

## Antimicrobial prescribing patterns for respiratory diseases including tuberculosis in Russia: a possible role in drug resistance?

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**Background:** Inappropriate antibiotic prescribing exposes patients to the risk of side effects and encourages the development of drug resistance across antimicrobial groups used for respiratory infections including tuberculosis (TB).

**Aim:** Determine among Russian general practitioners and specialists: (1) sources of antimicrobial prescribing information; (2) patterns of antimicrobial prescribing for common respiratory diseases and differences between primary and specialist physicians; (3) whether drug resistance in TB might be linked to over-prescribing of anti-TB drugs for respiratory conditions.

**Methods:** Point-prevalence cross-sectional survey involving all 28 primary care, general medicine and TB treatment institutions in Samara City, Russian Federation. In this two-stage study, a questionnaire was used to examine doctors' antimicrobial (including TB drugs) prescribing habits, sources of prescribing information, management of respiratory infections and a case scenario ('common cold'). This was followed by a case note review of actual prescribing for consecutive patients with respiratory diseases at three institutions.

**Results:** Initial questionnaires were completed by 81.3% (425/523) of physicians with 78.4% working in primary care. Most doctors used standard textbooks to guide their antimicrobial practice but 80% made extensive use of pharmaceutical company information. A minority of 1.7% would have inappropriately prescribed antibiotics for the case and 0.8–1.8% of respondents would have definitely prescribed TB drugs for non-TB conditions. Of the 495 respiratory cases, 25% of doctors prescribed an antibiotic for a simple upper respiratory tract infection and of 8 patients with a clinical diagnosis of TB, 4 received rifampicin monotherapy alone. Ciprofloxacin was widely but inappropriately used.

**Conclusion:** Doctors rely on information provided by pharmaceutical companies; there was inappropriate antibiotic prescribing.

Keywords: antibiotics, tonsillitis, bronchitis, pneumonia

### Introduction

Incorrect antibiotic prescribing exposes patients to the risk of side effects with little therapeutic benefit. It may encourage the emergence of drug resistance which has increased dramatically

across a wide range of important antimicrobial chemotherapeutic groups including those used to treat tuberculosis (TB).<sup>1,2</sup>

Factors encouraging the spread of antimicrobial drug resistance include: unrestricted public access to antibiotics, poor institutional infection control policies, excessive and inappropriate

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medical or self-prescribing; general over-prescribing; brand name prescribing; and patients' high expectations of antibiotic treatment.<sup>3,4</sup>

In the UK and other European countries, inappropriate prescribing and patients' expectations of antibiotic therapy were identified as important sources of drug resistance.<sup>2,5,6</sup> Overuse of antibiotics seems widespread, and has been described amongst primary and secondary care physicians across medical specialties.<sup>7</sup>

There is limited information on antibiotic resistance in respiratory infections, other than TB, in Russia but it is believed to be high.<sup>8,9</sup> Little is known about antibiotic prescribing in Eastern Europe and former states of the Soviet Union and very little on prescribing for respiratory infections in modern Russia. Pavin *et al.*,<sup>3</sup> for example, demonstrated that primary care doctors from rural areas of Uzbekistan over-prescribed antibiotics (57% of all prescribed drugs), with a bias for brand name prescribing rather than using generic compounds.

Drug-resistant organisms, such as some strains of multidrug-resistant TB [i.e. resistant to at least isoniazid and rifampicin (MDR-TB)], are potentially untreatable. High rates of drug-resistant TB, and MDR-TB in particular, have been documented in Russia.<sup>10</sup> First-line anti-TB agents such as isoniazid and rifampicin, and second-line agents such as the fluoroquinolones, as well as other antibiotics can be purchased without prescription in Russia. Inappropriate self-administration or medical prescribing of antibiotics may contribute to the emergence of drug resistance. We describe the pattern of prescribing for common respiratory diseases and the sources of information used by medical practitioners to guide their antibiotic prescribing.

## Materials and methods

### *Study population and design*

A preliminary drug resistance survey conducted in Samara, one of 89 regions of the Russian Federation, showed that inadequate TB treatment regimens differing from internationally adopted standards have been employed in Russia. This, and patients' poor compliance, may have been the cause of the high rates of antituberculous drug resistance documented during previous studies in this region.<sup>10</sup> However, no studies have been carried out to detect antibiotic prescribing patterns for this and other respiratory diseases.

We conducted a point-prevalence cross-sectional survey of primary care and hospital physicians in all 28 medical institutions managing respiratory tract infections in Samara City, Russian Federation (population, 1.3 million) to address the study aims. These were to determine among Russian general practitioners and specialists: (1) sources of antimicrobial prescribing information; (2) patterns of antimicrobial prescribing for common respiratory diseases and differences between primary and specialist physicians; (3) whether drug resistance in TB might be linked to over-prescribing of anti-TB drugs for respiratory conditions.

The study was conducted in two parts. Initially physicians completed a semi-structured questionnaire (see below) and this was followed by a detailed retrospective analysis (see below).

### *Questionnaires*

The questionnaire was designed to ascertain antimicrobial prescribing habits for different respiratory diseases. It included questions on sources of antibiotic prescribing information, on antimicrobial

prescribing habits, and the management of a clinical scenario (an upper respiratory infection or 'common cold'). Respiratory physicians (523 individuals) were invited to take part and participation was voluntary and anonymous.

The questionnaire included a clinical case which read: "A 29 year-old female patient presented with a two day history of coryzal symptoms and mildly sore throat which was almost completely relieved by self-prescribed lozenges. She had no fever or lymphadenopathy, no muscular or joint pain or tenderness and no rash. She had no drug allergies. A throat swab was negative following comprehensive bacteriological culture." Respondents were asked what further treatment, if any, they would prescribe.

Respondents were also asked what antimicrobial drugs they would prescribe (if any) for a hypothetical patient aged 35 with (1) acute bronchitis, (2) chronic obstructive pulmonary disease (COPD), (3) pneumonia or (4) tonsillitis, selecting from a defined list of drugs which included all classes of antibiotics (more than one answer was allowed) including TB drugs.

In the second part of this study, the medical notes of consecutive patients presenting with a respiratory illness were analysed, using a standardized case-review document, during a 2 week period in November 2003. This was conducted at three representative provider units, comprising two primary care outpatient institutions (one located in the industrial part of the city and the other located in the city centre), and one inpatient site (a respiratory ward at a main teaching hospital). Data on the symptoms, respiratory diagnoses made [which included acute bronchitis, tonsillitis, COPD, community-acquired pneumonia, upper respiratory tract infections (URTI), asthma, pleuritis, lung cancer and TB] and the antibiotics and other medications prescribed were collected from 495 consecutive patients. Specific data on drug doses (or duration) were not collected as these were comparable to doses used in the UK. The study was approved by the local Ethics Committee and Oblast Health Authority.

### *Statistical analyses*

Data were entered and processed using EpiInfo 6.04d and Excel packages. The accuracy of data entry was checked by selecting and examining a random sample of 20% of the questionnaires. Antibiotic prescribing rates of primary care physicians (who were prescribing in an outpatient role) and hospital specialists (exclusively inpatient role) were compared for the same respiratory illnesses. In the second part of the study, descriptive statistics were used to describe the prescribing patterns. The prescribing differences were determined using the  $\chi^2$  test for comparison of proportions (at the 95% confidence level).

## Results

### *Questionnaire-based analysis*

There was a high response rate [81.3% (425/523) questionnaires completed] during the first stage of the study. The majority of respondents (78.4%; 333/425) were primary care doctors with 21.6% (92/425) secondary care specialists including respiratory physicians.

Two Russian language pharmacological textbooks were identified as the main sources of antibiotic information by 86.1% (366/425) of practitioners.<sup>11,12</sup> One of these is updated annually and is analogous to, and has the same status as, the British National Formulary. Medical journals, professional meetings, and advice from colleagues were described as important sources

## Antimicrobial prescribing views and patterns among Russian physicians

of information by 73.4%, 39.5% and 41.9% of practitioners, respectively. Antimicrobial information provided by pharmaceutical companies was drawn upon by 80.0% (340/425) of doctors.

For the clinical case, the majority of respondents correctly suggested prescribing only symptomatic relief including aspirin (acetylsalicylic acid) or paracetamol preparations, vitamin C and throat lozenges. Nevertheless, 1.7% (7/411) would have given antibiotics inappropriately.

Analysis of the initial questionnaires revealed that penicillins would be the most commonly prescribed class of antibiotics: 30.2%, 25.9%, 23.4% and 44.1% of all prescriptions for acute bronchitis, COPD, pneumonia and tonsillitis, respectively. Within the class, ampicillin was the first choice for COPD, pneumonia and tonsillitis, and amoxicillin was the first choice for the treatment of acute bronchitis. Macrolides were the second most common choice overall with 21.8% of all prescriptions for acute bronchitis, 17.3% for COPD, 20.5% for pneumonia and 25.2% for tonsillitis (Table 1). There was little difference between the specific rates of drug class prescribing (data not shown) for acute bronchitis and tonsillitis, between primary and secondary care doctors, and between TB specialists and all other doctors. There was greater use of cephalosporins by primary care doctors compared with hospital-based physicians and fluoroquinolones

by general primary and secondary care physicians compared with TB doctors.

From the initial survey, a small proportion of doctors would prescribe anti-TB drugs in the empirical management of non-TB diseases: 0.9% (25/2821) of prescriptions were for TB drugs in treatment of bronchitis, 1.7% (51/3072) in the treatment of COPD, and 1.8% (67/3773) and 0.8% (16/1995) for pneumonia and tonsillitis, respectively. As doctors could give multiple answers, the total number of prescriptions formed the denominator. A larger proportion of doctors would consider the possible use of TB drugs as indicated in Table 2 where doctors were asked whether they would 'never' prescribe anti-TB drugs for acute bronchitis, COPD, pneumonia and tonsillitis (and this supports local anecdotal evidence).

### Respiratory cases review

This study showed that all patients with acute tonsillitis (100%; 88/88) and nearly all with acute bronchitis (90.8%; 129/142) received antibiotics. The majority of patients with COPD received at least one antibiotic (80.0%; 40/50) and 24.0% (12/50) received two. Similar prescribing patterns were demonstrated for patients with pneumonia: 96.7% of them received at

**Table 1.** Top six drugs chosen in order of preference for the treatment of acute bronchitis, COPD, pneumonia and tonsillitis by questionnaire-response ( $n = 425$ )

Choice	Acute bronchitis ( $n = 2821$ ) <sup>a</sup>	COPD ( $n = 3072$ ) <sup>a</sup>	Pneumonia ( $n = 3773$ ) <sup>a</sup>	Tonsillitis ( $n = 1995$ ) <sup>a</sup>
1	penicillins total 853 (30.2%) benzylpenicillin 191/853 (22.4%) amoxicillin 295/853 (34.6%) <sup>b</sup> ampicillin 261/853 (30.6%) flucloxacillin 30/853 (3.5%) co-amoxiclav 76/853 (8.9%)	penicillins total 797 (25.9%) benzylpenicillin 127/797 (15.9%) amoxicillin 242/797 (30.4%) ampicillin 332/797 (41.7%) <sup>b</sup> flucloxacillin 34/797 (4.3%) co-amoxiclav 62/797 (7.8%)	penicillins total 881 (23.4%) benzylpenicillin 184/881 (20.9%) amoxicillin 240/881 (27.2%) ampicillin 348/881 (39.5%) <sup>b</sup> flucloxacillin 29/881 (3.3%) co-amoxiclav 80/881 (9.1%)	penicillins total 879 (44.1%) benzylpenicillin 201/879 (22.9%) amoxicillin 236/879 (26.8%) ampicillin 365/879 (41.5%) <sup>b</sup> flucloxacillin 18/879 (2.0%) co-amoxiclav 59/879 (6.7%)
2	macrolides total 614 (21.8%) erythromycin 328/614 (53.4%) <sup>b</sup> azithromycin 226/614 (36.8%) clarithromycin 60/614 (9.8%)	macrolides total 531 (17.3%) erythromycin 214/531 (40.3%) azithromycin 228/531 (42.9%) <sup>b</sup> clarithromycin 78/531 (14.7%)	macrolides total 773 (20.5%) erythromycin 191/773 (24.7%) azithromycin 459/773 (59.4%) <sup>b</sup> clarithromycin 105/773 (13.6%)	macrolides total 502 (25.2%) erythromycin 345/502 (68.7%) <sup>b</sup> azithromycin 111/502 (22.1%) clarithromycin 46/502 (9.2%)
3	folate antagonists 379 (13.4%)	fluoroquinolones 395 (12.9%)	cephalosporins 628 (16.6%)	fluoroquinolones 143 (7.2%)
4	fluoroquinolones 256 (9.1%)	cephalosporins 356 (11.6%)	aminoglycosides 500 (13.3%)	tetracyclines 118 (5.9%) <sup>c</sup>
5	aminoglycosides 209 (7.4%)	aminoglycosides 351 (11.4%)	fluoroquinolones 392 (10.4%)	aminoglycosides 101 (5.1%) folate antagonists 102 (5.1%)
6	cephalosporins 197 (7.0%)	tetracyclines 209 (6.8%)	tetracyclines 209 (5.5%)	cephalosporins 100 (5.0%)

<sup>a</sup>Multiple answers were possible hence total number of prescriptions used as denominator.

<sup>b</sup>Most commonly prescribed within the group.

**Table 2.** Rates of doctors who would prescribe and who would 'never' prescribe anti-TB drugs for acute bronchitis, COPD, pneumonia and tonsillitis

Anti-tuberculosis drug	Number of doctors choosing the agent for possible prescription (%)	Number of doctors who would never prescribe TB drugs (%)
Ftivazide <sup>a</sup>	96 (22.6%)	329 (77.4%)
Isoniazid	90 (21.2%)	335 (78.8%)
Myrin P <sup>b</sup>	87 (20.5%)	338 (79.5%)
Rifampicin	78 (18.4%)	347 (81.6%)

*n* = 425

<sup>a</sup> An isoniazid preparation.

<sup>b</sup> A locally used fixed-dose combination of isoniazid, rifampicin, ethambutol and pyrazinamide.

least one antibiotic and 30.1% (28/93) received two. One-fourth of the patients with a diagnosis of simple 'URTI' (20/80) were also prescribed an antibiotic (Table 3).

Table 4 shows the actual antibiotic prescription rates for the patients at the three sites. Penicillins were the mostly commonly prescribed drugs for all patients with respiratory diseases and fluoroquinolones and macrolides were the next most common choices: 36.3% (165/454), 14.1% (64/454) and 14.3% (65/454) of all prescriptions, respectively. These three groups were also more often prescribed for outpatients by primary practitioners than inpatients—the attributive risk was 30.3% (95% CI 21–39%), 18.1% (95% CI 14–22%) and 8.1% (95% CI 1–15%), respectively.

The analysis of prescriptions for COPD illustrates the management differences between in- and outpatients as the latter were more commonly prescribed penicillins (attributive risk of 31.9%, 95% CI 8–56%) and aminoglycosides (attributive risk of 18.6%, 95% CI 7–30%).

In the treatment of acute tonsillitis, penicillins and macrolides were the drugs of choice—the prescription rates overall were 38.6% (34/88) and 27.3% (24/88), respectively. These findings support the answers given by physicians to the earlier questionnaire. Penicillins were also the first choice for treatment of acute bronchitis [50.4% (66/131)], followed by fluoroquinolones [19.8% (26/131)], although in the earlier questionnaire-based stage of the study macrolides were the second choice. Where fluoroquinolones were used, ciprofloxacin was chosen by respondents to treat acute bronchitis (96.2%) and tonsillitis (100%), but these would be of little likely benefit.

Cephalosporins [34.7% (42/121)] and penicillins [24.0% (29/121)] were the most commonly used antibiotic classes in the treatment of patients with community-acquired pneumonia, whereas penicillins and macrolides were the first and the second choices made by the respondents empirically in the questionnaire. Penicillins [35.8% (19/53)] and cephalosporins [17.0% (9/53)] were the drugs of choice for COPD therapy.

As for COPD, in the management of community-acquired pneumonia, hospital doctors prescribed more cephalosporins and primary care physicians prescribed more fluoroquinolones (attributive risk of 32.4%, 95% CI 49–16% and 16.4%, 95% CI 8–25%, respectively).

Within the Russian medical system, a differential diagnosis of TB should trigger a referral to the TB service for investigation and treatment, i.e. no TB treatment would be expected in the general health service. Of 8 patients with a clinical diagnosis of TB, 4 received rifampicin monotherapy alone.

## Discussion

We have shown that doctors in Russia draw upon a variety of media to inform themselves on antibiotic prescribing including 86.1% (366/425) who use standard pharmaceutical textbooks including one which is updated annually and equivalent to the British National Formulary. A high proportion (80%; 340/425), however, relied on information provided by pharmaceutical companies reflecting the links between physicians and the promotional influence of the pharmaceutical industry noted previously in other countries.<sup>13</sup>

Doctors were presented with a clinical case scenario describing a young woman with a 'common cold'. A Cochrane review of the efficacy of prescribing antibiotics for the 'general cold' indicated that there was insufficient evidence to support the use of antibacterial treatment.<sup>1</sup> Although the majority of respondents correctly suggested prescribing symptomatic relief, 1.7% would have prescribed antibiotics.

Doctors were asked whether they would select known TB drugs for the treatment of four respiratory syndromes and between 0.8% and 1.8% of them said that they would do so for the different scenarios. A larger proportion would consider the use of TB drugs.

The mostly widely prescribed antibiotics for respiratory diseases overall were in order: penicillins, fluoroquinolones, macrolides and cephalosporins.

Major guidelines including those of the American and British Thoracic Societies have indicated the role and importance of antibiotic therapy in the management of community or hospital pneumonia and in infective exacerbations of COPD.<sup>14–17</sup> Russian physicians made reasonable empirical and practical choices (penicillins, cephalosporins and macrolides) when compared with local and national Russian, American, or British guidelines<sup>18–21</sup> for community pneumonia and COPD. Fluoroquinolones were over-prescribed and where used ciprofloxacin rather than the 'respiratory fluoroquinolones' were used. We focused, therefore, on acute bronchitis and tonsillitis as antibiotic therapy has a more limited role here.

Acute bronchitis is caused primarily by respiratory viruses with a small proportion caused by bacteria, e.g. *Mycoplasma pneumoniae*, *Bordetella pertussis* and *Chlamydia pneumoniae*. Treatment is therefore directed at symptomatic relief and the use of antibiotics "is not recommended as a general practice".<sup>15</sup> For those cases of proven atypical bacterial aetiology, macrolides are effective and would be a reasonable option (as might be doxycycline or other tetracyclines).<sup>17</sup> In this study, we show that nearly all physicians would prescribe an antibiotic. Only 21.8% of prescriptions were for a macrolide (correctly) and antibiotics might be prescribed inappropriately in over two-thirds of cases. In actual practice, 90.8% (129/142) of the patients with acute bronchitis received at least one antibiotic.

Although most cases of tonsillitis are viral in origin, 5–30% of cases are due to group A streptococci<sup>18–20</sup> (*Streptococcus pyogenes*) which is an important differential diagnosis due to

**Table 3.** Proportion of patients with each respiratory condition treated with antibiotics and number of antibiotics prescribed

	Acute tonsillitis (n = 88)	Acute bronchitis (n = 142)	Community-acquired pneumonia (n = 93)	COPD (n = 50)	URTI (n = 80)	Asthma (n = 26)	Pleuritis (n = 3)	Lung cancer (n = 5)	TB (n = 8)
At least one antibiotic	88/88 (100%)	129/142 (90.8%)	90/93 (96.7%)	40/50 (80.0%)	20/80 (25.0%)	10/26 (38.5%)	2/3 (66.7%)	5/5 (100%)	8/8 (100%)
Two antibiotics	0	2/142 (1.4%)	28/93 (30.1%)	12/50 (24.0%)	0	0	2/3 (66.7%)	5/5 (100%)	8/8 <sup>a</sup> (100%)
Three antibiotics	0	0	3/93 (3.2%)	0	0	0	0	0	1/8 (12.5%)
Four antibiotics	0	0	0	1/50 (2.0%)	0	0	0	0	0

Total antibiotics prescribed for all patients combined for each respiratory condition.

n, number of patients.

<sup>a</sup>Four out of eight received rifampicin monotherapy for TB (second antibiotic was not for TB).

the sequelae of acute rheumatic fever and acute glomerulonephritis. Nevertheless, although penicillin or macrolide therapy is effective, in most cases no antibiotics are needed as the risk of complications is relatively low.<sup>22–26</sup> All patients with acute tonsillitis (100%; 88/88) received an antibiotic. Russian physicians would have over-prescribed antibiotics according to UK and USA guidelines but the actual choice in most cases (penicillins or macrolides) would have been correct although a significant minority of prescriptions were for fluoroquinolones.

This is the largest reported study conducted in Russia. The validity of the findings are strengthened through triangulation of research findings using questionnaires, scenario setting, and detailed case notes review of real practice. All relevant institutions were included. A limitation was that the study was carried out in one region, albeit with a population of 3.3 million, and our analyses may not be generalizable to the whole of Russia.

This study demonstrated that the use of antibiotics was excessive as even 25.0% of patients with a simple upper respiratory tract infection received an antibiotic. There is limited systematic data on the rates of drug resistance for respiratory pathogens other than TB, but studies suggest that resistance may be high in Russia. In a study of antibiotic resistance in European ICUs, antibiotic resistance across all species and drugs was, with some exceptions, highest in southern European countries and Russia, and lowest in Scandinavia.<sup>8</sup> Nevertheless, in a recent worldwide review of drug resistance among paediatric isolates,  $\beta$ -lactamase production among *Haemophilus influenzae* isolates ranged from approximately 4% in Russia to 26% in the United States and to 31% in France.<sup>27</sup> In a further study, the susceptibilities of 468 Russian clinical *Streptococcus pneumoniae* isolates and 600 *Streptococcus pyogenes* isolates, from 14 centres in Russia, to telithromycin, erythromycin, azithromycin, clarithromycin and penicillin G were tested. Penicillin-susceptible *S. pneumoniae* strains were rare except in Siberia, where their prevalence rate was 13.5%; most were of penicillin intermediate susceptibility. Overall, 2.5% of *S. pneumoniae* isolates were resistant to erythromycin. All *S. pyogenes* isolates were susceptible to penicillin, and 11% were erythromycin-resistant.<sup>28</sup> It is probable that, as in the UK and other European countries, inappropriate prescribing is a driver of drug resistance; similarly overuse of antibiotics seems to be widespread amongst both primary and secondary care physicians.<sup>2,5,6</sup> For some of these syndromes, Russian physicians were following local guidelines which need to be amended. For example, there are Russian guidelines for tonsillitis which recommend the empirical use of penicillins or macrolides (mainly because of the view that group A streptococci are very common causes of tonsillitis).<sup>29</sup>

High rates of drug resistance have been reported for *M. tuberculosis* in Samara,<sup>10</sup> and it is likely that inappropriate medical prescribing contributes to this. Although only a minority of doctors would prescribe anti-TB drugs inappropriately for non-TB illness, where treatment was given for suspected but unconfirmed TB, it was often monotherapy. Normal practice would be for patients in which TB was suspected to be referred for further investigation including microscopy, bacterial culture and radiography within the parallel structure of the TB 'dispensary' system. Doctors within the TB dispensary would attempt to obtain microbiological confirmation of TB and arrange therapy. For TB, greater effort should be made to obtain a microbiological diagnosis and to microbiologically exclude other causes of

**Table 4.** Antibiotics chosen from review of medical notes ( $n=495$ ) in order of preference for treatment of upper and lower respiratory diseases by clinical diagnosis, by antibiotic class and by commonest member within each class

Choice	Acute tonsillitis $n=88$	Acute bronchitis <sup>a</sup> $n=131$	Community- acquired pneumonia <sup>a</sup> $n=121$	COPD <sup>a</sup> $n=53$	Simple URTI $n=20$	Lung cancer $n=10$	Asthma $n=10$	TB $n=17$	Pleuritis $n=4$
1	penicillins 34 (38.6%) amoxicillin 22/34 (64.7%)	penicillins 66 (50.4%) amoxicillin 22/66 (33.3%)	cephalosporins 42 (34.7%) cefotaxime 13/42 (31.0%)	penicillins 19 (35.8%) amoxicillin, co-amoxiclav 6/19 (31.6%)	penicillins 10 (50.0%) amoxicillin 7/10 (70.0%)	penicillins 4 (40.0%) ampicillin 3/4 (75.0%)	cephalosporins 8 (80%) ceftriaxone 4/8 (50.0%)	TB drugs 12 (70.6%) rifampicin 8/12 (66.7%)	penicillins 1 (25.0%) ampicillin 1/1 (100%)
2	macrolides 24 (27.3%) erythromycin 13/24 (54.2%)	fluoroquinolones 26 (19.8%) ciprofloxacin 25/26 (96.2%)	penicillins 29 (24.0%) ampicillin 14/29 (48.3%)	cephalosporins 9 (17.0%) cefuroxime 3/9 (33.3%)	sulphanilamides 4 (20.0%) co-trimoxazole 4/4 (100%)	aminoglycosides 3 (30.0%) gentamicin 3/3 (100%)	tetracyclines 1 (10%) doxycycline 1/1 (100%)	aminoglycosides 3 (17.6%) gentamicin 3/3 (100%)	cephalosporins 1 (25.0%) cefazolin 1/1 (100%)
3	fluoroquinolones 22 (25.0%) ciprofloxacin 22/22 (100%)	macrolides 15 (11.5%) erythromycin 9/15 (60.0%)	fluoroquinolones 12 (9.9%) levofloxacin 5/12 (41.7%)	aminoglycosides 8 (15.1%) amikacin 8/8 (100%)	macrolides 3 (15.0%) clarithromycin 3/3 (100%)	tetracyclines 1 (10.0%) doxycycline 1/1 (100%)	aminoglycosides 1 (10%) gentamicin 1/1 (100%)	penicillins 2 (11.8%) ampicillin 1/2 (50%)	lincosamines 1 (25.0%) lincomycin 1/1 (100%)
4	tetracyclines 8 (9.1%) doxycycline 8/8 (100%)	tetracyclines 11 (8.4%) doxycycline 11/11 (100%)	macrolides 18 (14.9%) spiramycin 6/18 (33.3%)	macrolides 5 (9.4%) roxithromycin 2/5 (40.0%)	aminoglycosides 3 (15.0%) gentamicin 3/3 (100%)	lincosamines 1 (10%) lincomycin 1/1 (100%)			TB drugs 1 (25.0%) rifampicin 1/1 (100%)
5		lincosamides 4 (3.1%) lincomycin 4/4 (100%)	aminoglycosides 14 (11.6%) gentamicin 14/14 (100%)	fluoroquinolones 4 (7.5%) ciprofloxacin 3/4 (75.0%)		TB drugs 1 (10.0%) rifampicin 1/1 (100%)			
6		aminoglycosides 4 (3.1%) gentamicin 3/4 (75.0%)	lincosamides 3 (2.5%) lincomycin 3/3 (100%)	lincosamides 3 (5.7%) lincomycin 3/3 (100%)					
7		cephalosporins 4 (3.1%) cefoperazone 4/4 (100%)	TB drugs 2 (1.7%) rifampicin 2/2 (100%)	tetracyclines 2 (3.8%) doxycycline 2/2 (100%)					

 $n$ , total number of prescriptions.<sup>a</sup>First seven choices listed.

respiratory illness. Where an empirical clinical diagnosis of TB is made, treatment should be with standardized multi-drug therapy and never with monotherapy.

Current prescribing practice may be a contributing factor to the development of drug resistance in respiratory pathogens in Russia. Studies elsewhere which have demonstrated high inappropriate antibiotic use for the treatment of upper respiratory infections have demonstrated that it is possible to reduce over-prescribing.<sup>30,31</sup> The USA Centers for Disease Control and Prevention suggested that “multifaceted interventions may be effective in promoting appropriate drug prescribing”.<sup>32</sup> There remains a great need to restrict the use of antibiotics by doctors in general and to manage the expectations of patients over the value and necessity of antibiotics for simple infections particularly where they are of viral aetiology. There is also a need for further training of physicians, including reducing their reliance on pharmaceutical industry information, as well as legal measures to control the sale and spread of antibiotics.

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