### Duration of antibiotic treatment for respiratory tract infections in primary care

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**Objectives:** The primary driver of antimicrobial resistance is excessive antibiotic use, posing a global threat to public health. Reducing individual exposure to antibiotics is a key to addressing the problem. This study aimed to assess the duration of antibiotic courses administered to patients with acute respiratory tract infections (RTIs) in primary care.

**Methods:** Consecutive patients presenting with RTI symptoms were prospectively included from general practices and out-of-hours services in France, Greece, Lithuania, Poland and Spain for two winter periods (February to April 2022 and 2023). Data were collected using a paper-based Audit Project Odense template, with clinicians recording patient age, gender, RTI diagnosis, type of antibiotic prescribed and treatment duration.

**Results:** A total of 196 doctors (133 in general practice and 63 in out-of-hours services) registered 11270 cases, with 34.0% (3835) receiving antibiotics. The mean antibiotic course duration was 7.52 days (SD 2.11), which was significantly longer for pneumonia, COVID-19 infection and pharyngotonsillitis (8.01, 8.00 and 7.74 days, respectively), and lowest for predominantly viral infections, such as the common cold and flu infection, laryngitis and acute bronchitis (6.32, 6.48 and 6.98 days, respectively; P < 0.001). A total of 26.7% of the courses were prescribed for 10 days or longer.

**Conclusions:** Antibiotic courses for common RTIs are often prolonged, which does not align with current recommendations for course duration. Antibiotics should be avoided in cases of predominantly viral infections and most mixed infections; however, if deemed necessary, the courses should be substantially reduced to minimize unnecessary exposure.

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#### Introduction

Antimicrobial resistance (AMR) is a significant global health threat, which was worsened by the overuse and misuse of antibiotics. The rising prevalence of AMR leads to more severe infections, complications, prolonged hospitalizations and increased mortality rates.<sup>1,2</sup> The over-prescription of antibiotics, often for self-limiting conditions, plays a key role in the development of AMR.<sup>3</sup> This issue is particularly pronounced in primary healthcare settings, where most infections are viral. General practitioners are responsible for approximately 80% of all antibiotic prescriptions, with acute respiratory tract infections (RTIs) being the most common indication for antibiotic use.<sup>4</sup>

The key strategy in combating AMR is minimizing unnecessary antibiotic use and prescribing these drugs only when needed. Effective strategies to kerb antibiotic overuse include enforcing policies that prohibit over-the-counter antibiotic sales, promoting antibiotic deprescribing when clinicians deem it unnecessary based on clinical grounds, implementing antimicrobial stewardship programmes, involving clinicians in audits, adopting valid and reliable rapid point-of-care tests, enhancing communication skills with patients with the aid of information brochures and advocating delayed antibiotic prescribing strategies, which involve providing an antibiotic prescription with the advice to delay filling it if symptoms do not improve or worsen after a given number of days.<sup>5-8</sup> A promising approach emerging in recent years involves minimizing the exposure of individuals to antibiotic therapy by shortening courses, which should be implemented as rapidly as new evidence emerges and should become a matter of course when there is clear evidence of its effectiveness.<sup>9</sup> This approach was initially advocated for uncomplicated urinary tract infections in the early 2000s and is clearly supported in current guidelines<sup>10</sup>; however, an increasing body of evidence suggests that shorter durations of antibiotics are also effective in treating most bacterial RTIs.<sup>11-13</sup> Some recent clinical guidelines, such as the WHO AWaRe antibiotic book, advocate 5 day courses of antibiotics for acute rhinosinusitis, exacerbations of chronic obstructive pulmonary disease (COPD) and community-acquired pneumonia.<sup>14</sup> The latest update of the NICE guidelines also advocates shorter durations of antimicrobial therapy for RTIs in primary care.<sup>15</sup> Despite this evidence, most clinicians still use standard or longer courses.<sup>16,17</sup> A limited number of studies have evaluated the current prescribing behaviour of clinicians regarding the duration of antibiotic courses for these infections. The aim of this study was to investigate the duration of antibiotic prescriptions for different acute RTIs in general practice across five European countries.

#### Methods

#### Ethics approval

In Spain, the study protocol was approved by the Ethics Committee of the IDIAP Jordi Gol, Institute of Research in Primary Health Care, and the trial registration number is 21-121-P. The Ethical Committee Boards of Greece deemed it necessary to review the project and gave their approval. In Lithuania, Poland and France, there was no need for the Ethical Committee to review this type of project.<sup>18</sup>

#### Study design

This paper presents a secondary analysis of a before-and-after study conducted to enhance antibiotic prescribing practices in the primary care setting, focusing on reducing unnecessary antibiotic use and the prescription of non-first-line antibiotics.<sup>19</sup> A prospective study was carried out in five European countries with different cultural backgrounds and different healthcare organizations: France, Greece, Lithuania, Poland and Spain. The intervention involved presenting the results of the initial audit registration and engaging in discussions with peers. Additionally, it encompassed improvements in communication skills, the provision of communication tools such as materials and leaflets for patients and relatives and the introduction of an e-learning platform accessible to all participants. However, the intervention did not address the duration of antibiotic therapy.

#### Measurements and data

All participating clinicians were asked to complete a template for each consecutive patient with a community-acquired infection during the registration period. The data were recorded following the methodology of the Audit Project Odense (APO), using a prospective self-registry approach in which a simple reporting template was used.<sup>20</sup> Clinicians from the two primary care settings-general practice and out-of-hours services-were instructed to complete these registrations twice, with the initial registration taking place from February to April 2022 and the second registration period from February to April 2023. Participants registered the age and gender of the patients, RTI diagnosis given, type of antibiotic prescribed and duration, with a specific template designed for each setting. Figure S1 (available as Supplementary data at JAC-AMR Online) shows the templates used in the two settings. The templates for both clinicians in general practice consultations and primary care out-of-hours services considered the following RTIs: common cold or influenza infection, COVID-19, acute otitis media, acute rhinosinusitis, acute pharyngotonsillitis, acute bronchitis, acute exacerbations of COPD and pneumonia. The general practice template also included acute laryngitis.

#### Statistical analyses

Descriptive statistics were conducted, along with Chi-squared tests to compare categorical variables and Student's *t*-tests and analysis of variance to compare two or more quantitative groups, respectively. We considered a course to be prolonged when the doctor recommended the antibiotic to be taken for 10 days or more. We considered significant differences when P < 0.05. The data analysis was performed using SPSS v29.

#### Results

## General information on the infections collected and antibiotics prescribed

A total of 196 clinicians, with 133 practicing in general medicine and 63 in out-of-hours services, registered 11270 RTIs. Among these, information on 7850 (69.7%) infections were collected in general practice consultations and 3420 (30.3%) were registered in out-of-hours services. Women accounted for 6226 registrations (55.2%), and the mean age of the entire sample was 33.4 years (SD 25.6 years). Of all the patients with recorded ages, 3875 were children and 7339 were adults. Antibiotics were prescribed in 3835 (34.0%) cases, with higher rates observed for pneumonia (85.0%), acute otitis media (82.9%), acute COPD exacerbations (77.9%), acute rhinosinusitis (67.8%) and acute pharyngotonsillitis (63.7%) (Table 1). The percentage of antibiotics prescribed for patients with acute bronchitis was 47.8%. The antibiotics most frequently prescribed for RTIs were amoxicillin and clavulanate. Overall, penicillins were prescribed in 61.5% of all patients with RTIs. The prescription rate varied across countries, ranging from 51.5% in Greece to 25.7% in Spain (P<0.001). It was higher during

Table 1. General characteristics of the different	t diagnoses, antibiotic therapy	prescribed and duration of the antibiotic courses

	Total number of cases		Treated with antibiotics		Duration registered		Duration parameters, (days)				Prolonged courses prescribed <sup>a</sup>	
	n	%	n	%	n	%	Mean	SD	Median	IQR	n	%
Common cold/influenza	3985	35.4	83	2.1	82	98.8	6.32	1.27	7.00	6.00-7.00	1	1.2
COVID-19	1148	10.2	146	12.7	144	98.6	8.00	2.79	8.00	7.00-10.00	28	19.4
Acute otitis media	573	5.1	475	82.9	465	97.9	7.46	1.92	7.00	6.00-10.00	126	27.1
Acute rhinosinusitis	485	4.3	329	67.8	326	99.1	7.34	2.07	7.00	6.00-8.00	69	21.2
Acute pharyngotonsillitis	1782	15.8	1135	63.7	1119	98.6	7.74	1.89	7.00	7.00-10.00	392	35.0
Acute laryngitis <sup>b</sup>	324	4.1	63	19.4	59	93.6	6.48	1.69	7.00	5.00-7.00	6	10.2
Acute bronchitis	1204	10.7	576	47.8	565	98.1	6.98	1.84	7.00	6.00-7.00	80	14.2
Pneumonia	700	6.2	595	85.0	518	87.1	8.01	2.31	7.00	7.00-10.00	179	34.6
COPD exacerbation	271	2.4	211	77.9	205	97.2	7.40	2.27	7.00	7.00-10.00	48	23.4
Other infections	798	7.1	222	30.5	200	90.1	7.32	3.05	7.00	7.00-10.00	52	26.0
Total	11270	100.0	3835	34.0	3683	96.0	7.52	2.11	7.00	7.00-10.00	981	26.7

<sup>a</sup>Antibiotic courses of 10 days or more.

<sup>b</sup>Only available on the template filled out by general practitioners in general practice (n = 7850).

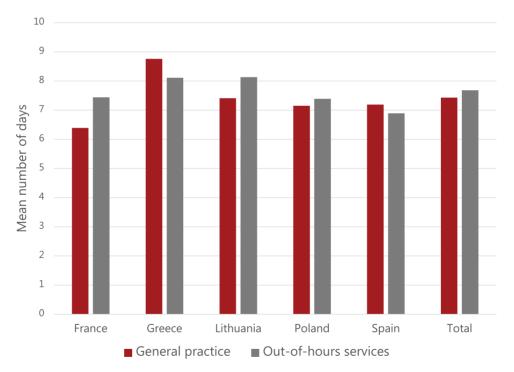


Figure 1. Treatment duration by country and setting.

the first audit (35.4% versus 32.7% in the second registration audit; P < 0.001) and in out-of-hours services compared with general practice (39.3% versus 28.7%; P < 0.001).

#### Mean duration of the antibiotic courses prescribed

The mean duration of the antibiotic courses was 7.52 days (SD 2.11), with a median of 7 days (IQR: 7–10 days), with no differences observed between the two registration periods (Table S1). Table 1

outlines the varying durations for different diagnoses in both settings—general practice consultations and out-of-hours services. The mean duration of antibiotic treatment was longest in Greece and shortest in France (8.54 versus 6.53 days, respectively; P < 0.001) and was longer in out-of-hours services compared with general practice (7.68 versus 7.43 days; P < 0.001) (Table S2). Figure 1 shows the mean duration of the antibiotic courses prescribed in the different settings and countries. The mean duration of the antibiotic courses was statistically longest for pneumonia (8.01 days; SD 2.3), followed by COVID-19 infection (8.0 days; SD 2.8) and acute pharyngotonsillitis (7.74 days; SD 1.9), and was shortest for colds and influenza infections (6.32 days; SD 1.3; P < 0.001). The mean durations for acute laryngitis and acute bronchitis were 6.48 days (SD 1.7) and 6.98 days (SD 1.8), respectively. Combining all the predominantly viral infections, the pooled mean duration was 7 days (SD 1.9).

A total of 981 courses (26.7%) were prolonged, prescribed for 10 days or longer, which was >30% in patients with pneumonia and pharyngotonsillitis and lowest in patients with the common cold (Table 1). The mean duration was longer in adults than in children (7.49 days, SD 1.88 versus 7.52 days, SD 2.22; P<0.05), with high variability among countries, but the percentage of prolonged courses was slightly greater among children (Table S3).

As shown in Table S4, amoxicillin was the predominant antibiotic for acute otitis media and acute pharyngotonsillitis, while amoxicillin and clavulanate were the most frequently prescribed antibiotics for lower RTIs and acute rhinosinusitis. Most of the penicillins prescribed for RTIs corresponded to 7 day courses, except in the case of acute otitis media, for which amoxicillin and clavulanate prescriptions mostly corresponded to 10 day courses. Similarly, for acute pharyngotonsillitis, 75% of the penicillin V prescriptions were for 10 day courses.

#### Discussion

The main finding of this study indicates that clinicians favour longduration antibiotic courses when treating RTIs. Although significantly longer durations of antibiotic therapy are prescribed for infections primarily caused by bacteria, such as pneumonia, most treatments for other RTIs last more than 6 days. Not only are these extended courses unnecessary, but they also subject individuals to prolonged therapy, carrying potential deleterious effects.

The study included over 10000 infections. The intervention prior to the second registration did not specifically address treatment duration, focusing instead on reducing unnecessary antibiotic prescribing as the primary goal and increasing the use of first-line antibiotics for different diagnoses, based on national guidelines from the participating European countries, as a secondary objective. Although treatment duration was not addressed during the intervention, we included this item on the template during both registration periods. The duration of the antibiotic courses prescribed during the second registration period was comparable with that observed during the first audit. This prospective study involved participating clinicians to register RTIs on the templates provided. This method provides a reflection of actual practices during consultations when prescribing antibiotic courses. Furthermore, the study was conducted across various European countries, allowing for the extrapolation of results to diverse contexts. This inclusivity is particularly valuable, considering the variation in antibiotic prescribing practices among different nations, such as Greece, which ranked first in European antibiotic consumption in 2023, and Lithuania, with a reported antibiotic consumption below the European average.<sup>21</sup>

One limitation lies in the potential impact of self-registration on prescribing habits. However, it is important to note that the APO methodology, employed in this study, has demonstrated high reliability across various European projects and shows a strong correlation with actual prescribing practices.<sup>22</sup> We cannot rule out the

possibility that clinicians did not record the actual treatment duration on the registration forms. Instead, they may have provided treatment durations they deemed more socially acceptable and aligned with good professional practice standards. Nevertheless, even in such cases, the data collected would likely still reflect the doctors' views on what they consider the most appropriate treatment duration. The voluntary participation of clinicians is another factor to consider, as studies have indicated that healthcare professionals who volunteer may demonstrate a greater interest in quality improvement programmes and research compared with the general population of doctors.<sup>23</sup> Theoretically, the ideal sequence involves treatment decisions following diagnostic decision-making. Diagnostic procedures and treatment decisions are intricately linked, and clinicians may determine antibiotic prescriptions concurrently with, or even prior to, conclusively diagnosing the patient's condition. Consequently, prescribers might adjust the diagnosis to align with the treatment decision, introducing the possibility of diagnostic misclassification bias.<sup>24</sup> In the second year, there was a documented shortage of certain first-line antibiotics, primarily in Eastern European countries.<sup>25</sup> While this shortage might have influenced the treatment prescribed, it is unlikely to have affected the duration of the therapies administered, which was the main focus of this analysis.

A major objective of antimicrobial stewardship programmes has been to reduce the use of non-first-line and broad-spectrum antibiotics. Few studies have assessed interventions to reduce the duration of treatment in outpatient settings.<sup>26,27</sup> The issue of longer-than-recommended treatment durations was mainly addressed in an English study that used a primary care database.<sup>28</sup> Based on a 2013 report from Public Health England, the study considered a 10 day antibiotic course for acute pharyngotonsillitis. 7 day courses for pneumonia and acute rhinosinusitis and 5 day courses for acute bronchitis, COPD exacerbations and acute otitis media. In this study, 80% or more of these treatment courses exceeded guideline recommendations for upper RTIs and acute bronchitis.<sup>28</sup> A 2019 study of patients with pneumonia concluded that two-thirds of patients received excess antibiotic durations, with 93.2% of the excess attributed to antibiotics prescribed at discharge. Each excess day was associated with a 5% increase in the odds of a patient having an antibiotic-associated adverse event.<sup>29</sup>

Clinical trials comparing short- and long-course antibiotic therapy for RTIs are accumulating, with most of the trials supporting the use of short-course therapy. Some recent clinical guidelines, such as the WHO AWaRe antibiotic book, advocate for 5 day courses of antibiotics for common RTIs.<sup>14</sup> A useful online tool summarizes the benefits of using short courses for 22 different infectious conditions, based on more than 130 clinical trials, most of which are managed in the hospital setting.<sup>30</sup> However, there are some notable exceptions. On one hand, some meta-analyses of treatment trials for streptococcal pharyngitis found that bacterial eradication rates were higher with 10 day courses of penicillin, although these differences were less pronounced with non-penicillin antibiotic treatments.<sup>31</sup> On the other hand, a recent network meta-analysis conducted of randomized controlled trials for acute otitis media in children showed that 7 day regimens of amoxicillinclavulanate were not inferior to 10 day courses, but 5 day regimens of amoxicillin and clavulanate were inferior to 10 day courses.<sup>32</sup>

The doubts arising with streptococcal tonsillitis and acute otitis media might hinder the generalization of using shorter antibiotic durations. This is also reflected in different recommendations. For example, even in a close-knit, small communities such as in the Scandinavian countries, the recommendations for streptococcal pharyngitis, acute otitis media and community-acquired pneumonia differ significantly in terms of doses and duration of penicillin V.<sup>33</sup> The same variability in the duration of antibiotic regimens exists in the current recommendations between France and Spain, two neighbouring countries that participated in this study.<sup>34,35</sup>

Despite clinicians in this study using 8 day antibiotic courses for pneumonia, which exceed the 5 day regimens recommended in the latest guidelines, the primary concern is the long durations prescribed for other RTIs, which are usually self-limiting and predominantly viral. Additionally, for these RTIs, the majority of antibiotics should be avoided. The evidence indicates that convincing doctors to refrain from prescribing antibiotics for certain viral RTIs, such as acute bronchitis in patients with otherwise healthy lungs, is challenaina; however, encouraging them to prescribe a minimal duration of therapy is more feasible.<sup>36</sup> In this study, doctors prescribe mean antibiotic courses of 7 days for infections in which viruses are predominant or plausible—common cold, flu infection, acute laryngitis, COVID-19 infection and acute bronchitis—according to the Centers for Disease Control and Prevention classification.<sup>37</sup> However, we observed that more than one guarter of all the antibiotic courses prescribed were for 10 days or longer, especially in pneumonia and pharyngotonsillitis. Despite the statistical significance of the difference in mean duration based on the diagnosis, age groups and setting, it is clinically irrelevant, as many patients are unnecessarily exposed to 1 week antibiotic regimens. However, important differences in the mean duration of the antibiotic courses were observed depending on the country, with a range of 2 days between the two countries with the longest and shortest durations. These results highlight the need to consider treatment duration as a crucial outcome for antimicrobial stewardship interventions in primary care. Convincing doctors to prescribe a short-course is much easier than encouraging them not to prescribe antibiotics if they feel uncertain about the aetiology and/or prognosis of the RTI.<sup>38</sup> In addition, promoting shorter regimens should be accompanied by changes in the regulation of antibiotic dispensing in community pharmacies. This includes favouring unit-dose dispensing for shorter courses, replacing the still-available full-box dispensing. Our key aim is to reduce unnecessary antibiotic exposure. By substantially limiting the duration of antibiotic courses, we can more successfully prevent side effects and kerb AMR.

#### Conclusions

We found a mean duration of antibiotic therapy slightly over 7 days for RTIs in two primary care settings, with durations being statistically longer for pneumonia, despite current guidelines recommending 5 day courses. Although antibiotics are prescribed less frequently for other RTIs, the mean duration for these infections was 7 days or more. It is crucial to restrict antibiotic exposure, particularly for these self-limiting and predominantly viral RTIs, to mitigate AMR and minimize adverse effects.

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#### **Transparency declarations**

None to declare.

#### Author contributions

The initial idea for this study was proposed by C. Ll. C. Ll., M. P. H., J. L., J. O. and L. B. designed the study. P. T. L., P. B., A. K., C. Li., R. R., L. J. and A. G. -S. collected the data. All authors were involved in the analysis or interpretation of the data, and all authors reviewed and critically revised the manuscript, approved the final draft and are accountable for the accuracy and integrity of the content.

#### Supplementary data

Figure S1 and Tables S1–S4 are available as Supplementary data at JAC-AMR Online.

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