



## Prescription of antibiotics in children in primary care. Study in an administrative area of Osakidetza-Basque Health Service

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### Abstract

**Introduction:** based on the current literature, the consumption of antibiotics in children is high in Spain. However, there may be large differences even between small geographic areas. The objective of the study was to establish the frequency of antibiotic prescription in the paediatric age group and describe the characteristics of these prescriptions in the in the Barrualde-Galdakao integrated health care area of the Osakidetza-Basque Health System.

**Methods:** we made a retrospective analysis of antibiotic prescriptions made to children aged 0 to 13 years in years 2015, 2016 and 2017. We retrieved the data from the Presbide database of the Osakidetza-Basque Health System. We calculated rates of antibiotic-treated episodes and the prevalence of antibiotic use, and analysed the distribution by type of antibiotic.

**Results:** We analysed 56 974 antibiotic prescriptions dispensed to 40 824 children over a 3-year period. The number of antibiotic-treated episodes per 1000 children/year was 465.20. The percentage of children who received at least one antibiotic per year was 30.72. The highest rates of antibiotic use occurred in children aged 1 and 2 years (826 and 827 episodes treated/1000 children/year respectively), and 64.61% of the dispensed prescriptions were for amoxicillin

**Conclusion:** The frequency of antibiotic use in children found in our study was high compared to countries with a low frequency of antibiotic prescription in Europe and significantly lower compared to the results of other studies conducted in Spain and other Mediterranean countries.

### Key words:

- Antibiotics
- Children
- Pharmacoepidemiology
- Prescription
- Primary Care

## Prescripción de antibióticos en niños en Atención Primaria. Estudio en un área administrativa de Osakidetza-Servicio Vasco de Salud

### Resumen

**Introducción:** según los estudios disponibles, el consumo de antibióticos en niños es elevado en España. No obstante, puede haber grandes diferencias territoriales incluso entre áreas geográficas pequeñas. El objetivo del estudio es conocer la prescripción de antibióticos en la edad pediátrica y describir sus características en el área administrativa de la Organización Sanitaria Integrada (OSI) Barrualde-Galdakao del Servicio Vasco de Salud-Osakidetza.

**Material y métodos:** se han estudiado retrospectivamente las prescripciones antibióticas realizadas a niños de 0 a 13 años a lo largo de los años 2015, 2016 y 2017. Los datos han sido extraídos de la base de datos Presbide del Servicio Vasco de Salud-Osakidetza. Se han determinado tasas de episodios tratados con antibiótico y su prevalencia, así como tipos de antibióticos utilizados.

**Resultados:** se han analizado 56 974 prescripciones de antibiótico dispensado a 40 824 niños a lo largo de tres años. El número de episodios tratados con antibiótico por 1000 niños/año fue de 465,20. El porcentaje de niños que recibió al menos una dispensación antibiótica/año fue de 30,72. La máxima incidencia de prescripción se dio en niños de uno y dos años (826 y 827 episodios tratados/1000 niños/año respectivamente). El 64,61% de las dispensaciones fueron de amoxicilina.

**Conclusión:** nuestras cifras de prescripción de antibióticos en niños son elevadas en comparación con los países poco prescriptores del norte de Europa y sensiblemente inferiores a los datos disponibles de estudios hechos en España y de otros países del área mediterránea.

### Palabras clave:

- Antibióticos
- Atención Primaria
- Farmacoepidemiología
- Niños
- Prescripción

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## INTRODUCTION

Inappropriate antibiotic use not only causes individual harm and increases health care expenditure, but may also contribute to the development of drug-resistant bacteria,<sup>1</sup> which leads to serious public health problems.<sup>2</sup> Most antibiotics are prescribed at the primary care level,<sup>3</sup> with the highest frequency of prescriptions corresponding to the 0-4 years age group.<sup>3,4</sup>

In up to 60% of cases, antibiotics are used for treatment of respiratory infections,<sup>5</sup> most of which are viral, and some authors estimate that antibiotic use may be inappropriate in up to 50% of cases.<sup>6</sup>

Spain, along with other countries in the Mediterranean region, is one of the greatest consumers of antibiotics in Europe,<sup>7</sup> and the few studies conducted on the subject in children have identified the same trend.<sup>8</sup> However, there may be significant differences in the use of antibiotics in children not only between countries,<sup>8,9</sup> but also between regions in the same country<sup>10</sup> and between prescribers in smaller geographical areas.<sup>11,12</sup>

Overall, antibiotic use in the Basque Country is high, with figures that are very similar to those of other regions in Spain,<sup>13</sup> but we are not aware of any studies of antibiotic prescription in children in this autonomous community.

The aim of our study was to describe antibiotic prescription in the paediatric age group and its characteristics in the Barrualde-Galdakao integrated health care area (IHCA) of the public health system of the Basque Country (Osakidetza).

## MATERIAL AND METHODS

We conducted a retrospective cohort study in the Barrualde-Galdakao IHCA, making a descriptive analysis of antibiotic prescription in children. The Barrualde-Galdakao IHCA of the Osakidetza-Basque Health System includes 17 primary care units (PCUs) serving a catchment population of 313 000 inhabitants. We included children aged 0 to 13 years that received prescriptions in 2015, 2016 and 2017.

We obtained the data from the outpatient prescription database of the Osakidetza-Basque Health System (Presbide). This database includes information on the type of antibiotic prescribed using Anatomical, Therapeutic, Chemical (ATC) classification system codes, the date of prescription and dispensation, the patient identification code and the age, sex and PCU of the patient. We analysed with ATC code J01 (antibacterials for systemic use); thus excluding drugs for treating tuberculosis, antifungal and antiparasitic drugs and topical antibacterials. We excluded prescriptions that were not dispensed by the pharmacy system. If we found records of the same antibiotic being dispensed 2 or more times within a period of up to 14 days, we counted it a single instance of dispensation (1 treated episode).

We analysed the following variables: number of antibiotic dispensations or episodes treated with antibiotics per 1000 children per year (rate of antibiotic-treated episodes) and the distribution of antibiotic prescription by age, month of year and PCU, the percentage of children that received at least 1 antibiotic dispensation per year (prevalence of antibiotherapy) and the distribution by age group and sex. We also analysed the type of antibiotics used and corresponding proportions, and the distribution by subgroups, for which we established the categories of first- and second-line penicillins, first- and second-generation macrolides, cephalosporins and other (Table 1).

To perform this analysis, we used absolute frequency and percent distributions and compared them between groups by means of the  $\chi^2$  test.

We obtained data regarding the population from the Osabide database of the Osakidetza-Basque Health System.

All the analyses were made with the statistical software SAS 9.4.

## RESULTS

The study population consisted of 40 901 children in 2015, 41 059 in 2016 and 40 512 in 2017, of which 48.12% were girls.

**Table 1. Classification of antibiotics**

<b>First-line penicillins</b>	Amoxicillin, ampicillin, dicloxacillin, oxacillin, penicillin V potassium
<b>Second-line penicillins</b>	Amoxicillin-clavulanic acid
<b>First-generation macrolides</b>	Erythromycin, josamycin
<b>Second-generation macrolides</b>	Azitromicina, clarithromycin, roxithromycin
<b>Cephalosporins</b>	Cefaclor, cefadroxil, cefixime, cefuroxime, ceftibuten, cefalexin, ceftibuten, cefditoren, cefpodoxime, cefprozil
<b>Others</b>	Quinolones, clindamycin, doxycycline, minocycline, nitrofurantoin, vancomycin, linezolid, trimethoprim-sulfamethoxazole

We analysed a total of 56 974 dispensed antibiotic prescriptions corresponding to the period under study. There were 7814 prescriptions (12.06%) that were never dispensed through the pharmacy system. We did not include 6375 dispensations (10.06%) in the count because they were instances of repeated dispensation of the same antibiotic to the same patient within a 14-day window.

In the period under study, the rate of antibiotic-treated episodes was of 465.20/1000 children/year and the percentage of children with at least 1 treated episode/year was 30.72%.

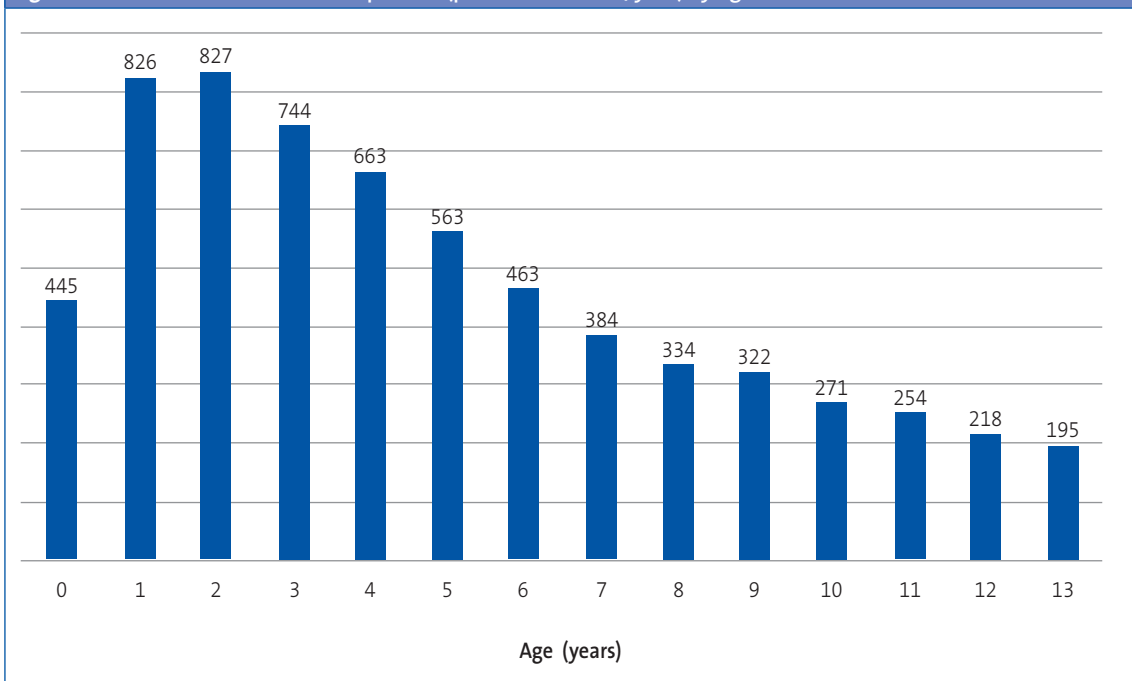
The age distribution of antibiotic-treated episodes (Figure 1) shows that the incidence peaked at ages

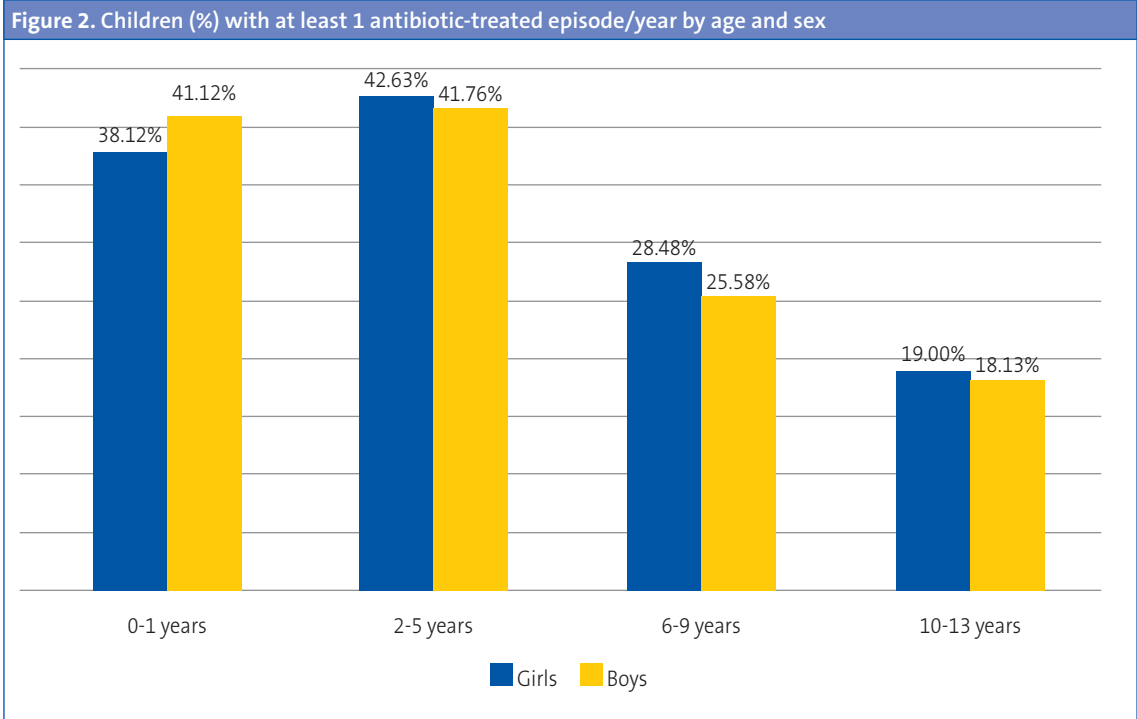
1 and 2 years (826 and 827 treated episodes per 1000 children/year, respectively), with a fairly even decrease at later ages.

Figure 2 shows that early childhood (ages 2-5 years) was the age range corresponded to the highest frequency of antibiotic use ( $p < 0.0001$ ). The prevalence was also greater in male infants compared to female infants (0-1 years;  $p < 0.0001$ ), but this predominance inverted starting at pre-school age, when prescription became more frequent in girls.

In the years under study, 59.43% of antibiotic treatments took place in the first and last trimesters of the year, with an incidence of treated episodes of

**Figure 1. Rate of antibiotic-treated episodes (per 1000 children/year) by age**

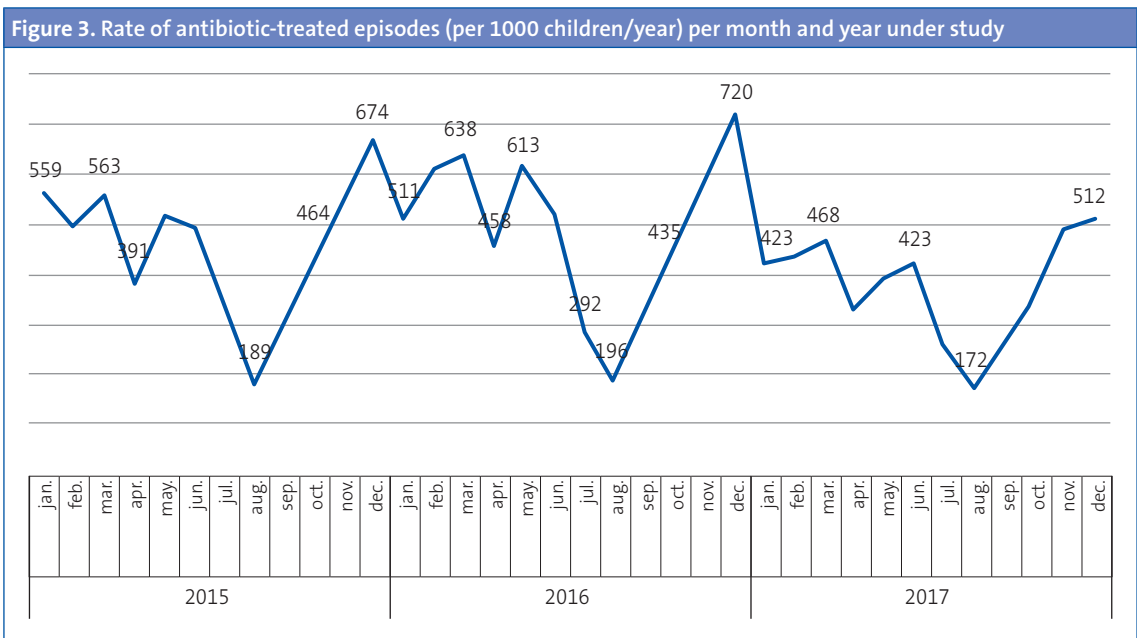


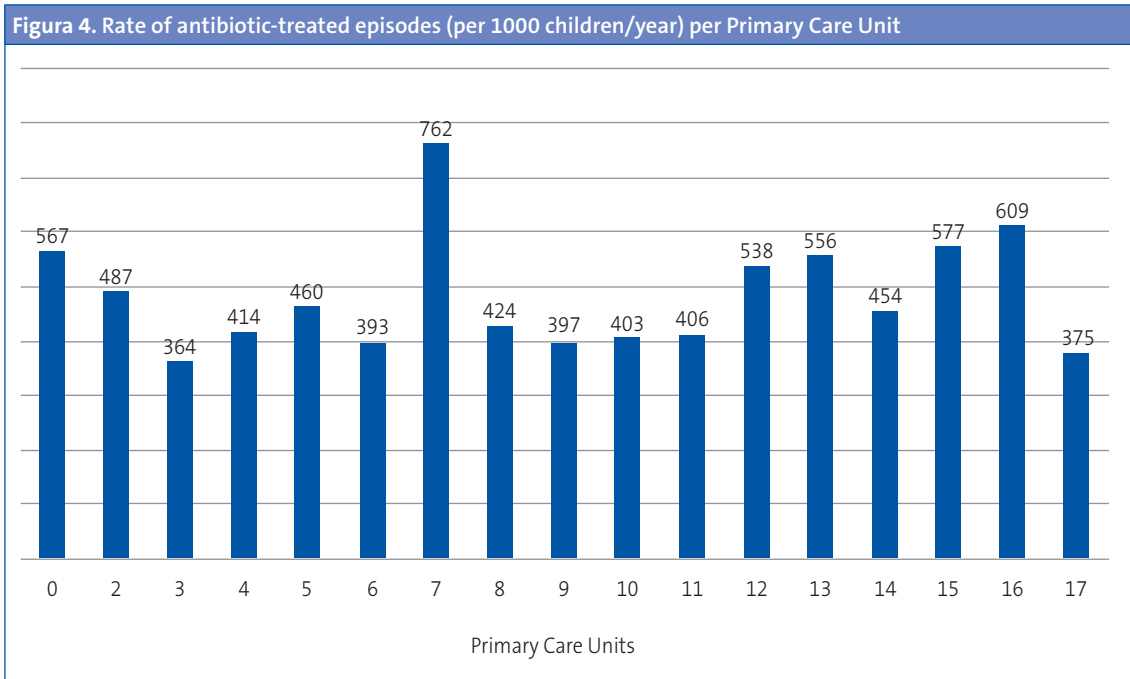


553/1000 children/year, higher compared to the April-September semester, in which the incidence was 378/1000 children/year. In the aforementioned trimesters, antibiotic prescriptions exceeded prescriptions made the rest of the year by 32%.

Figure 3 shows the differences between months in the frequency of antibiotic-treated episodes in the years under study.

The frequency of antibiotic-treated episodes in the different PCUs ranged from 364/1000/children/





year to 762/1000 children/year, and many of these were statistically significant ( $p < 0.0001$ ). **Figure 4** presents the figures for the 17 PCUs.

**Table 2** shows the most frequently used antibiotics. Three antibiotics accounted for more than 90% of the total dispensations: amoxicillin, amoxicillin-clavulanic acid and azithromycin. This was also the case in 15 of the 17 PCUs included in the study. We ought to highlight the infrequent use of cephalosporins (1.87%) penicillin V (1.62%), erythromycin (0.24%) and cloxacillin (0.07%).

**Figure 5** presents the distribution of the dispensed antibiotics by subgroup. We found that 66.3% of prescriptions corresponded to first-line penicillins, with amoxicillin accounting for nearly all of these prescriptions (97%). Azithromycin accounted for 91% of the macrolides.

## DISCUSSION

The rate of 465.34 antibiotic-treated episodes per 1000 children/year and an annual antibiotic use prevalence of 30.72% indicates that in our region, antibiotic prescription in children is higher com-

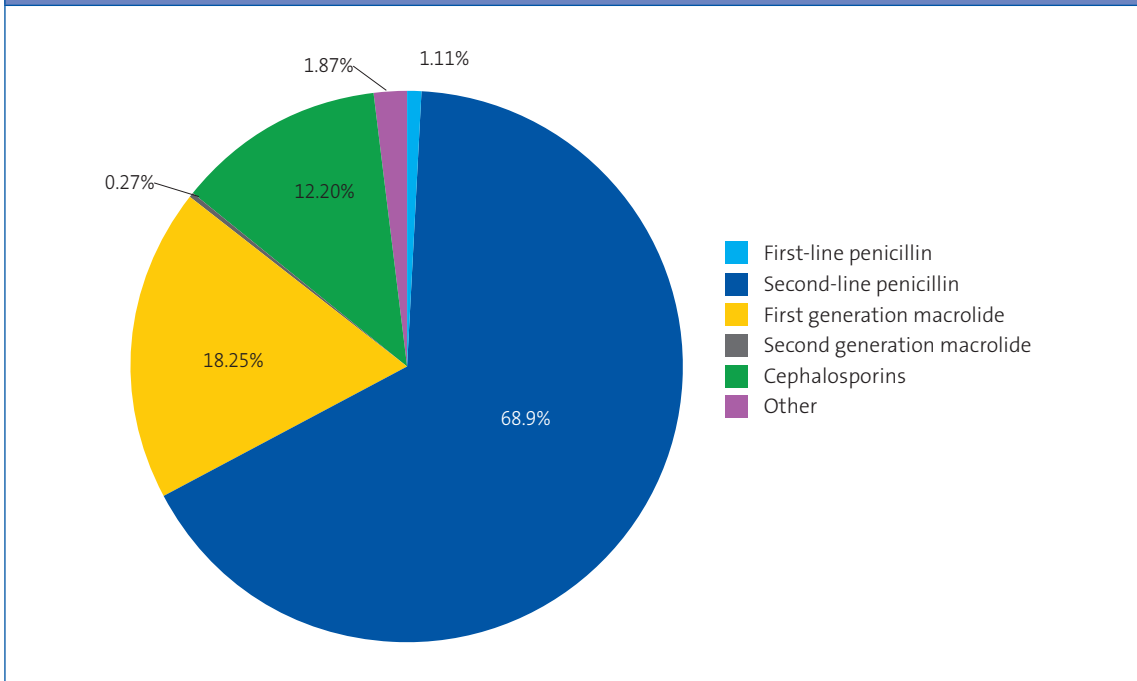
**Table 2. Antibiotics prescribed most frequently**

Antibiotic	Dispensaciones (n)	%
Amoxicillin	36 811	64.61
Amoxicillin-clavulanic acid	10 401	18.25
Azithromycin	5927	10.40
Other	3835	6.73

pared to countries that with historically low rates of antibiotic prescription, such as the Netherlands<sup>9,14,15</sup> and Norway<sup>8</sup>, but also substantially lower, based on the available data, to the frequency in other areas of Spain<sup>4,8,16</sup> and other countries in the Mediterranean region.<sup>8,10,17</sup> The antibiotic dispensation figures we found were also lower compared to those reported in studies conducted in Germany<sup>8,9,18</sup> and similar to those reported in the United Kingdom.<sup>9,14,19</sup>

The seasonal variation in dispensation in our catchment area reflects the high antibiotic prescription pattern associated with winter outbreaks of disease, which are known to be caused by viruses. Seasonal peaks have been found to be most pronounced in countries with high antibiotic utilization,<sup>9</sup> but we did not find any studies that meas-

**Figure 5. Percent distribution by subgroup of prescribed antibiotics**



ured these variations in the paediatric population, which in our study was of 32%.

We found significant homogeneity in the antibiotics selected by clinicians, which may be indicative of adherence to protocols or clinical guidelines.

Although 66.3% of antibiotic treatments were done with first-line penicillins, our data show a very infrequent use of narrow-spectrum antibiotics such as penicillin V and antistaphylococcal penicillins. Difficulties with the administration of oral dosage forms of these antibiotics (interactions with food, bad taste) are probably the main reason why they are displaced by other broader-spectrum drugs. The use of amoxicillin-clavulanic acid and cephalosporins in our study was much lower compared to previous studies of national scope.<sup>8,20</sup>

The significant differences in prescription observed between PCUs corroborated the findings of other studies<sup>10,12</sup> on the variability of antibiotic use, even in very small geographical areas. The prescription practices in clinicians are often influenced by how clinicians handle diagnostic uncer-

tainty and parental expectations, and this aspect is probably one of the greatest contributors to the observed variability.<sup>12</sup> We agree with other authors<sup>10,21</sup> that an awareness of clinicians of the characteristics of their prescribing practices and a more local approach to the development of antibiotic stewardship strategies are a necessary complement to strategies of a more general scope.

In conclusion, we present the first study of antibiotic prescription in children in the Basque Country. The antibiotic dispensation figures obtained in this study fell between those observed in high-prescription and low-prescription countries in Europe. We found substantial homogeneity in the selection of the antibiotics to use, and substantial variability in the frequency of prescription between PCUs. Most antibiotic treatments involved use of first-line penicillins, with infrequent use of narrow-spectrum antibiotics. We ought to mention some of the limitations of the study: our results underestimate the antibiotics given to children, as we did not have access to data from the private sector, and we did not know the diagnoses

that motivated the prescriptions, which limited our ability to assess whether the use of antibiotics was appropriate.

## CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare in relation to the preparation and publication of this article.

## ABBREVIATIONS

**ATC:** Anatomical, Therapeutic, Chemical Classification System • **IHCA:** Integrated Health Care Area • **PCU:** primary care unit.

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