; and
- duration of illness prior to the consultation.

Figure 3. Variation in antibiotic consumption by patients with acute cough/LRTI in 14 European primary care networks.



RESULTS

Figure 1 illustrates the recruitment process. In total, 387 GPs recruited 3398 patients who were eligible. Complete follow-up data (both case report form and diary) were obtained for 2690 (79.1%) patients. A total of 170 patients were prescribed delayed antibiotics, leaving 2520 for analysis. Of these, 1294 were prescribed antibiotics for immediate use and 1226 were prescribed no antibiotics at the index consultation. Of those who were prescribed antibiotics, data on the type of antibiotic consumed was missing for one participant and the reported number of days of consumption was missing for three participants.

Use of antibiotics

In total, 532 (41.2%) of the 1290 patients who were prescribed immediate antibiotics and for whom follow-up data were available did not consume any of their antibiotic course, and 392 (30.4%) did not consume any antibiotics during the follow-up period (Figure 2). Only 570 (44.2%) consumed the entire prescribed treatment course.

Of the 1226 who were not prescribed antibiotics at the index consultation, 142 (11.6%) consumed an antibiotic at some

Table 2. Association between clinical characteristics and adherence to prescribed antibiotic course in 1189 patients prescribed immediate antibiotics by 251 clinicians[a]

(Dependent variable: adherent to full prescribed course), 1189 patients nested within 251 clinicians	Odds ratio	95% CI Lower	95% CI Upper	*P*-value
Patient characteristics				
Age, decades	1.01	0.92	1.11	0.784
Sex (reference category: female)				
Male	1.09	0.83	1.43	0.529
Comorbidities (reference category: no comorbidities)				
At least one comorbidity	1.08	0.79	1.48	0.614
Days waited before consulting for this illness (reference category: ≤7 days)				
8–14 days	1.30	0.89	1.91	0.172
15–21 days	1.12	0.64	1.95	0.694
22–28 days	1.15	0.33	3.95	0.827
>28 days	2.92	1.04	8.20	0.042
Patient illness information, clinician-rated symptom severity at consultation[b]	1.03	0.93	1.14	0.566
Clinician's working diagnosis (reference category: LRTI)				
Asthma/COPD related	0.73	0.44	1.19	0.207
URTI	1.17	0.85	1.59	0.334
Non-specific RTI	1.48	0.88	2.49	0.137
Viral/other non-specific illness	1.36	0.83	2.21	0.217
Pneumonia	1.24	0.66	2.35	0.499
Clinician-level characteristic, prescribing rate[b]	1.02	0.94	1.10	0.538
Clinicians' perception that the patient wanted antibiotics (reference category: clinician does not agree)				
Clinician agrees	0.95	0.72	1.24	0.707
Patient behaviour (reference category: did not want antibiotics)				
Wanted antibiotics	0.82	0.62	1.09	0.177
Class of antibiotic prescribed (reference category: amoxicillin)				
Azithromycin	1.51	0.65	3.51	0.342
Cephalosporins	1.10	0.57	2.15	0.773
Clarithromycin	1.60	0.91	2.83	0.104
Co-amoxiclav	1.80	1.11	2.92	0.017
Doxycycline	0.72	0.38	1.39	0.333
Erythromycin	1.22	0.35	4.23	0.753
Other	1.99	0.85	4.63	0.112
Phenoxymethylpenicillins	0.87	0.35	2.17	0.773
Quinolones	2.76	1.29	5.91	0.009
Spiramycin	2.42	1.02	5.77	0.046
Frequency of antibiotic dose (reference category: once a day)				
Twice a day	0.84	0.53	1.31	0.438
3 times a day	0.92	0.51	1.68	0.791
≥4 times a day	1.12	0.44	2.83	0.816
Duration of antibiotic course (reference category: ≤5 days)				
6 or 7 days	0.57	0.39	0.86	0.007
8 or 9 days	0.19	0.10	0.38	<0.001
≥10 days	0.28	0.16	0.48	<0.001
Primary care network (reference category: Antwerp)				
Balatonfured	2.09	0.79	5.54	0.140
Barcelona	1.01	0.29	3.54	1.000
Bratislava	0.34	0.12	0.92	0.035
Cardiff	0.66	0.25	1.76	0.405
Helsinki	6.96	2.02	24.02	0.002
Jönköping	5.34	1.77	16.14	0.003
Lodz	1.43	0.53	3.84	0.476
Mataro	0.53	0.18	1.55	0.246
Milan	0.56	0.20	1.58	0.273
Rotenburg	0.92	0.33	2.59	0.877
Southampton	0.77	0.25	2.32	0.637
Tromsø	3.02	0.97	9.40	0.057
Utrecht	2.56	0.89	7.34	0.081

COPD = chronic obstructive pulmonary disease. LRTI = lower respiratory tract infection. RTI = respiratory tract infection. URTI = upper respiratory tract infection. [a]The clinician level intraclass correlation coefficient (using the standard $\pi^2/3$ estimator) was 0.03. [b]Odds ratio for a 10 percentage point increase.

point during the 28-day follow-up period. A total of 282 patients (11.2% of the total and 26.4% of those who reported taking an antibiotic at some point) took an antibiotic that was not prescribed for them at the index consultation (140 who were prescribed immediate antibiotics and 142 who were not prescribed antibiotics). Of the 260 of these for whom there were data on reconsultations, 99 (38.1%) reported no consultations with a healthcare professional (excluding pharmacist) during the study follow-up period. Antibiotic prescribing and consumption varied by primary care network (Table 1), and the relationship between antibiotic prescribing and consumption was not consistent across networks (Figure 3). Differences in the proportion of patients prescribed antibiotics between networks were much greater than differences in antibiotic consumption at any point during the follow-up period at the network level.

Factors associated with adherence

In the multivariable analysis, an antibiotic course of >5 days and being in the Bratislava network were both associated with a reduced odds of adhering to the antibiotic course. Waiting for >28 days with an illness before consulting (compared with waiting ≤7 days); being prescribed co-amoxiclav, quinolones, or spiramycin; and being in the Helsinki or Jönköping networks were all associated with an increase in the odds of adhering to the antibiotic course. Age, sex, comorbid illness, clinician-rated severity of illness at presentation, clinician working diagnosis, frequency of antibiotic dosing, clinician prescribing rate, patient desire for antibiotics, and clinicians' perception of patient expectations were not significantly associated with adherence to the antibiotic course (Table 2). There was little clustering by clinician (intracluster correlation coefficient = 0.03), suggesting that individual clinician factors play little role in influencing adherence.

Time until patient reported recovery

Survival analysis of time to recovery found no significant association in differences in recovery between:

- those who were prescribed antibiotics and were fully adherent (reference category), and those who were prescribed antibiotics and were not fully adherent but consumed some antibiotics (hazard ratio [HR] 1.09; 95% CI = 0.93 to 1.27; $P = 0.296$),
- those who were prescribed antibiotics but

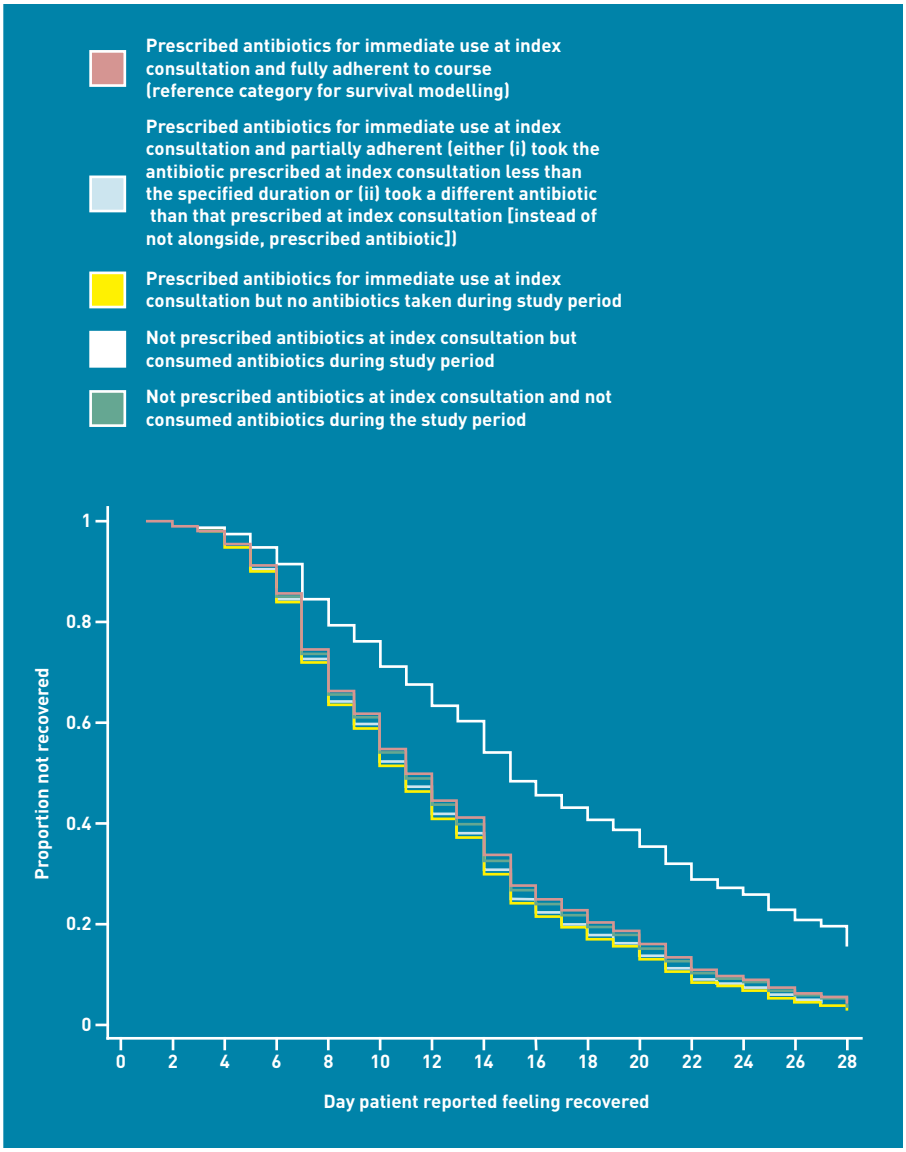


Figure 4. Time to patient-reported recovery in 2153 patients consulting for acute cough/LRTI with primary care clinicians in 14 European primary care networks.

did not consume any antibiotics (HR 1.11; 95% CI = 0.94 to 1.32; *P* = 0.209) and those who were not prescribed antibiotics and did not consume any antibiotics (HR 1.03; 95% CI = 0.90 to 1.18; *P* = 0.625).

However, those who were not prescribed antibiotics, but took antibiotics at some point in the study period, were associated with a slower recovery rate (HR 0.54; 95% CI = 0.43 to 0.68; *P*<0.001) (Figure 4).

DISCUSSION

Summary

Approximately 60% of adults prescribed antibiotics for acute cough/lower respiratory tract infection did not adhere fully to the prescription, and some 40% reported taking none of the antibiotics prescribed at the index consultation. More than one in 10 patients reported taking antibiotics not prescribed for them at the index consultation, and more than a third of those who consumed antibiotics not prescribed at the index consultation reported having no subsequent consultations during the study period. Duration of symptoms prior to consulting, duration of antibiotic course, choice of antibiotic, and regional factors were all associated with differences in adherence. Adherence to antibiotics prescribed for acute cough/lower respiratory tract infection was not associated with difference in recovery.

Strengths and limitations

This prospective study of >2500 adults presenting with acute cough/lower respiratory tract infection in the community included 14 primary care networks in 13 European countries and allowed for meaningful descriptions of antibiotic prescribing and adherence. The multinational nature of the study increases generalisability of findings and allowed for comparisons between primary care networks.

As there was no experimental intervention, clinicians were asked to record their usual practice and patients recorded antibiotic consumption prospectively; as such, these results are likely to closely represent the usual behaviour of clinicians and patients. Patients recorded the names of all medication consumed, together with the days on which the medication was taken. Although pharmacists were allowed to change from a branded to a generic prescription in some networks, the comparisons were based on the active ingredient and, therefore, this would not have affected this study's findings. As a result, the study was able to assess whether patients took the same antibiotic that was prescribed for them and whether they took it for the recommended length of time. The fact that patients reported the day they felt recovered allowed the impact of adherence with prescribed antibiotics on recovery to be assessed.

There is a risk of response bias; diary return rates varied from 60% in the Cardiff network to nearly 100% in the Bratislava network. There are no data to inform assumptions about the rate of adherence in those who did not return their diaries, but it seems unlikely that those who did not follow instructions to return a research diary would be more likely to follow instructions to consume antibiotics compared with those

who did return their diaries. Therefore, the adherence rate measured in this study may be an overestimate, rather than an underestimate, of actual adherence.

Ascertainment bias is also a possibility. Medication use was measured through self-report and, although the dosing frequency that was directed on the prescription was known, patients were only asked to record whether or not they consumed the medication on each day, and not how many times a day they took that medication. Electronic measurement of medication use may be more accurate than self-report. Leftover antibiotics were not counted but awareness that an electronic device is monitoring one's behaviour may, in itself, affect medication use. Furthermore, self-report by diary has been shown to have moderate-to-high concordance with measurement of adherence through objective measures.[8]

Conclusions about rates of recovery need to be interpreted with caution. As these are observational data, confounding by indication cannot be completely excluded.

Comparison with existing literature

A systematic review and meta-analysis of adherence to antibiotic therapies (for all indications) in the community, which used 51 estimates from 46 studies and included 29 291 participants, found an overall adherence rate of 62.2% (95% CI = 56.4 to 68.0).[15] In the 14 estimates involving 7204 participants in whom antibiotics were prescribed for respiratory tract infections, the rate of adherence was slightly higher at 72.6% (95% CI = 65.5 to 79.7). However, there were studies included in this review that included only children,[16–19] were conducted in resource-poor[17,20,21] or secondary care settings,[7] and/or included small numbers. Furthermore, a number of different methods of measuring and defining adherence were used.

In studies where adherence was assessed by patient-completed questionnaire, most of which defined adherence as completing the antibiotic course, the mean adherence rate was 55.3% (95% CI = 44.4 to 66.1).[15] Adherence was also lower in studies of adults than in studies of children or studies of children and adults.[15] The adherence rate of 44.2% is lower than all of these estimates, although the CIs overlap with other studies that used patient-completed questionnaires (use of diaries was not reported) and was higher than the adherence rate found in studies using the electronic Medication Event Monitoring System devices (30.0%; 95% CI = 18.0 to 41.9).

An observational study of antibiotic treatment of lower respiratory tract infection in outpatients found higher rates of adherence than found in the study: 55% adherence to 80% of the prescribed medication for those with thrice daily dosing and 87% for those prescribed an antibiotic with once daily dosing.[7] However, those patients were recruited from a medical outpatient setting rather than primary care and, likely, had more severe illness. For example, 58% of participants in that study had exacerbations of COPD, compared with only 2.8% of participants in the current study.[13] No previous observational study has measured adherence to antibiotics for acute cough/lower respiratory tract infection in adults in primary care.

A lower number of daily antibiotic doses has been associated with greater adherence,[7,9,22–24] and this is consistent with evidence on adherence to non-antibiotic medication. A relationship between number of daily doses and adherence was not found in the current study. This may have been because antibiotic consumption was measured on a day-by-day basis rather than a dose-by-dose basis, or may have been because choice of antibiotic was included in the current model; this is closely correlated with the number of daily doses. The finding that those who had the longest duration of illness prior to consulting were more likely to adhere is not surprising; these individuals are more likely to be motivated to take treatment. However, waiting 1–3 weeks before consulting was not associated with greater odds of adherence.

It is not clear why greater adherence was found in those prescribed co-amoxiclav, quinolones, and spiramycin. Although the study controlled for symptom severity, there may have been some residual confounding, with those who had more severe symptoms being more likely to be prescribed these antibiotics and more likely to adhere. This study's finding that a longer duration of treatment was associated with lower adherence is consistent with other studies.[25] Illness severity and poor communication within the consultation,[25] country of residence, age, attitude to the doctor, and attitude to antibiotics have all been associated with differences in adherence to antibiotic prescriptions.[26]

Although no attempt was made to measure aspects of clinician–patient communication, there is some evidence that clinicians do not consistently provide clear communication in consultations for

Funding

This study was funded by 6th Framework Programme of the European Commission (LSHM-CT-2005-518226). The South East Wales Trials Unit and the Wales School of Primary Care Research are funded by the National Institute for Social Care and Health Research. Dr Nick Francis is a senior clinical research fellow with the Wales School of Primary Care Research. The Antwerp Primary Care Network was supported by the Research Foundation — Flanders

Ethical approval

Ethical approval was obtained from ethics committees in all participating countries.

Provenance

Freely submitted; externally peer reviewed.

Competing interests

The authors have declared no competing interests.

Acknowledgements

We would like to thank all patients, clinicians, and networks who participated in the GRACE-01 study. We acknowledge the entire GRACE team for their expertise, hard work, and enthusiasm.

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respiratory tract infections;[27] this may contribute to poor adherence. An association was also shown in the current study between management in certain networks and adherence, with one network (Bratislava) being associated with worse adherence and two networks (Helsinki and Jönköping) being associated with better adherence. The reasons for these differences are not yet clear. However, it is interesting to note that, along with Tromsø (which was borderline significant), the three networks associated with greatest adherence are all in Nordic countries.

This study's finding that adherence to acute antibiotic prescriptions was not associated with faster recovery is consistent with the previous finding that antibiotic prescribing is not associated with differences in recovery at the primary care network level,[6] as well as being consistent with evidence that there is little meaningful benefit from antibiotics for acute bronchitis.[28] Those who were not prescribed antibiotics at the index consultation but ended up taking them during the study period had a significantly slower rate of recovery; this could be because those who were recovering more slowly may have been more likely to reconsult and be prescribed antibiotics at a subsequent consultation.

Taking antibiotics that have been prescribed for others or prescribed for a previous illness is common.[3] A systematic review and meta-analysis of 18 estimates from 16 755 participants in nine studies reported a mean rate of leftover antibiotic use of 28.6% (95% CI = 21.8 to 35.4).[15] A survey of 7120 members of the public in the UK found that 15.8% (95% CI = 14.3 to 17.4) reported keeping antibiotics at some point during the previous year.[3] These data are consistent with this study's findings that antibiotic courses are frequently not adhered to, and that >10% of patients, more than one-third of whom had not reconsulted, consumed an antibiotic that had not been prescribed for them in the index consultation.

Implications for practice and research

These findings provide the most convincing evidence so far that adults frequently do not adhere to antibiotics that are prescribed for acute cough/lower respiratory tract infection in primary care settings. Duration of antibiotic course, choice of antibiotic, and regional factors all seem to be associated with differences in adherence, but the reasons why patients do not adhere remain unclear. The finding that the variation in consumption at a network level was less than the variation in prescribing suggests that patients may 'vote with their feet'; that is, be less likely to take prescribed antibiotics in high-prescribing networks and more likely to take their prescribed antibiotic and/or obtain antibiotics subsequent to their initial consultation in low-prescribing networks. Patients may also stop taking antibiotics because they are starting to feel better or have an adverse reaction. Nevertheless, low levels of adherence suggest a degree of misunderstanding, miscommunication, or failure to reach common ground in these consultations, and may result in:

- worse health outcomes (if prescribed for appropriate indications);
- waste resources (if prescriptions are collected and not used);
- antibiotics being kept for future use (which may be used later for inappropriate indications); and
- a distortion of data on antibiotic use.

There is a need for further research, including both quantitative and qualitative studies, to better understand the reasons for these diverse behaviours.

The study found that antibiotic prescribing at the initial consultation for a presumed infectious episode is a crude indicator of antibiotic use; antibiotic consumption during the entire period of the usual illness course is a more meaningful consideration. This is important for research into the association between antibiotic prescribing and antimicrobial resistance.[29]

The finding that adherence to acute antibiotic treatment was not associated with improved recovery is consistent with increasing evidence that antibiotics do not benefit most adult patients with acute cough/lower respiratory tract infection who are otherwise well. This may be because most of these infections are caused by viruses and might not be expected to respond to antibiotic treatment. Clinicians do not yet have the tools to adequately identify patients with acute cough/lower respiratory tract infection who will, and will not, benefit from antibiotic treatment.

These data will have implications for GPs when considering the use of antibiotics for acute cough/lower respiratory tract infection. Communication in these consultations needs to encompass not only the likely effect of antibiotic treatment, but also issues about adherence, such as

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