

Antibiotic prescribing and expenditures in outpatient paediatrics in Greece, 2010–13

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Objectives: The objectives of this study were to provide a nationally representative analysis of antibiotic prescribing in outpatient paediatrics and to assess overall and class-specific antibiotic costs in Greece.

Methods: Data on antibiotic prescriptions for patients aged ≤ 19 years old between July 2010 and June 2013 in Greece were extracted from the IMS Health Xponent database. Antibiotics were grouped into narrow- and broad-spectrum agents. The number of prescribed antibiotics and census denominators were used to calculate prescribing rates. The total costs associated with prescribed antibiotics were calculated.

Results: More than 7 million antibiotics were prescribed during the study period, with an annual rate of 1100 antibiotics/1000 persons. Prescribing rates were higher among children aged < 10 years old. Acute respiratory tract infections (ARTIs) accounted for 80% of prescribed antibiotics, with acute otitis media (22.3%), acute tonsillitis (19.5%) and acute bronchitis/bronchiolitis (13.9%) being the most common clinical diagnoses. Cephalosporins (32.9%), penicillins (32.3%) and macrolides (32.1%) were the most commonly prescribed antibiotic classes. The majority (90.4%) of antibiotics were broad spectrum. Antibiotic expenditures totalled \sim €50 million.

Conclusions: Broad-spectrum antibiotic prescribing is common in outpatient paediatric patients. These data provide important targets to inform the development of an outpatient antimicrobial stewardship programme targeting specific practices, providers and conditions.

Keywords: antimicrobial prescription, ambulatory paediatric patients, acute respiratory infections, cost

Introduction

In the EU, antibiotic prescribing is highest in young children^{1,2} and outpatient acute respiratory tract infections (ARTIs) account for the majority of these prescriptions.^{2,3} It has been estimated that almost 50% of antibiotic prescriptions given to children are unnecessary or inappropriate.⁴

There is accumulating evidence linking overuse/misuse of antibiotics to increased antibiotic resistance and increased healthcare costs.^{5,6} This problem is more pronounced in Greece, which has the highest rates of antibiotic consumption and antibiotic resistance compared with other European countries.⁷ Recently, Greece has experienced a significant economic crisis, which has resulted in healthcare budgetary constraints. In this context, the reduction of healthcare costs is, more than ever before, a top priority for policy makers. Therefore, curtailing inappropriate antibiotic prescribing in Greece could be

an effective method to lower costs and reduce antibiotic resistance pressure.

To most effectively target interventions to improve outpatient antibiotic prescribing in Greece, it is critical to first understand prescribing patterns. Although national data on antibiotic prescribing for children are available for many European countries,^{1,8–11} such data are lacking for Greece.

Hence, we aimed to generate a nationally representative analysis of antibiotic prescribing in outpatient paediatrics and to assess overall and class-specific antibiotic costs in Greece.

Methods

Data source and design

The IMS Health Xponent Greece database was used to obtain data on the annual incidence of and indications for antibiotic prescriptions in the

paediatric outpatient setting (0–19 years old) between July 2010 and June 2013 in Greece. Xponent is a unique source of data capturing local and regional prescription drug dispensing.

This database contains longitudinal data that represent a 100% projection of prescribing activity in the community on the basis of prescriptions given by a random cluster sample, by specialty and region, of 625 physicians (2.5% of all doctors in Greece). IMS data directly link antibiotic prescriptions to the clinical indications. We restricted the analysis to the most common clinical diagnoses for which antibiotics were prescribed.

Antibiotic classification

Antibiotic prescriptions were categorized into two groups: narrow-spectrum antibiotics, which included narrow-spectrum penicillins (i.e. pivmecillinam, penicillin and amoxicillin); and broad-spectrum antibiotics, which included all other systemic antibiotics, as suggested by European Surveillance of Antimicrobial Consumption (ESAC) and National Institute for Health and Care Excellence (NICE) guidelines.

Cost data

The total antibiotic expenditures for outpatient paediatrics from the perspective of the national health insurance (EOPYY) were calculated by combining the daily dose, frequency and duration of each prescribed antibiotic with the corresponding reimbursed drug prices. These prices were obtained from the reimbursed drug list published by the Ministry of Health, reduced by the patient relevant copayment (25%). Costing data reflect the year 2013.

Statistical analysis

All collected variables were analysed descriptively. Nominal variables were analysed using frequencies and percentages. In order to calculate antibiotic prescribing rates, we used the number of antibiotics prescribed and census denominators from the Hellenic Statistical Authority (www.statistics.gr). Analyses were performed using SPSS 20.

Results

Antibiotic prescribing patterns

During the study period, an estimated 7 million antibiotic prescriptions were given to paediatric outpatients, resulting in an annual rate of 1100 antibiotics/1000 persons (95% CI: 1099–1101) (Table 1). Antibiotic prescribing rates were higher among children <10 years old (1632 prescriptions/1000 persons) compared with older children aged 10–19 years (579 prescriptions/1000 persons). Time trend analysis for the period under investigation showed a decline of 21.3% for the prescription of antibiotics between July 2010 and June 2013, although no statistically significant trend was detected.

The majority of prescribed antibiotics (90.4%) were broad spectrum. The most commonly prescribed antibiotic agents were cephalosporins (32.9%), penicillins (32.3%, of which only 1.1% were narrow spectrum) and macrolides (32.1%). Specifically, clarithromycin (25%), amoxicillin/clavulanic acid (22.6%) and cefprozil (18.4%) represented 66% of all prescribed antibiotics. Amoxicillin was prescribed for only 8.5% of patients (Table 2).

Antibiotic prescribing across clinical diagnoses

ARTIs accounted for 80% of all antibiotics prescribed, with acute otitis media (22.3%), acute tonsillitis (19.5%) and acute

Table 1. Antibiotic prescribing rates in outpatient paediatrics in Greece for the period July 2010–June 2013

	Number of prescribed antibiotics (millions)	Greek population 2011 ^a	Prescriptions per 1000 persons per year (95% CI)
Age (years)			
0 to <1	0.359	103 877	1152 (1148–1156)
1–4	2.548	433 366	1960 (1957–1962)
5–9	2.234	512 596	1453 (1451–1455)
10–14	0.873	519 429	560 (559–561)
15–19	0.991	553 276	597 (596–598)
Total	7.005	2 122 544	1100 (1099–1101)

^aBased on the 2011 census (www.statistics.gr).

bronchitis/bronchiolitis (13.9%) being the most common clinical diagnoses (Table 2).

Broad-spectrum antibiotics were prescribed for 83.9%, 94.4% and 87.3% of acute otitis media, acute tonsillitis and acute bronchitis/bronchiolitis episodes, respectively.

Clarithromycin was the most commonly prescribed antibiotic for acute tonsillitis (36.4%) and acute bronchitis/bronchiolitis (40.2%), while amoxicillin/clavulanic acid was the most commonly prescribed antibiotic for acute otitis media (31.7%).

Antibiotic expenditures

During the 3 year study period, the total expenditures for prescribed antibiotics were ~€50 million. Cephalosporins and macrolides each represented 40% of the total expenditures for antibiotics. Clarithromycin alone accounted for almost one-third (32.7% or €16.1 million) of the total antibiotic expenditures, followed by cefprozil (21.9% or €10.8 million). Although amoxicillin/clavulanic acid was the second most frequently prescribed antibiotic, only 13.1% (€6.5 million) of the total antibiotic expenditure was attributed to this agent (Table 2).

Discussion

Several studies have monitored outpatient antibiotic consumption in the general population. For example, ESAC, a network of national surveillance systems, collects comparable and reliable data on antibiotic use across various countries including Greece.⁷ When reporting antibiotic consumption in the total population (adults included), consumption was much higher in Greece compared with most other countries. In the present study, we focused on the paediatric population, which is known to have higher rates of prescribing. To the best of our knowledge, this is the first study describing antibiotic prescribing patterns in ambulatory paediatrics in Greece.

We found a high annual rate of antibiotic prescribing in outpatient paediatrics in Greece, but this decreased over time. The vast majority of antibiotics prescribed were broad spectrum, with clarithromycin, amoxicillin/clavulanic acid and oral cephalosporins being the most commonly prescribed antibiotics as

Table 2. Antibiotic prescribing patterns and expenditures in outpatient paediatrics in Greece for the period July 2010–June 2013

	Number of prescribed antibiotics (in millions)	Percentage of prescribed antibiotics	Expenditures (in €)	Percentage of total expenditures
Total	7.005		49176361	
Type of antibiotics				
cephalosporins	2.305	32.9	19774139	40.21
macrolides	2.246	32.1	19712793	40.09
penicillins	2.260	32.3	8560851	17.41
tetracyclines	0.086	1.2	366624	0.75
trimethoprim	0.060	0.9	98733	0.20
fluoroquinolones	0.036	0.5	459629	0.93
other β -lactams excluding penicillins and cephalosporins	0.012	0.2	203591	0.41
Antibiotic				
clarithromycin	1.752	25.0	16095485	32.73
amoxicillin/clavulanic acid	1.582	22.6	6458358	13.13
cefprozil	1.289	18.4	10752742	21.87
amoxicillin	0.596	8.5	1639687	3.33
cefaclor	0.536	7.7	3946483	8.03
cefuroxime	0.453	6.5	4893132	9.95
azithromycin	0.438	6.2	3236451	6.58
penicillins	0.079	1.1	446015	0.91
Broad versus narrow spectrum				
narrow spectrum	0.676	9.6	2096610	4.26
broad spectrum	6.329	90.4	47079750	95.74
Clinical diagnosis				
acute otitis media	1.560	22.3	9954119	20.24
acute/chronic sinusitis	0.204	2.9	1710229	3.48
acute tonsillitis	1.369	19.5	10968513	22.30
acute bronchitis/bronchiolitis	0.975	13.9	6897667	14.03
cystitis/other urinary tract infections	0.281	4.0	1831919	3.72
acute pharyngitis	0.340	4.9	2302502	4.68
acute lower respiratory infections	0.242	3.5	3339988	6.79
other	2.033	29.0	12171422	24.75

Narrow-spectrum antibiotics included amoxicillin and penicillin.

opposed to amoxicillin. Eighty percent of antibiotic use was for ARTIs. Antibiotic prescriptions represented a significant health-care expenditure for the national healthcare system.

Antibiotic prescribing rates identified in our study are consistent with those reported in previous studies, indicating that the rate is higher in young children and decreases with age.^{8,12,13} Comparing the overall estimated antibiotic prescription rate in Greece with that provided in other countries for corresponding populations, we reveal that our rate (1.1/person-year) is amongst the highest along with Italy (1.3/person-year in children ≤ 13 years in 2006)⁹ and Canada (0.9/person-year in children < 19 years in 2001)¹⁴ in contrast to rates reported in Germany (0.7/person-year in 2004–06).⁸ These comparative data raise concerns about the appropriateness of antibiotic prescribing for children in Greece.

As for antibiotic prescribing across diagnostic conditions, our results revealed that ARTIs accounted for 80% of total antibiotic

prescriptions in outpatient paediatrics, slightly higher than that reported in a corresponding population in the USA (i.e. almost 75%).¹² Professional guidelines from the USA and other European countries support the treatment of most bacterial ARTIs with narrow-spectrum antibiotics,^{15,16} which is at odds with the high rate of broad-spectrum antibiotic prescribing. The implications of antibiotic overuse are profound. Considering that > 6 million broad-spectrum antibiotics were prescribed to children in Greece during the study period, an intervention that could produce a modest 10% reduction in broad-spectrum prescribing would result in $\sim 600\,000$ fewer unnecessary broad-spectrum antibiotic prescriptions and savings of $\sim \text{€}4.7$ million to the national health-care system.

Overall, our study indicates that antibiotic overprescribing is a significant problem in Greece. These data provide important targets for interventions to improve judicious antibiotic prescribing. Parental pressure to prescribe antibiotics and inadequate

knowledge around appropriate utilization of antibiotics are some of the factors leading to antibiotic overuse.¹⁷ There are many examples of countries that have succeeded in reducing the amount of antibiotics prescribed to children, including the Netherlands, Sweden and the USA, after promoting rational antibiotic prescribing by educational, antimicrobial stewardship with feedback and regulations.^{18,19}

Our study had several limitations. First, IMS data are obtained from a sample of 625 practitioners. Although selected following a cluster procedure by specialty and region, the sample may not be representative of the population of physicians and region under study. Second, we report on antibiotic prescriptions not actual antibiotic use, as we did not capture antibiotics dispensed by pharmacists without a physician's prescription, a not uncommon practice in Greece.²⁰ Third, we believe that our study likely underestimated the national antibiotic prescribing rate because we did not have access to prescribing data from emergency departments and outpatient departments located in hospitals. Fourth, the reasons for the reduction in antibiotic prescriptions over the study period (2010–13) cannot be definitely determined with our data. Finally, it should be noted that the costs related to antibiotic use throughout the study period may be underestimated; drug prices as published at the end of the year 2013 were used in our calculations when there was known to be a sharp reduction in drug prices in Greece.

Conclusions

In conclusion, we observed a high rate of antibiotic prescribing in outpatient paediatrics in Greece, with clarithromycin, amoxicillin/clavulanic acid and oral cephalosporins being the most commonly prescribed antibiotics as opposed to amoxicillin. These data indicate that broad implementation of outpatient antimicrobial stewardship interventions targeting specific practices, providers and conditions should be a public health priority for Greece.

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Transparency declarations

None to declare.

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