The relationship between primary care antibiotic prescribing and bacterial resistance in adults in the community: a controlled observational study using individual patient data

Alastair D. Hay1*, Michael Thomas2, Alan Montgomery1, Mark Wetherell3, Andrew Lovering4, Cliodna McNulty5, Deirdre Lewis6, Becky Carron7, Emma Henderson8 and Alasdair MacGowan4

1Academic Unit of Primary Health Care, Department of Community Based Medicine, University of Bristol, Cotham House, Cotham Hill, Bristol, BS6 6JL, UK; 2Department of General Practice and Primary Care, University of Aberdeen, Foresterhill Health Centre, Westburn Road, Aberdeen, AB25 2AY, UK; 3Department of Social Medicine, University of Bristol, Canynge Hall, Whiteladies Road, Bristol, BS8 2PR, UK; 4Bristol Centre for Antimicrobial Research and Evaluation, Department of Medical Microbiology, Southmead Hospital, Bristol, BS10 5NB, UK; 5Health Protection Agency, Primary Care Unit, Microbiology Department, Gloucestershire Royal Hospital, Great Western Road, Gloucester, GL1 3NN, UK; 6Health Protection Agency South West, The Wheelhouse, Bonds Mill, Stonehouse, Gloucestershire, GL10 3RS, UK; 7City of Bristol College, Bedminster, Bristol, BS3 5JL, UK; 8Richard Bright Renal Unit, Southmead Hospital, Bristol, BS10 5NB, UK

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Objectives: To examine the relationship between primary care prescribed antibiotics and the development of antibiotic resistance in perineal flora contaminating unselected urinary isolates from a large sample of asymptomatic adults representative of the general community.

Patients and methods: Escherichia coli isolates contaminating urine samples were obtained from asymptomatic adults aged >16 years registered with general practices in the former Avon and Gloucestershire health authority areas. Data on antibiotic exposure during the 12 months prior to providing the urine samples were collected from the primary care electronic and paper medical records. The main outcome measure was resistance to amoxicillin or trimethoprim or both.

Results: Two thousand nine hundred and forty-three adults submitted urine samples. Susceptibility among E. coli isolates and antibiotic prescribing data were available from 618 patients. We found no evidence of an association between resistance and patients’ exposure to any antibiotic prescribed in primary care in the previous 12 months [adjusted odds ratio (OR) 1.12, 95% confidence interval 0.77–1.65, P = 0.52]. Secondary analyses demonstrated greater resistance in patients exposed to antibiotics within 2 months (adjusted OR 1.95, 1.08–3.49, P = 0.03), a dose–response relationship to increasing exposure to trimethoprim in the previous 12 months (adjusted OR 1.01, 1.01–1.02, P = 0.001) and that individuals who had been prescribed any β-lactam antibiotic in the previous 12 months had amoxicillin MICs more than twice (adjusted 95% CI 1.23–3.31, P = 0.009) that of those who had not been prescribed any β-lactams.

Conclusions: Whether or not adults receive a prescription for any antibiotic during a 12 month period does not appear to influence the antimicrobial resistance of perineal flora. However, the temporal and dose–response relationships found may be suggestive of a causative association and should be the focus of further research.

Keywords: primary health care, antibiotics, drug resistance, patient level data

*Corresponding author. Tel: +44-117-954-6632; Fax: +44-117-954-6677; E-mail: alastair.hay@bristol.ac.uk

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Primary care antibiotic prescribing and the development of bacterial resistance

Introduction

Resistance to antibiotics has been described as a major threat to public health. Antibiotics contribute to the development of resistance through ‘selective grooming’ from three sources: medical prescription to humans, veterinary prescription and non-prescription use, and waste antibiotics reaching the environment.

In the UK, general practitioners (GPs) are responsible for 80% of all antibiotics prescribed to humans, mostly for respiratory tract infections, despite evidence of limited or marginal effectiveness for the most common respiratory primary care presentations. Patient expectations for antibiotics are a powerful determinant of prescribing and can result in treatment, even when the prescriber feels that the patient’s condition does not warrant their use. GPs are aware of the problem, but may see antibiotic resistance as a theoretical or minimal risk.

The relationship between GP prescribing and resistance is currently incompletely understood, and the ecology of the emergence and spread of resistance is not straightforward. There have been repeated calls to examine the role of antibiotics in the development of antibiotic resistance. Given their convenience, many studies have used routine laboratory urine samples from patients with suspected urinary tract infection (UTI) and population-based aggregate antibiotic exposure data, such as prescribing analysis and cost (PACT) data in the UK. However, two important limitations to these studies exist. First, although reflecting active infection, studies of routine samples from symptomatic patients are prone to selection bias. Samples are more likely to be sent from older patients, those not cured on first line therapy and those with more severe infection or complications due to co-morbidities. Furthermore, studies in which repeated samples have been sent from the same individual can overestimate resistance rates. Second, population-based data give an average prescribing rate, not an estimate of individual antibiotic exposure, and prevent the use of multivariable analysis to adjust for individual characteristics such as age, gender or comorbidity, or to examine for dose–response relationships between increasing exposure and resistance. Associations arising from such aggregate data do not necessarily apply to individuals (the so-called ‘ecological fallacy’), as demonstrated by comparing the aggregate and individual analyses in a recent paper investigating trimethoprim-resistant bacteria. Importantly, using individual level data, this study demonstrated an association between antibiotic prescribing and resistance in routine urine samples lasting up to 6 months, not apparent at the aggregate level analysis. UK studies using aggregate data or routine laboratory data, examining whether primary care antibiotic prescribing leads to resistance have shown contrasting results, from modest to stronger relationships. One American study, using individual-level data, found a dose–response association between antibiotic exposure and resistance in elderly patients with UTI and another Swedish (aggregate data) study showed that the degree of non-hospital antimicrobial consumption correlated with multidrug-resistant E. coli in patients with UTI.

Bacteria in low concentrations commonly contaminate urine from healthy, asymptomatic adults, usually from the urethra. Our premise is that these organisms are representative of perineal flora and may be the same organisms associated with UTI in women, the so-called ‘faecal–perineal–urethral’ aetiology. Thus, any resistance in such urinary isolates from asymptomatic adults may reflect the impact of antibiotics on the perineal and gut flora. Therefore, our aim was to quantify the relationship between prescribed antibiotics at the individual level and the development of antibiotic resistance in perineal flora contaminating unselected urinary isolates obtained from a large sample of asymptomatic adults as representative as possible of the general community.

Methods

Practices and participants

This study was part of an ongoing investigation of antibiotic resistance surveillance and was approved by the Southmead and Gloucester Local Research Ethics Committees (062/99 and 99/51G, respectively). We selected practices of a medium to large size and attempted to find a mix of urban and rural practices in the former Avon and Gloucestershire health authority areas. Two groups of patients registered with 12 practices were invited to submit urine samples between April 2000–July 2002. The first group was patients aged 17 years or more attending their practice (GP or practice nurse) with a non-infection-related problem on days when a research nurse was present in the practice. The second group was patients aged 17 years or more who had not visited the surgery in the previous 6 months. Each practice generated a list of these patients, a random sample of whom were sent study information and invited to return by post a urine sample and questionnaire including demographic (age, gender and postcode) and co-morbidity (the presence of asthma, other chest disease, diabetes or hypertension) data.

Urinary isolates

In order adequately to sample bacteria contaminating the urethra, patients in both groups were given the same sampling instructions: to provide a first void urine sample without prior genital cleaning and to return the urine sample by post to the laboratory. In the laboratory, 50 μL of urine was inoculated onto a cystine lactose electrolyte deficient agar. After overnight incubation, the predominant organism was identified using conventional methods. Antimicrobial susceptibility testing was performed by BSAC agar incorporation methods. BSAC breakpoints were used to categorize isolates as susceptible or resistant (R > 32 mg/L amoxicillin; R > 2 mg/L trimethoprim). As previous research has demonstrated associations between trimethoprim exposure and amoxicillin resistance and vice versa, thought to be plasmid mediated, we classified patients as ‘resistant’ if E. coli isolates were resistant to either trimethoprim or amoxicillin, or both, and ‘sensitive’ if susceptible to both. We restricted our analysis to E. coli isolates as this is the most important group numerically, and other species, for example Klebsiella, exhibit resistance to amoxicillin independent of antibiotic exposure. As patients in neither group were known to be experiencing symptoms of urinary tract infection at the time of sampling, data from both groups were analysed together.

Antibiotic exposure data

Data regarding systemic (British National Formulary chapters 5.1.1 to 5.1.13) antibiotic exposure during the 12 months prior to providing the urine sample were collected from the primary care electronic and paper medical records. We defined primary care antibiotic exposure as any course prescribed by GPs (in or out of hours) or by practice and walk-in centre based nurse practitioners. For each course, data were collected regarding: the date of the prescription, the type, the number of units (capsules, tablets or suspension volume) per dose, the strength per unit, the total number of units and the dosing instructions. Two investigators, blind to the outcome, extracted data from a sample of records in practices with differing paper and electronic systems for storing the medical record to ensure data quality.
Sample size

An estimate of antibiotic exposure for the relevant age group in the general population is ~25%.” We assumed that 20% of ‘sensitive’ patients would have received one or more antibiotic prescriptions in the previous 12 months, and that an important absolute difference in antibiotic exposure is 10 percentage points. In other words, for exposure among ‘resistant’ patients of either 30 or 10%, this is equivalent to odds ratios of 1.71 and 0.44, respectively. Further, of the 3079 individuals who submitted a urine sample in the surveillance study, we anticipated that ~45% (1400) would yield an isolate, and that exposure data would be available for 80% of these individuals (1120). Data from the surveillance study suggested a ratio of susceptible to resistant isolates of 3:1. Therefore the study would yield at least 85% power to detect an absolute change in antibiotic exposure of 10% with 5% two-sided α.

Data analysis

All data were analysed using Stata version 8. We used summary statistics to describe the demographics and antibiotic exposure of individuals with susceptible and resistant isolates. The deprivation variable was generated from the Townsend scores (from the 2001 Census) associated with postcodes at the enumeration district level. Unfortunately, due to new postcode allocations since 2001, we were unable to assign a deprivation score to 55 patients in our final analysis group. Appropriate univariable and multivariable regression models were used to describe the unadjusted and adjusted [for age, gender, co-morbidity and group (attender and non-attender)] associations between exposures and outcomes. We did not adjust for deprivation as including this variable would have resulted in loss of power. Additionally, we allowed for any clustering effects by practice in the data using the ‘svy’ set of commands in Stata. For the multivariable models without deprivation, n = 5 individuals did not have complete data and therefore sensitivity analyses making different plausible assumptions for missing data were not considered necessary. The primary analysis examined the association between the prescription of any antibiotic in the previous 12 months and resistance to either amoxicillin or trimethoprim or both. Our secondary analyses investigated associations between exposure to different numbers of courses, recent (within 2 months of sample submission) antibiotic use, different classes of antibiotics, by type and/or dose, and resistance to amoxicillin, trimethoprim or both. For one of these secondary analyses, we generated a new variable, total β-lactam antibiotics, by summing the total number of milligrams of penicillin and cephalosporin antibiotics. In order to investigate associations between antibiotic exposure and resistance as a continuous rather than binary variable, we used amoxicillin and trimethoprim MIC data. The MICs tested are all logarithms to base two of antibiotics prescribed in the previous 12 months, of which 162 (52%) were penicillins, 55 (17%) macrolides, 39 (12%) were trimethoprim, 31 (10%) tetracyclines, nine (3%) were quinolones, five (2%) were cephalosporins and 12 (4%) were other types. There was a record of a further two courses prescribed outside of primary care, and these were excluded from the analyses.

Primary analysis

We found no evidence of an association between any antibiotic prescribed in the previous 12 months and resistance in E. coli organisms to either amoxicillin or trimethoprim or both (Table 2). There was no evidence of an interaction with age (P = 0.93), gender (P = 0.96) or group (P = 0.17) (data not shown).

Secondary analyses

We found no evidence of a dose–response relationship between resistance and the number of courses of antibiotics prescribed over a 12 month period (Table 3). However, recent (within 2 months of the sample submission) antibiotic use (adjusted odds ratio = 1.95, 95% CI 1.08 to 3.49, P = 0.03, Table 3) and increased use of trimethoprim in the last 12 months (adjusted odds ratio = 1.01, 95% CI 1.01 to 1.02, P = 0.001, Table 4) were associated with resistance independently of age, gender, co-morbidity, group origin and any clustering effects by practice. Finally, we found that individuals who had been prescribed a β-lactam antibiotic within 12 months had an amoxicillin MIC over twice (adjusted 95% CI 1.23 to 3.31, P = 0.009) that of those who not been prescribed any β-lactams (Table 5). There was no evidence of an association between trimethoprim prescription and trimethoprim MIC.

Urinary isolates

Of the 618 E. coli isolates in which antibiotic susceptibility status was known (Figure 1), resistance to amoxicillin was present in 223 (36%), to trimethoprim in 44 (7%) and in either or both (our primary outcome) in 239 (39%) (Table 1). Resistant isolates were more likely to be from female (P = 0.04) and younger (P = 0.05) individuals (Table 1).

Antibiotic prescribing

Among the 618 adults with E. coli urinary organisms in whom susceptibility status was known, there were a total of 313 courses of antibiotics prescribed in the previous 12 months, of which 162 (52%) were penicillins, 55 (17%) macrolides, 39 (12%) were trimethoprim, 31 (10%) tetracyclines, nine (3%) were quinolones, five (2%) were cephalosporins and 12 (4%) were other types. There was a record of a further two courses prescribed outside of primary care, and these were excluded from the analyses.

Results

Practices and participants

The 12 practices agreeing to participate were located in inner city, urban and rural areas, serving a total population of 126 000 patients, with list sizes ranging from 7000 to 14 000. The flow of participants through the study is shown in Figure 1. Regarding the practice attenders, 2969 adults visited the practices on the days a nurse was present and agreed to participate, completing a baseline questionnaire. Regarding the non-attenders, the practices identified 6239 adults who had not consulted within the previous 6 months. A random sample of 2800 was invited by post to participate, of whom 1162 returned the baseline questionnaire, giving a total of 4131 asymptomatic patients with baseline data. Of these, 2943 (71%) patients submitted a urine sample. Patients who submitted a sample were slightly older (52 years versus 51 years, P = 0.04) than those who did not return a sample but did not differ in terms of gender (comparison 1, Figure 1). Of the patients who submitted a sample, a predominant isolate was identified in 931, and in 618 the isolate was both identified as an E. coli organism and susceptibility status of the organism was known (the number available for analysis). Compared with all the other 2325 patients who submitted a urine sample, the 618 patients available for analysis were older (55 years versus 51 years, P < 0.001) and there was a greater proportion of females (83% versus 52%, P < 0.001) (comparison 2, Figure 1).

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Discussion

Summary of main results

We believe this is the first paper to describe the relationship between primary care antibiotic prescribing and resistance among perineal flora contaminating relatively unselected, community sourced, urinary samples using individual level data. In our observational controlled study, we found no evidence of an association between resistance in urinary \textit{E. coli} organisms from asymptomatic adults and their prior exposure to any antibiotic prescribed in primary care in the previous 12 months. However, our secondary analyses did demonstrate greater resistance in patients exposed to antibiotics within 2 months, a dose–response relationship to increasing exposure of trimethoprim, and increasing amoxicillin resistance with any exposure to \(\beta\)-lactam antibiotics.

Interpretation of results

Whether or not patients receive a prescription for any antibiotic over a 12 month period does not appear to influence antimicrobial resistance in perineal flora. However, in our six, secondary analyses, we observed statistically significant temporal and dose–response associations between recent antibiotics and trimethoprim, respectively, as well as quantitatively greater resistance following the use of any \(\beta\)-lactam antibiotics. The first suggests that the effects of antibiotic exposure could be temporary (lost somewhere between 2 and 12 months). The data were explored to see if it was possible to ascertain more precisely when the effects of antibiotic exposure are lost, but there were too few data to draw reasonable conclusions (data not shown). We also looked for associations between any antibiotic exposure in the previous 12 months and the separate development of trimethoprim and amoxicillin resistance. No associations were found (data not shown). The overall exposure of patients to antibiotics other than \(\beta\)-lactams and trimethoprim was too low to allow meaningful analysis. While requiring replication, the three significant associations may suggest a causal relationship. The implication of our results for future research is that there is a need to clarify the time-course of changes in resistance patterns in perineal organisms following antibiotic exposure, and for clinical practice, to give

Figure 1. Flow of participants through the study.
Table 1. Characteristics of 618 patients with *E. coli* urinary isolates sensitive to both antibiotics or resistant to amoxicillin and/or trimethoprim (full data available unless indicated otherwise)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sensitive</th>
<th>Resistant</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 379</td>
<td>n = 239</td>
<td></td>
</tr>
<tr>
<td>Mean (years) age (SD)</td>
<td>55.5 (15.5)</td>
<td>53.1 (14.3)</td>
<td>0.05</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>304 (80)</td>
<td>207 (87)</td>
<td>0.04</td>
</tr>
<tr>
<td>Recruited from group attending practices, n (%)</td>
<td>233 (61)</td>
<td>150 (63)</td>
<td>0.75</td>
</tr>
<tr>
<td>Mean Townsend deprivation score (SD)</td>
<td>-0.15 (2.82)</td>
<td>0.01 (2.88)</td>
<td>0.50</td>
</tr>
<tr>
<td>Presence of any co-morbidity, n (%)</td>
<td>107 (28)</td>
<td>57 (24)</td>
<td>0.26</td>
</tr>
<tr>
<td>Mean (SD) number of antibiotic courses in the last 12 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1 antibiotic prescribed in the last 12 months, n (%)</td>
<td>100 (26)</td>
<td>69 (29)</td>
<td>0.50</td>
</tr>
<tr>
<td>Courses of antibiotics in the last 12 months, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>279 (74)</td>
<td>170 (71)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>56 (15)</td>
<td>37 (15)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>23 (6)</td>
<td>17 (7)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>15 (4)</td>
<td>4 (2)</td>
<td></td>
</tr>
<tr>
<td>4 or more</td>
<td>6 (2)</td>
<td>11 (5)</td>
<td>0.10</td>
</tr>
<tr>
<td>≥1 courses of trimethoprim prescribed in the last 12 months, n (%)</td>
<td>18 (5)</td>
<td>14 (6)</td>
<td></td>
</tr>
<tr>
<td>Median (IQR) dose of trimethoprim if prescribed (mg)</td>
<td>2000 (1200–2800)</td>
<td>2200 (2000–4000)</td>
<td>0.56</td>
</tr>
<tr>
<td>≥1 courses of β-lactam antibiotics prescribed in the last 12 months, n (%)</td>
<td>65 (17)</td>
<td>50 (21)</td>
<td></td>
</tr>
<tr>
<td>Median (IQR) dose of β-lactams if prescribed (mg)</td>
<td>10000 (5250–14750)</td>
<td>7500 (5250–14500)</td>
<td>0.65</td>
</tr>
</tbody>
</table>

*Presence of diabetes, asthma, other chest disease or hypertension.

\( b \) n = 238.

\( c \) n = 350.

\( d \) n = 213.

\( e \) n = 378.

\( f \) n = 236.

Table 2. Association between prescription of any antibiotic in previous 12 months and resistance to amoxicillin and/or trimethoprim among patients with *E. coli* isolates

<table>
<thead>
<tr>
<th>Any antibiotic prescribed in last 12 months</th>
<th>Sensitive</th>
<th>Resistant</th>
<th>Crude OR</th>
<th>Adjusted* OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>no</td>
<td>279</td>
<td>170</td>
<td>1.13</td>
<td>1.12 (0.77–1.65)</td>
<td>0.52</td>
</tr>
<tr>
<td>yes</td>
<td>100</td>
<td>69</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted for age, gender, presence of comorbidity, group origin and practice clustering effects.

Table 3. Association between number of antibiotic courses and recent antibiotic use and resistance to amoxicillin and/or trimethoprim among patients with *E. coli* isolates

<table>
<thead>
<tr>
<th>Number of antibiotic courses in last 12 months</th>
<th>Sensitive</th>
<th>Resistant</th>
<th>Crude OR</th>
<th>Adjusted* OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>279</td>
<td>170</td>
<td>1.08</td>
<td>1.07 (0.76–1.52)</td>
<td>0.43</td>
</tr>
<tr>
<td>1</td>
<td>56</td>
<td>37</td>
<td>1.21</td>
<td>1.25 (0.46–3.39)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>23</td>
<td>17</td>
<td>0.44</td>
<td>0.42 (0.13–1.35)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>15</td>
<td>4</td>
<td>3.01</td>
<td>3.14 (0.63–15.6)</td>
<td></td>
</tr>
<tr>
<td>≥4</td>
<td>6</td>
<td>11</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any antibiotic prescribed in last 2 months</td>
<td>338</td>
<td>199</td>
<td>1.93</td>
<td>1.95 (1.08–3.49)</td>
<td>0.03</td>
</tr>
<tr>
<td>yes</td>
<td>22</td>
<td>25</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted for age, gender, presence of comorbidity, group origin and practice clustering effects.

\( ^{b} \) P value from Wald test.
consideration to the use of an alternative antibiotic from any recently prescribed. These data serve as a reminder that antibiotic resistance in primary care should not be regarded as a theoretical problem, and the possibility of increasing carriage of resistant bacteria needs to be a factor in the risk–benefit analysis in the decision to prescribe antibiotics. Of the three exploratory, non-statistically significant analyses, the first (increasing exposure to any antibiotic versus resistance to either amoxicillin or trimethoprim or both, Table 3) was in the expected direction, but the low numbers in the two or higher antibiotic course categories may mean we were inadequately powered to detect a relationship. In the second (increasing β-lactam dose versus amoxicillin resistance, Table 4), the odds ratio centres on the null and suggests an absence of association. The third relationship (any trimethoprim versus trimethoprim MIC, Table 5) was in the opposite to expected direction, but the 95% confidence limit for the odds ratio spans the null and so is probably due to chance (adjusted \( P = 0.11 \)). All these associations require further exploration using adequately powered studies. Comparing Tables 4 and 5 gives apparently conflicting results, but it should be noted that Table 4 makes most efficient use of the exposure data (treated as continuous variable) while Table 5 does the same for the outcome (MICs treated as a continuous variable). Therefore, given these different exposure and outcome classifications, it is not surprising that different results are obtained.

**Where this fits in with other research**

Our results complement those of Donnan *et al.*\(^{17}\) who found that associations at the individual level were obscured by analysis of aggregate data and that recent (up to 6 months) exposure to trimethoprim was associated with resistance in patients with UTI. Our study examined the impact of antibiotics on perineal flora, not those causing UTI, and also found an association between recent antibiotic exposure and resistance.

**Limitations**

Although patients submitting and not submitting urines appeared similar in gender and age, an *E. coli* organism was more likely to be isolated from older female patients, so the generalizability of our results may be limited to this group. Nevertheless, our subgroup analysis suggests that for the primary outcome at least, the lack of association is not confined to women. In addition, the representativeness of the results may be compromised by (an unmeasured) response bias occurring among the 42% of patients in the non-attending group who responded to the invitation to return the baseline questionnaire. This response bias may also be related to the higher return of urine samples and subsequent organism isolation rate in this group compared with the practice-attending patients. For example, it is possible that patients in the non-attenders returning samples were also more likely to experience mild urinary symptoms due to intercurrent or low-grade urinary infection. However, we think it unlikely that the difference in organism isolation rate between groups could be accounted for by differences in the method used to obtain the samples, since both groups were given the same sampling instructions. While primary care antibiotic prescribing is particularly common in children,\(^{29}\) our study sample consisted entirely of adults. This would be an important group in which to replicate this research. Although we used an objective measure of antibiotic exposure, an antibiotic prescription does not equate to antibiotic consumption. Estimates of primary non-compliance vary from 5%\(^{30}\) to 14.5%\(^{31}\) and could lead to an underestimation of the strength of association. Nevertheless, our results relate to the GP’s prescribing decision, which is made without knowledge of the patient’s future compliance. Also, although

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### Table 4. Association between increasing trimethoprim exposure and resistance to trimethoprim and increasing β-lactam dose and resistance to amoxicillin among patients with *E. coli* isolates

<table>
<thead>
<tr>
<th></th>
<th>Crude OR</th>
<th>Adjusted(^a) OR (95% CI)</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds ratio of resistance to trimethoprim associated with change in trimethoprim dose of 200 mg in the previous 12 months</td>
<td>1.02</td>
<td>1.01 (1.01–1.02)</td>
<td>0.001</td>
</tr>
<tr>
<td>Odds ratio of resistance to amoxicillin associated with change in β-lactam dose of 500 mg in the previous 12 months</td>
<td>1.00</td>
<td>1.00 (0.99–1.01)</td>
<td>0.62</td>
</tr>
</tbody>
</table>

\(^a\)Adjusted for age, gender, presence of comorbidity, group origin and practice clustering effects.

### Table 5. Association between prescription of trimethoprim and β-lactam antibiotics and trimethoprim and amoxicillin MICs

<table>
<thead>
<tr>
<th>Prescription of antibiotic in last 12 months</th>
<th>Trimethoprim</th>
<th>β-Lactam</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no (n = 596)</td>
<td>no (n = 515)</td>
</tr>
<tr>
<td>Trimethoprim MIC (mg/L), geometric mean (SD)</td>
<td>0.28 (4.11)</td>
<td>1.03 (45.75)</td>
</tr>
<tr>
<td>Crude ratio of geometric means (95% CI)</td>
<td>0.76 (0.54–1.08), ( P = 0.12 )</td>
<td>1.94 (1.23–3.07), ( P = 0.009 )</td>
</tr>
<tr>
<td>Adjusted ratio of geometric means(^a) (95% CI)</td>
<td>0.77 (0.56–1.07), ( P = 0.11 )</td>
<td>2.02 (1.23–3.31), ( P = 0.009 )</td>
</tr>
</tbody>
</table>

\(^a\)Adjusted for age, gender, presence of comorbidity, group origin and practice clustering effects.
prescribed in smaller quantities than in primary care, patients could have received antibiotics from other sources, such as secondary care, dentists and genitourinary medicine clinics, without entry in the primary care record. The effect of this prescribing to resistance should be quantified in future studies. Although we collected prescribing data prior to urine sample submission, we cannot be certain that patients had not already been colonized by resistant bacteria before they received the antibiotic. Measuring other potential confounding factors, such as population density, was beyond the resources of this study.

Conclusions

Whether or not adults receive a prescription for any antibiotic during a 12 month period does not appear to influence antimicrobial resistance in perineal flora. However, the use of antibiotics within 2 months may impact on resistance, suggestive of a temporary effect on microbial flora. The other analyses may suggest important, and possibly causative, associations between increasing trimethoprim exposure and resistance and the use of any β-lactam and increased amoxicillin MICs. Further research is needed to clarify the temporal associations between prescribing and resistance and to replicate the dose–response relationships.

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Transparency declaration

The authors declared that there were no conflicts of interest.

References

Primary care antibiotic prescribing and the development of bacterial resistance


