High Rates of Prescribing Antimicrobials for Prophylaxis in Children and Neonates: Results From the Antibiotic Resistance and Prescribing in European Children Point Prevalence Survey

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Background. This study was conducted to assess the variation in prescription practices for systemic antimicrobial agents used for prophylaxis among pediatric patients hospitalized in 41 countries worldwide.

Methods. Using the standardized Antibiotic Resistance and Prescribing in European Children Point Prevalence Survey protocol, a cross-sectional point-prevalence survey was conducted at 226 pediatric hospitals in 41 countries from October 1 to November 30, 2012.

Results. Overall, 17,693 pediatric patients were surveyed and 36.7% of them received antibiotics (n = 6,499). Of 6,818 inpatient children, 2,242 (32.9%) received at least 1 antimicrobial for prophylactic use. Of 11,899 prescriptions for antimicrobials, 3,400 (28.6%) were provided for prophylactic use. Prophylaxis for medical diseases was the indication in 73.4% of cases (2,495 of 3,400), whereas 26.6% of prescriptions were for surgical diseases (905 of 3,400). In approximately half the cases (48.7% [1,656 of 3,400]), a combination of 2 or more antimicrobials was prescribed. The use of broad-spectrum antibiotics (BSAs), which included tetracyclines, macrolides, lincosamides, and sulfonamides/trimethoprim, was high (51.8% [1,761 of 3,400]). Broad-spectrum antibiotic use for medical prophylaxis was more common in Asia (risk ratio [RR], 1.322, 95% confidence interval [CI], 1.202–1.653) and more restricted in Australia (RR, 0.619; 95% CI, 0.521–0.736). Prescription of BSA for surgical prophylaxis also varied according to United Nations region. Finally, a high percentage of surgical patients (79.7% [721 of 905]) received their prophylaxis for longer than 1 day.

Conclusions. A high proportion of hospitalized children received prophylactic BSAs. This represents a clear target for quality improvement. Collectively speaking, it is critical to reduce total prophylactic prescribing, BSA use, and prolonged prescription.

Key Words: antimicrobials; inpatients; pediatrics; point-prevalence survey; prophylactic prescribing.

Antimicrobial agents are among the most commonly prescribed medications, especially for children and neonates. Although the appropriate selection and administration of antibiotics certainly saves lives, their widespread overuse—especially of broad-spectrum antibiotics—has also contributed to significant increases in antimicrobial resistance [1, 2]. Therefore, pediatric-specific antibiotic stewardship programs are urgently needed [3]. These programs must specifically address the substantial differences that exist between children and adults [4].

Prophylactic use of antibiotics to prevent infections is contentious. National guidelines emphasizing short duration and focused use already exist for surgical prophylaxis [5, 6]. Because pediatric-specific surgical prophylaxis data are sparse, pediatric recommendations have been extrapolated from adult data [5, 6]. Guidelines for medical antibiotic prophylaxis can only be found for a few specific medical conditions, such as congenital heart anomalies, vesicoureteral reflux, acute rheumatic fever, asplenia and sickle cell disease, meningococcal and pertussis exposure, Pneumocystis pneumonia prophylaxis, and latent tuberculosis infection [7]. To date, data on which children receive antimicrobial prophylaxis and why they do have not been available. Cross-sectional point-prevalence surveys (PPS) are a validated method for analyzing data on antimicrobial usage and for determining quality indicators [8, 9]. We analyzed data on prophylactic antibiotic prescribing from the Antibiotic Resistance and Prescribing in European Children (ARPEC) project [8], a multicenter, cross-sectional study investigating prescription variations for systemic antimicrobial agents at 226 pediatric hospitals in 41 countries worldwide [10].
METHODS

Data Source and Study Population
Data were extracted from the global ARPEC internet-based PPS, which was performed between October 1 and November 30, 2012, at 226 pediatric hospitals in 41 countries worldwide [10]. The study included all children who were hospitalized and received at least 1 antimicrobial for prophylactic indications on the day of the survey.

Data Collection
The cross-sectional, hospital-based PPS used the standardized ARPEC-PPS protocol, which consisted of 2 sets of data collection forms: one for patients on pediatric wards and a second for infants on neonatal wards [8, 10]. Participating hospitals were asked to conduct a 1-day PPS during a regular working day during October–November 2012. To capture meaningful information about antimicrobial prophylaxis from the previous 24-hour period, pediatric surgical wards were not audited on Mondays. This included all children under 18 years old who had been admitted before midnight the previous day and were still present in hospital at 8:00 AM on the day of the survey. The surveillance mainly focused on systemic antimicrobial agents, but it also included antibiotics and other antimicrobials used as intestinal anti-infectives (following the Anatomical Therapeutic Chemical classification system) [11]. This included antibacterials for systemic use, antibiotics used for treatment of tuberculosis or leprosy, antibiotics used as intestinal anti-infectives, nitroimidazole derivatives, antifungals, antivirals for systemic use, tuberculosis or leprosy, antibiotics used for treatment of tuberculosis or leprosy, antibiotics used as intestinal anti-infectives, nitroimidazole derivatives, antifungals, antivirals for systemic use, and antimalarials [10]. The following antibiotics were arbitrarily classified as broad-spectrum: tetracyclines, penicillins with extended spectrum (eg, piperacillin ± tazobactam, ticarcillin + clavulanic acid); second-, third-, and fourth-generation cephalosporins; carbapenems; sulfonamides and trimethoprim; macrolides; lincosamides; aminoglycosides; and fluoroquinolones and polymyxins. We classified carbapenems, fluoroquinolones, and glycopeptides as reserve antibiotics. In addition to the antimicrobial agents (name, application route, dose per administration, number of doses per day), the following information was collected: patient age, gender, current weight, underlying diagnoses, and type of prophylaxis. Two types of prophylaxes were distinguished: surgical and medical. In addition, the duration of surgical prophylaxis was categorized as single dose, equal to 24 hours or else greater than 24 hours. All data were collected anonymously [8]. Countries were classified according to the United Nations Standard Country and Area Codes [12].

Data Analysis
Anonymous patient data were collected on paper forms, and then all data were mandatorily entered using a web-based system for data collection, validation, and reporting. For statistical analysis, GraphPad Prism version 6 (GraphPad Software, La Jolla, CA) was used. A patient-level analysis focused on the use of prophylactic antimicrobials. Results were expressed as a percentage of the total number of patients treated. Proportional differences were compared using either a χ² test or a Fisher’s exact test, as appropriate. Prophylactic prescribing in Europe was used as the comparison point. All statistical tests were 2-tailed and considered significant if the P value was <.05. Data regarding prophylactic prescriptions in African and Eastern European hospitals were excluded from statistical analysis, either because the number of prescriptions was too low to provide for meaningful data interpretation (Africa) or because data on prophylactic prescribing were not reported (Eastern Europe).

RESULTS

Study Population and Antimicrobial Rate
Prophylactic antimicrobial prescribing practices were evaluated for 17 693 surveyed children and infants hospitalized at 226 hospitals (H) in 41 countries (C) worldwide, including Europe (172H; 24C), Africa (6H; 4C), Asia (25H; 8C), Australia (6H), Latin America (11H; 3C), and North America (4H; 1C [all from the United States]) [10]. In Europe, there was overrepresentation (ie, >50%) of hospitals and patients from the United Kingdom (65H) [10]. Overall, 6818 hospitalized children and neonates received 11 899 antimicrobial prescriptions, among whom 2242 patients (32.9%) received at least 1 antimicrobial for prophylactic use. Rates for prophylactic antimicrobial prescribing in children ≥30 days of age were 70.4% for medical prophylaxis (corresponding to 19.9% of all antimicrobial prescriptions) and 29.6% (or 8.3% of all antimicrobials) for surgical prophylaxis. In neonates <30 days of age, the rates were 83.5% (or 24.9% of all antimicrobials) and 16.5% (or 4.9% of all antimicrobials) (Table 1). Systemic antibiotics were prescribed in 36.7% of all patients surveyed (6499 of 17 693) [10].

Therapeutic Versus Prophylactic Antimicrobial Use
Antimicrobials were provided for therapeutic use in 70.7% of prescriptions (8408 of 11 899), whereas 28.6% (3400 of 11 899) were for prophylactic use and 0.8% of indications were reported to be unknown (n = 91). Of the 3400 prescriptions for prophylactic use, 2482 were given to children ≥30 days of age and 918 were given to neonates <30 days of age. Prophylaxis for medical diseases was the indication in 73.4% of cases (2495 of 3400), whereas one quarter of prescriptions were for surgical diseases (26.6% [905 of 3400]; Table 1). Prescribing for medical prophylaxis was significantly higher in infants <30 days of age. In addition, children from Western Europe, Australia, and North America received more antimicrobials for medical prophylaxis compared with children from northern Europe, southern Europe, Asia, and Latin America (Table 1). Except for patients in Africa, in over 90% of cases, the antimicrobial selection was empiric.

The administration route for antimicrobial prophylaxis was parenteral in 46.6% of prescriptions (1583 of 3400) and oral in 52.6% (1790 of 3400). A single antimicrobial agent was given
for prophylactic purposes in 63.3% of patients (1420 of 2242), a combination of 2 antimicrobials in 25.7% (576 of 2242), and 3 or more agents in 11.0% (246 of 2242). A combination of 2 or more antimicrobials was more commonly prescribed in medical prophylaxis (38.9% [615 of 1582]) than in surgical prophylaxis (28.8% [183 of 636]; risk ratio [RR], 1.391; 95% confidence interval [CI], 1.199–1.613).

### Indications and Types of Antimicrobial Prophylaxis

Our survey did not specifically collect data regarding the reason for medical prophylaxis. However, it did gather information about patients’ underlying diseases.

For children ≥30 days of age receiving a prophylactic prescription, the most common underlying disease was oncological (33.0% [536 of 1623]), surgical (19.5% [316 of 1623]), and/or related to a chronic heart condition (6.6% [107 of 1623]). In 12.5% (203 of 1623) of children ≥30 days of age, there was no underlying disease. The 2 most common indications for antimicrobial prophylaxis in children ≥30 days of age were prophylaxis for medical problems (910 of 1623 [56.1%]) and prophylaxis for surgical disease (466 of 1623 [28.7%]).

In infants <30 days of age, the 3 most common underlying conditions were respiratory distress (22.3% [138 of 619]), premature rupture of membranes (17.8% [110 of 619]), and surgical disease (12.0% [74 of 619]). In 14.2% (88 of 619) of infants <30 days of age, no underlying disease was present. Four indications accounted for >80% of antimicrobial prophylaxis in infants <30 days of age; namely, medical prophylaxis (29.2% [181 of 619]), prophylaxis for neonatal risk factors (27.9% [173 of 619]), prophylaxis for maternal risk factors (16.2% [100 of 619]), and surgical prophylaxis (11.0% [68 of 619]).

### Antimicrobials Used for Medical Prophylaxis in Children ≥30 Days of Age

The 3 most common classes of antimicrobials for medical prophylaxis in children ≥30 days of age were trimethoprim/sulfonamides, antifungals, and antivirals (Figure 1). Together, these accounted for two thirds (1233 of 1854 [66.5%]) of all prescriptions for medical prophylaxis. In children ≥30 days of age, 1130 antibiotic prescriptions were written for medical prophylaxis. The 3 most common antibiotic classes for systemic use were trimethoprim/sulfonamides (532 of 1130 [47.1%]), narrow-spectrum penicillins (148 of 1130 [13.1%]), and macrolides/lincosamides (99 of 1130 [8.8%]). Fewer trimethoprim/sulfonamides were prescribed in Asia (RR, 0.725; 95% CI, 0.530–0.992) and Latin America (RR, 0.599; 95% CI, 0.370–0.969). Prescriptions of narrow-spectrum penicillins had an equal distribution globally. Within Northern Europe, the rate was higher than the rest of Europe (RR, 2.221; 95% CI, 1.507–3.272). Macrolides and lincosamides were administered considerably more often to patients in North America (RR, 3.873; 95% CI, 2.516–5.963). Notably, in Northern Europe, this antibacterial class was more commonly used (RR, 5.744; 95% CI, 3.873–9.198). Antimicrobials prescribed for medical prophylaxis varied according to region (Table 2). In Southern Europe and Asia, broad-spectrum antibiotics were prescribed significantly more often (as were reserve antibiotics in Asia), whereas in Australia, their use was more restricted (as were reserve antibiotics in Western Europe; Table 2).

### Table 1. Prophylactic Antimicrobial Prescriptions by Indication, Type of Treatment, and UN Region

<table>
<thead>
<tr>
<th>Region</th>
<th>No.</th>
<th>No. %</th>
<th>(95% CI)</th>
<th>No.</th>
<th>No. %</th>
<th>(95% CI)</th>
<th>No.</th>
<th>No. %</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe</td>
<td>7142</td>
<td>1562</td>
<td>21.9</td>
<td>1.000</td>
<td>528</td>
<td>7.4</td>
<td>1.000</td>
<td>1960</td>
<td>93.8</td>
</tr>
<tr>
<td>Eastern Europe</td>
<td>2802</td>
<td>537</td>
<td>19.2</td>
<td>0.812</td>
<td>150</td>
<td>5.4</td>
<td>0.615</td>
<td>639</td>
<td>93.0</td>
</tr>
<tr>
<td>Northern Europe</td>
<td>2802</td>
<td>537</td>
<td>19.2</td>
<td>0.812</td>
<td>150</td>
<td>5.4</td>
<td>0.615</td>
<td>639</td>
<td>93.0</td>
</tr>
<tr>
<td>Southern Europe</td>
<td>2120</td>
<td>438</td>
<td>19.0</td>
<td>0.817</td>
<td>261</td>
<td>11.3</td>
<td>2.050</td>
<td>670</td>
<td>95.6</td>
</tr>
<tr>
<td>Western Europe</td>
<td>1884</td>
<td>563</td>
<td>29.9</td>
<td>1.573</td>
<td>117</td>
<td>6.2</td>
<td>0.795</td>
<td>627</td>
<td>92.2</td>
</tr>
<tr>
<td>Africa</td>
<td>900</td>
<td>55</td>
<td>6.1</td>
<td>n.d.</td>
<td>9</td>
<td>1.0</td>
<td>n.d.</td>
<td>28</td>
<td>43.8</td>
</tr>
<tr>
<td>Asia</td>
<td>1635</td>
<td>298</td>
<td>18.2</td>
<td>0.833</td>
<td>196</td>
<td>12.0</td>
<td>1.622</td>
<td>447</td>
<td>90.5</td>
</tr>
<tr>
<td>Australia</td>
<td>839</td>
<td>278</td>
<td>33.1</td>
<td>1.515</td>
<td>66</td>
<td>7.9</td>
<td>n.s.</td>
<td>340</td>
<td>98.8</td>
</tr>
<tr>
<td>Latin America</td>
<td>74</td>
<td>115</td>
<td>15.5</td>
<td>1.000</td>
<td>52</td>
<td>7.0</td>
<td>n.s.</td>
<td>155</td>
<td>92.8</td>
</tr>
<tr>
<td>North America</td>
<td>639</td>
<td>187</td>
<td>29.3</td>
<td>1.338</td>
<td>54</td>
<td>8.5</td>
<td>n.s.</td>
<td>235</td>
<td>97.5</td>
</tr>
<tr>
<td>Children ≥30 days of age</td>
<td>9327</td>
<td>1854</td>
<td>19.9</td>
<td>1.000</td>
<td>778</td>
<td>8.3</td>
<td>1.000</td>
<td>2446</td>
<td>92.9</td>
</tr>
<tr>
<td>Infants &lt;30 days of age</td>
<td>2572</td>
<td>641</td>
<td>24.9</td>
<td>1.254</td>
<td>127</td>
<td>4.9</td>
<td>0.592</td>
<td>719</td>
<td>93.6</td>
</tr>
<tr>
<td>Grand Total</td>
<td>11899</td>
<td>2495</td>
<td>21.0</td>
<td>1.000</td>
<td>905</td>
<td>7.6</td>
<td>1.000</td>
<td>3165</td>
<td>93.1</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; n.d., not done; n.s., nonsignificant; RR, risk ratio (comparison point in bold); UN, United Nations.
Antimicrobials Used for Surgical Prophylaxis

One quarter of all antimicrobial prophylactic prescriptions were for surgical prophylaxis (905 of 2495 [26.6%]; Table 1). The 4 most common classes of antimicrobials for surgical prophylaxis in children ≥30 days of age were first-generation cephalosporins, narrow-spectrum penicillins, second-generation cephalosporins, and third- or fourth-generation cephalosporins (Figure 2A). Together, these accounted for two thirds (509 of 778 [65.4%]) of all prescriptions for surgical prophylaxis. Overall, the most frequently prescribed class of antibiotics for surgical prophylaxis was first-generation cephalosporins (140 of 761 [18.4%]). This was particularly true for hospitals in North America (RR, 5.929; 95% CI, 4.154–8.463) and Australia (RR, 5.536; 95% CI, 3.839–7.982). Narrow-spectrum penicillins were more commonly prescribed in Northern Europe (RR, 2.721; 95% CI, 1.933–3.830). Second-generation cephalosporins were more frequently used in Western Europe (RR, 1.681; 95% CI, 1.123–2.514). In Asia, more children received third- or fourth-generation cephalosporins (RR, 1.881; 95% CI, 1.348–2.626) and fluoroquinolons (RR, 17.19; 95% CI, 2.085–141.7).

Prescription of broad-spectrum and reserve antibiotics for surgical prophylaxis was high (55.0%; Table 2) and varied according to region (Table 2). Broad-spectrum antibiotics were less frequently used in Northern Europe, Australia, and North America, whereas they were more commonly prescribed in Asia and Western Europe (Table 2). The only region with an increased use of reserve antibiotics for surgical prophylaxis was Southern Europe. Meanwhile, its use in Northern Europe was limited (Table 2).

### Table 2. Prophylactic Broad-Spectrum and Reserve Antibiotic Use by Indication and UN Region

<table>
<thead>
<tr>
<th>Region</th>
<th>Medical Prophylactic Use</th>
<th>Surgical Prophylactic Use</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Broad-Spectrum Antibiotics</td>
<td>RR (χ² Test) and Reserve Antibiotics</td>
</tr>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Europe</td>
<td>785</td>
<td>50.3</td>
</tr>
<tr>
<td>Northern Europe</td>
<td>263</td>
<td>49.0</td>
</tr>
<tr>
<td>Southern Europe</td>
<td>244</td>
<td>55.7</td>
</tr>
<tr>
<td>Western Europe</td>
<td>269</td>
<td>47.8</td>
</tr>
<tr>
<td>Africa</td>
<td>28</td>
<td>50.9</td>
</tr>
<tr>
<td>Asia</td>
<td>192</td>
<td>64.4</td>
</tr>
<tr>
<td>Australia</td>
<td>91</td>
<td>32.7</td>
</tr>
<tr>
<td>Latin America</td>
<td>60</td>
<td>52.2</td>
</tr>
<tr>
<td>North America</td>
<td>107</td>
<td>57.2</td>
</tr>
<tr>
<td>Grand Total</td>
<td>1263</td>
<td>50.6</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; n.d., not done; n.s., nonsignificant; RR, risk ratio ([in bold] in comparison to Europe); UN, United Nations.
The 4 most common classes of antimicrobials for surgical prophylaxis in infants <30 days were aminoglycosides, narrow-spectrum penicillins, imidazole derivates, and glycopeptides (Figure 3A). Together, these accounted for 69.3% (88 of 127) of all surgical prophylaxis prescriptions. Overall, the most frequently prescribed class of antibiotics for surgical prophylaxis was aminoglycosides and narrow-spectrum penicillins (28 of 127 [22.0%] each). For glycopeptides, prescription was the highest in European hospitals (RR, 2.474; 95% CI, 1.020–5.999). Within Europe, narrow-spectrum penicillins were used only in Northern Europe (P < .0001 [no RR or CI]). In North America, more children received first-generation cephalosporins (RR, 6.324; 95% CI, 2.696–14.83).

Duration of Surgical Antibiotic Prophylaxis
In the vast majority of cases, surgical prophylaxis was given for longer than 1 day. In children ≥30 days of age, 80.1% of cases (623 of 778; range, 68.2%–87.2%) received prophylaxis for over 24 hours (Figure 2B). A single dose was administered only in a small minority of cases (6.8% [range, 3.7%–10.6%]). A similar prescription pattern was observed among infants <30 days of age (Figure 3B). In 80.0% of these cases (99 of 127), surgical prophylaxis was given for more than 1 day.

DISCUSSION
This cross-sectional survey represents the first assessment of antimicrobial prescription practices for prophylaxis in pediatric patients hospitalized worldwide. The majority of prescriptions was for medical prophylaxis (73.4%), with only one quarter for surgical prophylaxis. This rate was even higher in infants <30 days of age (ie, 83.5%). Among those, the 3 main indications—medical prophylaxis, prophylaxis for neonatal risk factors, and prophylaxis for maternal risk factors—accounted for 73.3% of all prescriptions (data not shown). For half of the medical prophylaxis prescriptions in neonates (ie, 50.4%),
broad-spectrum antibiotics were used (data not shown). Despite our study's lack of data regarding the specific indications for medical prophylaxis, this high rate cannot be considered evidence-based [13]. The high rate of prophylactic prescribing is similar to data shown by the 2008 European Surveillance of Antibiotic Consumption (ESAC) PPS study, which included 32 pediatric departments in 21 European countries and analyzed systemic antimicrobial prescriptions from 1799 children [14]. The ESAC study showed that in 171 cases, antimicrobials were given for prophylaxis [14], and in 66% of cases, a medical prophylaxis was the indication [14]. In our study, there was a higher prevalence of medical prophylaxis in Western Europe, Australia, and North America. This overrepresentation is likely due to the greater number of patients admitted to highly specialized tertiary-care pediatric hospitals that provide care to those with oncological or other complex underlying diseases [10]. Regarding medical prophylaxis, oncological diseases were the most common underlying conditions in children ≥30 days of age. These and other variations in practice among the regions may be explained by disparities among hospital care systems as well as by the patient case-mix in the different parts of the world [15]. In comparison to the ESAC PPS 2008 study, our study showed a lower rate of parenteral administration (46.6% vs 62.5% in 2008) [14]. More importantly, however, the ESAC PPS study reported route of administration at a patient level, whereas our data were based on a prescription level. For this reason, meaningful trends cannot be deduced from comparing the two. GARPEC (Global Antimicrobial Resistance, Prescribing, and Efficacy Among Neonates and Children) [16], the global follow-up study of ARPEC, will use the same PPS method. In the future, this will allow us to draw comparisons over time.

We have identified several key strategies for improving prophylactic prescription practices. The first performance indicator is the high rate of antimicrobial combination prescriptions. In 36.7% of cases, 2 or more systemic antimicrobials were administered. This result is in line with the 37.4% shown by the ESAC PPS 2008 study conducted among European hospitals only [14]. The high rate of combination therapy in our study

![Figure 3. (A) Proportion (%) of infants <30 days of age with antimicrobial agents for surgical prophylactic use (ATC4 level) by United Nations (UN) region (numbers in proportions >5% are shown in the graph). (B) Proportion (%) of infants <30 days of age with surgical prophylactic use by duration and UN region.](https://academic.oup.com/jpids/advance-article-abstract/doi/10.1093/jpids/piy019/4939181)
was observed for both medical (38.9%) and surgical prophylaxis (28.8%), with the latter percentage clearly indicating inappropriate usage. Multiple studies in adults have shown that antibiotic combinations do not provide additional coverage and do not result in lower rates of postoperative surgical site infections (SSIs) [5, 6]. According to a study by Tamma et al [17], even in pediatric patients with Gram-negative sepsis—a high-mortality disease—combination antibiotic therapy did not translate into a survival benefit. Both the ASHP report and World Health Organization (WHO)'s global guidelines state that for most surgical procedures, a single-agent regimen (e.g., a first-generation cephalosporin) is the preferred option [5, 18]. In addition to the lack of clinical benefits offered by combination therapies, these therapies have numerous potential negative ramifications, including drug interactions, the need for drug monitoring, increased costs, and additional side effects.

The second quality indicator is the high rate of prophylactic broad-spectrum antibiotic prescribing worldwide. In our study, this accounted for half the cases of both medical and surgical prophylaxis. This prescription pattern was particularly notable in Asia (for both indications) and in Western Europe (for surgical prophylaxis). In Asia, colonization and infection rates with multiresistant organisms are the highest in the world—a fact that may explain the higher use of broad-spectrum antibiotics in this region [1]. Use of broad-spectrum antibiotics itself is associated with an increased risk of antimicrobial resistance [1]. This is particularly true for third- and fourth-generation cephalosporins as well as for fluoroquinolones [1].

The third performance indicator is the prolonged (>24 hour) duration of surgical prophylaxis. In our study, 80% of surgical patients—including infants <30 days as well as children ≥30 days of age—received surgical prophylaxis for >1 day. The new WHO guidelines on prevention of SSIs strongly recommend against prolonging surgical antibiotic prophylaxis (SAP) beyond a single dose due to the lack of benefit in reducing SSIs [18]. According to WHO, prolongation should only be considered in cardiac, vascular, and orthognatic surgery for a period of up to 24 hours. However, the quality of evidence demonstrating a beneficial effect is low to very low [18]. Unfortunately, our study protocol did not include questions about the type of surgery associated with SAP. Although extended therapy does not decrease the risk of postsurgical infections, its prolonged use is in fact associated with adverse events and antimicrobial resistance [19].

It is important to recognize limitations of our study. The study design is cross-sectional and provides a snapshot of antimicrobial prescribing practices at the hospital level. Participation was voluntary and the researcher did not receive payment. Both of these factors could lead to a participation bias whereby primarily highly motivated parties participated in the survey. However, how this bias might influence the observed rates is unclear. There are no generally accepted consensus definitions of medical prophylaxis. For this reason, definitions of prophylaxis were not preset in the study protocol. There is a clear overlap between medical prophylaxis for maternal or neonatal risk, early empiric therapy, and then prolonging antibiotic therapy in high-risk babies in settings with a very high prevalence of hospital-acquired infection. However, it is clear that a consensus definition of medical prophylaxis is needed for research purposes. Training of researchers collecting hospital data was not performed in person; rather, it was done by means of an online training tool, a frequently asked questions list, and a helpdesk. Therefore, data accountability cannot be independently validated. Nevertheless, data were subjected to inconsistency checking, with requests for clarification directed towards participating centers when needed. Despite the large number of patients included in the study, it should be noted that tertiary care hospitals were overrepresented. For this reason, the generalizability of the data for other types of pediatric hospitals cannot be guaranteed. Moreover, geographic regions outside Europe were underrepresented. Accordingly, findings are only representative for the hospitals captured. Finally, but crucially, we were hampered in our determination of whether or not antibiotic classes were used appropriately by the fact that indications for prophylaxis were not specifically collected with the survey.

Although acknowledging the above limitations, we nevertheless believe our study contains several unique strengths. The survey was global and hospitals from 41 countries participated. A large number of patients (3400 prescriptions for prophylaxis) were eligible and included in the current analysis. The study used a standardized protocol, which ensured uniformity of data and of conclusions to be drawn from it. Such a standardized method facilitates comparisons among hospitals and countries, while also paving the way for longitudinal analyses when the survey becomes repeated [16]. Therefore, the PPS method easily can be used to test the efficacy of interventions deployed for the purpose of improving prophylactic antimicrobial prescribing practices. Finally, the PPS method may provide a vital tool for initiating and evaluating interventions that are part of an antibiotic stewardship program. The survey method is inexpensive and therefore also feasible in resource-limited countries.

CONCLUSIONS

Our study is the first PPS on prescription practices for systemic antimicrobial agents used for surgical and medical prophylaxis for pediatric patients hospitalized worldwide, and it reveals several potential targets for quality improvements. We conclude that the following interventions are needed: (1) reduce the high rate of antimicrobial combination prescriptions, especially in medical prophylaxis; (2) limit the high rate of broad-spectrum antibiotic usage; and (3) combat the extended duration of surgical prophylaxis.

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Notes

Acknowledgment. We are grateful to all members of the Antibiotic Resistance and Prescribing in European Children (ARPEC) project group for their participation in data collection: We thank all colleagues who contributed to the success of this project: Graciela Maria Caile, Hospital de Pediatría Juan P. Garrahan, Buenos Aires, Argentina; Julia Clark, Royal Children's Hospital, Brisbane, Australia; Celia Cooper, Women's and Children's Hospital, North Adelaide, Australia; Christopher C. Blyth and Joshua Reginald Francis, Princess Margaret Hospital for Children, Perth, Australia; James Alsalman, Salamaniya Medical Complex, Manama, Bahrain; Hilde Janssen and Ludo Mahieu, University Hospital Antwerp, Antwerp, Belgium; Paul Van Rossom, General Hospital KU, Brasschaat, Belgium; Wouter Vandewal, AZ Sint Lucas, Brugge, Belgium; Philippe Lepage and Sophie Blumenthal, Hôpital Universitaire des Enfants Reine Fabiola, Brussels, Belgium; Caroline Briquet, Université 'Catholique de Louvain, Cliniques Universitaires Saint-Luc, Brussels, Belgium; Dirk Robbrecht, General Hospital A. Z. Daniaan, Ostend, Belgium; Pierre Maton, NICU-CHC St. Vincent, Rocourt, Belgium; Patrick Gabriels, Sint-Trudo ziekenhuis, Sint-Truiden, Belgium; Zana Rubin and Tanja Kovacevic, University Hospital Centre Split, Croatia; Jens Peter Nielsen, Pediatric Department, Regionshospital Viborg, Viborg, Denmark; Jes Reinholdt Petersen, Department of Neonatology, Righospitalitet, University of Copenhagen, Copenhagen, Denmark; Pornpita Poorisrisak, Department of Pediatrics, Naestved Hospital, Naestved, Denmark; Lise Heilmann Jensen, Roskilde University Hospital, Roskilde, Denmark; Mari Laan, Tallinn Children's Hospital, Tallinn, Estonia; Ema Tamm, Children's Clinic of Tartu University Hospital, Tartu, Estonia; Maire Mattisen and Maija-Liisa Rummukainen, Central Finland Health Care District, Jyväskylä, Finland; Vincent Gajdos and Romain Olivier, Hopitaux Universitaires Paris Sud; Antoine Beclere, Clamart, France; Flore Le Marechal, Department of Pediatrics and Neonatology, University Hospital Dijon, Dijon, France; Alain Martinot, François Dubos, Marion Lagrée, CHR Lille, Lille University Hospital, Lille, France; Sonia Prot-Labarthe and Mathie Lorrot, AP-HP Hôpital Robert-Debré, Paris, France; Daniel Orbach, Institut Curie, Paris, France; Karaman Pagava, Thilisi State Medical University, Thilisi, Georgia; Markus Knut, Children's Hospital, Dr Horst-Schmidt-Kliniken, Wiesbaden, Germany; Stephanie A. A. Schlag and Johannes Liese, University Children's Hospital, University of Würzburg, Würzburg, Germany; Lorna Renner, Prof. Kore Bu Teaching Hospital, Accra, Ghana; Anthony Enimil and Marah Awunyo, Komfo Anokye Teaching Hospital, Kumasi, Ghana; Garyfallia Syridou and Nikos Spyridis, Aglaia Kyriakou Children's Hospital, Athens, Greece; Elena Critselis, First University Department of Pediatrics, 'Aghia Sophia' Children's Hospital, Athens, Greece; Sofia Kouni and Katerina Moukgou, University of Athens Collaborative Center for Clinical Epidemiology and Outcome Research, Athens, Greece; Fani Ladomenou, University Hospital of Heraklion, Crete, Greece; Despoina Gkentzi, University General Hospital of Patras, Patras, Greece; Elias Iosifidis and Emmanuel Rolildes, 3rd Department of Pediatrics, Faculty of Medicine, Aristotel University School of Health Sciences, Hippokration Hospital, Thessaloniki, Greece; Suneeta Sahu, Microbiology, Apollo Hospitals, Bhubaneswar, Odisha, India; Srinivas Murki, Fernandes Hospital, Hyderabad, India; Manoj Malviya and Durga Bhavani Kalavapalli, Nice Hospital for Women, Newborns and Children, Hyderabad, India; Sanjeev Singh, Amrita Institute of Medical Sciences, Kochi, India; Tanu Singhal, Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute, Mumbai, India; Garima Garg, Escorts Heart Institute, New Delhi, India; Pankaj Garg, Sir Ganga Ram Hospital, Rajinder Nagar, New Delhi, India; Neelam Kler, Sir Ganga Ram Hospital, Rajinder Nagar, New Delhi, India; Jafar Soltani, Besat Tertiary Hospital affiliated to Kurdistan University of Medical Sciences, Sanandaj, Kurdistan, Iran; Zahra Jafarpour and Gholamreza PouSadaf, Professor Alborz Clinical Microbiology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran; Giangiacomo Nicolini, San Martino Hospital, Pediatric Department, Belluno, Italy; Carlotta Montagnani and Luisa Galli, Department of Health Sciences, University of Florence, Meyer Children's Hospital, Florence, Italy; Susanna Esposito, Pediatric Highly Intensive Care Unit, and Rossana Tenconi, Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; Andrea, Lo Vecchio, University of Naples Federico II, Naples, Italy; Daniele Dona' and Carlo Giaquinto, Department for Woman and Child Health, Padua, Italy; Eleonora Borgia, University Hospital of Padova, Padua, Italy; Patrizia D'Argenio and Maia De Luca, Bambino Gesù Children's Hospital, Rome, Italy; Chiara Centenari, Paediatric and Neonatal Unit, Hospital of Viareggio, Viareggio, Italy; Luk Raka, National Institute of Public Health of Kosovo and University of Pristina, and Denis Raka, University of Pristina, Pristina, Kosovo; Abeer Omar and Hafaa Al-Moussa, Directorate of Infection Control, Ministry of Health, Kuwait City, Kuwait; Dzintars Mozgis, Centre for Diseases Prevention and Control, Riga, Latvia; Ines Siestena, University Children's Hospital, Riga, Latvia; Sigita Brukienè, Children's Hospital, Affiliate of Vilnius University Hospital Santariskiu Klinikos, Vilnius, Lithuania; Vytautas Uonis, Vilnius University, Vilnius, Lithuania; Gabriela Tavchivoka, General Hospital 'Borka Taleski', Prilep, Macedonia; Antonia Hargadon-Lowe, Queen Elizabeth Central Hospital, Blantyre, Malawi; Peter Zarb and Michael A. Borg, Mater Dei Hospital, Msida, Malta; Carlos Agustin Gonzalez Lozano and Patricia Zárate Cañasto, Instituto Nacional de Pediatría, México D.F., México; Martha E. Cancino, Universidad Autónoma de Nayarit, México and DURG-LA (Para la Investigación de la Utilización de los Medicamentos-America Latina), Tepic, Nayarit, México; Bernadette McCullagh, South Eastern Health and Social Care Trust, Belfast, Northern Ireland; Ann McCorry, Southern Health and Social Care Trust, Craigavon, Northern Ireland; Caireine Gormley, Western Health and Social Care Trust, Derry, Northern Ireland; Zaina Al Maskari and Amina Al-Jardani, Royal Hospital, Muscat, Oman; Magdalena Piata, Department of Children's Infectious Diseases, Medical University of Warsaw, Poland, Warsaw, Poland; Fernandez Rodrigues and Ana Brett, Hospital Pediatrico, Centro Hospitalario y Universitario de Coimbra, Coimbra, Portugal; Isabel Esteves, Hospital de Santa Maria, Pediatric Department, Pediatric Infectious Diseases Unit, Lisbon, Portugal; Laura Marques, Centro Hospitalar do Porto, Porto, Portugal; Jannetel Ali AlAjmi, Hamad Medical Corporation, Doha, Qatar; Simona Claudia Cambrea, Faculty of Medicine, 'Ovidiu' University, Constantanta, Romania; Asia N. Rashed, King Abdulaziz Medical City—Jeddah, Jeddah, Saudi Arabia; Aeshah Abdu Muhammad Al Azmi, Ministry of National Guard Health Affairs, King Abdulaziz Medical City, Pharmaceutical Care Services Department, Jeddah, Saudi Arabia; Sin Min Chan, Khoo Teck Puat-National University Children's Medical Institute, National University Health System, Singapore, Singapore; Mas Suhaila Isla, National University Hospital, Singapore; Peter Najdenov, General Hospital Jesenice, Jesenice, Slovenia; Milan Cizman, University Medical Centre, Ljubljana, Slovenia; Sibila Unuk, University Medical Center Maribor, Maribor, Slovenia; Heather Finlayson, Department of Paediatrics and Child Health, Stellenbosch University, Cape Town, South Africa; Angela Dramowski, Tygerberg Hospital, Cape Town, South Africa; Irene Mat-Cano, Hospital Universitario del Henares, Coslada, Madrid, Spain; Beatriz Soto, Hospital Universitario de Getafe, Getafe, Madrid, Spain; Cristina Calvo, Severo Ochoa Hospital, Leganés, Madrid, Spain; Beogoña Santiago and Jesus Saavedra-Lozano and Amaya Bustigina, Gregorio Marañon Hospital, Madrid, Spain; Luis Escosa-Garcia, Hospital Infantil Universitario La Paz, Madrid, Spain; Noelia Ureta, Elisa Lopez-Varela and Pablo Rojo, Hospital Universitario 12 de Octubre, Madrid, Spain; Alfredo Tagarro, Hospital Universitario Infantil Sofia, San Sebastian de Los Reyes, Madrid, Spain; Pedro Terol Barrero, Hospital Universitario Virgen Macarena, Sevilla, Spain; Elena Maria Rincon-Lopez, Hospital Universitario y Politecnico La Fe, Valencia, Spain; Ismaela Abubakar, Edward Francis Small Teaching Hospital/Royal Victoria Teaching Hospital, Banjul, The Gambia; Jeff Aston, Mitul Patel and Alison Bedford Russell, Birmingham Children's Hospital NHS Foundation Trust, Birmingham, UK; Maggie Heginbothom, Public Health Wales, Cardiff, UK; Prakash Satodia, University Hospitals Coventry and Warwickshire NHS Trust, Coventry, UK; Mehdi Garbassy, County Durham and Darlington NHS Foundation Trust, Durham and Darlington, UK; Alison Johnson, Wye Valley NHS Trust, Hereford, UK; David Sharpe, Alder Hey Children's NHS Foundation Trust, Liverpool, UK; Christopher Barton, Institute of Child Health, University of Liverpool, Liverpool, UK; Esse Menson and Sara Arenas-Lopez, Evelina London Children's Hospital, London, UK.
London, UK; Suzanne Luck, Kingston Hospital NHS Foundation Trust, London, UK; Katja Doerholt, St George’s Hospital, London, UK; Paddy McMaster, North Manchester General Hospital, Manchester, UK; Neil A. Caldwell, Wirral University Teaching Hospital NHS Foundation Trust, Merseyside, UK; Andrew Lunn, Nottingham Children’s Hospital, Nottingham, UK; Simon B. Drysdale, Oxford University Hospitals NHS Trust, Oxford, UK; Rachel Howe, Peterborough City Hospital, Peterborough, UK; Tim Scorrer and Florian Gahleitner, Queen Alexandra Hospital, Portsmouth, UK; Richa Gupta, Royal Preston Hospital, Lancashire Teaching Hospitals, Preston, UK; Clare Nash, Sheffield Children’s NHS Foundation Trust, Sheffield, UK; John Alexander, University Hospital of North Midlands, Stoke on Trent, UK; Mala Raman, Torbay Hospital, South Devon Health Care NHS Foundation Trust Torquay, UK; Emily Bell, Royal Cornwall Hospitals NHS Trust, Truro, Cornwall, UK; Veena Rajagopal, St George's NHS Trust, London, UK; Stephen Kohlhoff, SUNY Downstate Medical Center, Brooklyn, NY; Elaine Cox, Kristen Nichols, and Elaine Cox, Riley Hospital for Children at IU Health, Indianapolis, IN; Theoklis Zaoutis, The Children’s Hospital of Philadelphia, Philadelphia, PA.

Disclaimer. The collaborators did not receive compensation from the funder for their contributions. The funders had no role in the design and conduct of the study, collection, management, analysis, review, or approval of the manuscript, and decision to submit the manuscript for publication.

Financial support. This work was co-funded by a grant from the European Commission Directorate General for Health and Consumers (DG Sanco) through the Executive Agency for Health and Consumers (http://ec.europa.eu/health/index_en.htm; Grant number 2009 11 01). The October–November 2012 Antibiotic Resistance and Prescribing in European Children Point Prevalence Survey was cofunded by the Paediatric European Network for Treatment of AIDS (http://www.penta-id.org/).

Potential conflicts of interest. All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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