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Antibiotic Use and Stewardship Practices in a Pediatric Community-based Cohort Study in Peru: Shorter Would be Sweeter

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Background. There is a need to evaluate antibiotic use, duration of therapy, and stewardship in low- and middle-income countries to guide the development of appropriate stewardship programs that are global in scope and effectively decrease unnecessary antibiotic use.

Methods. We prospectively collected information on illness occurrence and antibiotic use from a cohort of 303 children. We evaluated the incidence, duration of therapy, and appropriateness of antibiotic prescriptions by 5 main antibiotic prescribers (physicians and nurses, pharmacists, nursing assistants, self-prescriptions, and neighbors or family members).

Results. Ninety percent of children received an antibiotic during follow-up, and on average, by the end of follow-up a child had spent 4.3% of their first 5 years of life on antibiotics. The most frequent prescribers were physicians/nurses (79.4%), followed by pharmacists (8.1%), self-prescriptions (6.8%), nursing assistants (3.7%), and family or neighbors (1.9%). Of the 3702 courses of antibiotics prescribed, 30.9% were done so for the occurrence of fever, 25.3% for diarrhea, 2.8% for acute lower respiratory disease, 2.7% for dysentery, and 38.2% for an undetermined illness. Courses exceeding the recommended duration were common for the principal diseases for which treatment was initiated, with 27.3% of courses exceeding the recommended length duration, representing a potential reduction in 13.2% of days on which this cohort spent on antibiotics.

Conclusions. Stewardship programs should target medical personnel for a primary care stewardship program even in a context in which antibiotics are available to the public with little or no restrictions and appropriate duration should be emphasized in this training.

Keywords. antimicrobial stewardship; primary healthcare; outpatient; antibiotic resistance; Iquitos.

Antibiotic-resistant infections are among the greatest global threats to public health [1, 2]. They are a complex problem that occurs because of the misuse of antibiotics in human and veterinary medicine, as well as in the production of livestock. The World Health Organization (WHO) Global Action Plan identifies a need to use an integrative approach to counter the improper use of antibiotics, including the implementation of effective stewardship programs in inpatient and outpatient settings [1, 3]. Human antibiotic prescription predominantly occurs in the outpatient setting, where estimates from the United States show that up to 30% are prescribed erroneously [4], but that appropriate stewardship in this setting can effectively reduce prescriptions [5–7]. However, despite the global misuse of antibiotics, the epidemiology of antibiotic use in most global contexts is poorly studied.

The extension of antimicrobial stewardship to low- and middle-income countries, where the majority of the world's population resides, is both an obvious necessity and a nascent concern already recognized by the International Disease Society of America [8]. Antibiotics are available without prescription in most of the world, and stewardship programs, if they are to be effective globally, must understand usage patterns in diverse contexts [9]. Yet, patterns of prescription have not been well characterized in low-resource settings. Among Latin American countries, by 2007, Peru was situated among the top 4 countries with highest antibiotic utilization, with 13.50 daily doses per 1000 inhabitants per day (only surpassed by Argentina and Venezuela), representing a 70.6% increase

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since 1997 [10]. Studies have characterized antibiotic prescriptions at tertiary level hospitals in Peru, showing a reduction of prescriptions as a result of stewardship programs [11]. However, antimicrobial stewardship at the primary healthcare level remains poorly described, even though that majority of antibiotic exposure occurs in the outpatient setting.

The objective of this study is to characterize antibiotic use to treat dysentery, diarrhea, acute lower respiratory infections (ALRIs), and fever within a community-based birth cohort study in a population living in extreme poverty with access to universal healthcare. Because individual children were followed over their early life course, the study comprehensively measured antibiotic exposure from both formal and informal health sectors in an unbiased manner. We aimed to delineate who the prescribers of antibiotics were for this cohort of children with the aim of guiding future context-specific antimicrobial stewardship interventions.

METHODS

Setting, Study Design, and Definition of Illnesses

The Etiology, Risk Factors, and Interactions of Enteric Infections and Malnutrition and the Consequences for Child Health and Development study was a prospective community-based cohort study conducted in a periurban community of Iquitos, Loreto, Peru, between 2012 and 2018. Specific details of the study design, enrollment, and surveillance have been described previously [12–14]. Briefly, a total of 303 healthy newborns were enrolled within the first 17 days of life and followed until 5 years of age. Surveillance was conducted 2 times a week, generating a continuous daily history of symptoms and antibiotic usage. Illness episodes were reported by caretakers and observed and recorded by trained healthcare workers. An illness episode was identified as being separated by at least 2 symptom-free days. ALRI was identified if the child presented cough or had difficulty breathing and if measured breathing rate was ≥60 breaths/min in children ≤2 months, ≥50 breaths/min in children 2–11 months, and ≥40 breaths/min in children 1–5 years as measured by an average of duplicate measures or lower chest wall indrawing as recommended by WHO [15, 16]. Diarrhea was defined as more than 3 loose stools in a 24-hour period, and dysentery was defined as diarrhea in which the mother reported seeing blood [17]. Fever was ascertained by caregiver report. Antibiotic courses were assigned to illness syndromes based on the symptoms reported on the day of or immediately before the date of course initiation. Assignment of syndromes to courses were mutually exclusive. The assignment of a course to ALRI took precedent to that of fever, dysentery, and diarrhea as per WHO guidelines regarding attributions for child mortality. The assignment of a course to dysentery took precedent to that of diarrhea and undifferentiated fever. Finally, the assignment of a course to diarrhea took precedent to that of fever. If none of the 4 syndromes were reported during that window, courses were assigned to a separate category, that of undetermined illness. These predominantly represent less-common diagnoses (ear infection, tonsillitis, skin infection, urinary tract infection), which were annotated by physician and nurses. Mothers reported daily injectable or oral antibiotics prescribed to the infant, the length of the antibiotic course, and who prescribed it. Fieldworkers asked to visually verify the use of the antibiotic by observing the antibiotic package or the prescription [18]. Validation of maternal reports has been described previously [18].

Antibiotic Use Categorization and Definitions

Endpoint definitions are the same as those presented previously [18]. Specifically, the length of the antibiotic course was defined as the total number of days on which a child received an antibiotic. A distinct antibiotic course was identified by being separated by 2 antibiotic-free days. An antibiotic course taken for an episode of dysentery, fever, diarrhea, or an undetermined illness was considered of standard duration if it lasted between 3 and 5 days (>3–≤5) according to national therapeutic guidelines, which were short if it lasted 3 days or less (≤3) and extended if it lasted for more than 5 days (>5). An antibiotic course taken for an episode of ALRI were considered of standard duration if it lasted between 5 and 7 days (>5–≤7) according to national therapeutic guidelines, which were short if it lasted 5 days or less (≤5) and extended if it lasted more than 7 days (>7) [19, 20]. Antibiotics were recorded with their specific names and analyzed as individual variables. Antibiotic prescribers were identified as either (1) medical doctor or nurse, (2) pharmacists, (3) nursing assistant, (4) neighbor, family, or friend, and (5) self-prescribed. Additional covariates analyzed included age and sex of the child, maternal primary education completion, and monthly household income (US dollars) recorded at baseline.

Statistical Analysis

Follow-up days are defined as the number of days each child was enrolled and observed within the cohort study. The percent of days a child spent on antibiotics within their first month, more than 1 month to 6 months, more than 6 months to 12 months, and more than 12 months to 60 months was calculated as the number of days receiving an antibiotic as a proportion of the total number of follow-up days. The average percent of follow-up days spent on any antibiotic and the average and total number of courses of antibiotics were calculated for the entire cohort and as prescribed by each specific prescriber. The incidence of antibiotic use was calculated as the number of antibiotic courses per child-year as prescribed by each specific prescriber.

The percent of days a child received antibiotics while experiencing ALRI, diarrhea, dysentery, and fever was calculated. Additionally, the number of antibiotic courses taken and the

Table 1. Average Percent of Follow-Up Days Children Spent on Antibiotics by Age Category

	Average Percent of Days of Follow-Up on Antibiotics (IQR)				
	0–1 Mo	1–6 Mo	6–12 Mo	12–60 Mo	0–60 Mo
Any antibiotic	**0.10 (0–0)**	**0.83 (0–0.97)**	**0.99 (0.27–1.25)**	**3.02 (1.83–4.20)**	**4.32 (2.42–5.98)**
Beta-lactams					
Amoxicillin	0.07 (0–0)	0.45 (0–0.5)	0.50 (0–0.71)	1.34 (0.54–1.96)	2.08 (0.82–3.00)
Cephalexin	0.01 (0–0)	0.01 (0–0)	0.01 (0–0)	0.02 (0–0)	0.05 (0.0–0.0)
Ceftriaxone	0.01 (0–0)	0 (0–0)	0.01 (0–0)	0.02(0–0)	0.05 (0.0–0.0)
Dicloxacillin	0.01 (0–0)	0.02 (0–0)	0.03 (0–0)	0.2 (0–0.29)	0.20 (0.0–0.32)
Penicillin	0.01 (0–0)	0.08(0–0)	0.10 (0–0.09)	0.3 (0–0.41)	0.41 (0.0–0.65)
Macrolides					
Erythromycin	0 (0–0)	0.13 (0–0)	0.26 (0–0.32)	0.49 (0–0.71)	0.77 (0.0–1.0)
Azithromycin	0 (0–0)	0.04 (0–0)	0.07 (0–0)	0.19 (0–0.32)	0.26 (0.0–0.38)
Clarithromycin	0.01 (0–0)	-	0 (0–0)	0 (0–0)	0 (0–0)
Quinolones					
Nalidixic acid	-	0 (0–0)	-	-	0 (0–0)
Ciprofloxacin	-	0 (0–0)	0.01 (0–0)	0.16 (0–0.22)	0.13 (0.0–0.20)
Norfloxacin	0.01 (0–0)	-	-	0 (0–0)	0.001 (0.0–0.0)
Aminoglycosides					
Gentamicin	0.01 (0–0)	0.01 (0–0)	0 (0–0)	0.03 (0–0)	0.04 (0.0–0.0)
Sulfas					
Trimethoprim-sulfamethoxazole	0 (0–0)	0.18 (0–0)	0.14 (0–0.11)	0.34 (0–0.60)	0.59 (0.0–0.72)
Lincosamide					
Clindamycin	0.01 (0–0)	-	-	0 (0–0)	0 (0–0)
Amphenicol					
Chloramphenicol	-	-	-	0 (0–0)	0.01 (0.0–0.0)
Nitrofuran					
Furazolidone	-	0 (0–0)	0 (0–0)	0.08 (0–0)	0.07 (0.0–0.0)
Nitroimidazole					
Metronidazole	-	0 (0–0)	0.01(0–0)	0.29 (0–0.41)	0.25 (0.0–0.34)

Abbreviations: -, no antibiotics received for the specific age category; IQR, interquartile range.

number of days spent on an antibiotic for each specific illness were calculated for each specific prescriber. The duration of the length of each antibiotic course was classified as short, standard, or extended. The percent of extended number of courses as well as the corresponding percent of additional days on antibiotics as fraction of total follow-up days were calculated for the entire cohort and by each specific prescriber.

Antibiotic use was analyzed as a time-varying repeated binary outcome and occurrences of each illness type as binary time-varying exposures. Odds ratios for the association between the prescription and intake of an antibiotic and the occurrence of illness (ALRI, dysentery, diarrhea, and fever) were modelled using log-binomial model regressions fitted with generalized linear models and robust variance estimation. Final models for each type of illness were adjusted for age (months), sex, maternal primary education completion (yes/no), and monthly household income, which are factors hypothesized to affect antibiotic purchasing capacity and decision to give antibiotics to their children. Statistical analysis was performed in Stata 17.0 (Stata Corp., College Station, TX).

Ethics Statement

Formal paternal informed consent was obtained for all children participating in the study. The study was approved by the ethics committee of Asociación Benéfica Prima, Lima, Peru, and the institutional review board of the Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA.

RESULTS

A total of 303 children were enrolled and followed for up for 372 199 child-days (median 1501 child-days or 4.1 child-years per child). Overall, the entire cohort of children received 3702 courses of antibiotics, representing 16 870 days. A total of 9109 illness episodes were recorded for the entire cohort. Of these, 29.7% (105/353) of ALRI episodes, 63.5% (99/156) of dysentery episodes, 31.0% (938/3027) of diarrhea episodes, and 20.5% (1144/5573) of fever episodes received an antibiotic course. An extra 1416 courses of antibiotics were prescribed for undetermined illness.

Table 2. Incidence of Antibiotic Courses Taken Per Child Year, Average Number of Antibiotic Courses, and Average Percent of Follow-Up Days a Child Spent on Antibiotics by Antibiotic Prescriber

Source of Prescription	Incidence (Courses/Child-Year)	Average Number of Courses	Total Number of Courses	Average Percent of Follow-up Days on Antibiotics	Total Number of Days on Antibiotics
All sources	3.63	12.22	3702	4.32	16 870
Physician/nurse	2.88	9.71	2941	3.60	14 079
Pharmacy	0.30	0.99	301	0.30	1268
Self-prescribed	0.25	0.83	251	0.22	761
Nurse assistant	0.13	0.45	136	0.13	544
Neighbor/family	0.07	0.23	71	0.06	212
Undetermined	0.002	0.006	2	<0.01	6

Table 3. Percent (Number) of Antibiotic Courses Prescribed According to the Associated Illness Episode

Illness Associated With Antibiotic Intake	Physician/Nurse Antibiotic Courses, % (n/N)	Pharmacy Antibiotic Courses, % (n/N)	Self-Prescribed Antibiotic Courses, % (n/N)	Nurse Assistant Antibiotic Courses, % (n/N)	Neighbor/Family Antibiotic Courses, % (n/N)	Undetermined Antibiotic Courses, % (n/N)
All causes	79.4% (2941/3702)	8.1% (301/3702)	6.8% (251/3702)	3.7% (136/3702)	1.9% (71/3702)	0.1% (2/3702)
Acute lower respiratory infection	97.1% (102/105)	2.9% (3/105)	0% (0/105)	0% (0/105)	0% (0/105)	0% (0/105)
Dysentery	96.0% (95/99)	1.0% (1/99)	3.0% (3/99)	0% (0/99)	0% (0/99)	0% (0/99)
Diarrhea	76.2% (715/938)	6.8% (64/938)	8.1% (76/938)	5.2% (49/938)	3.4% (32/938)	0.2% (2/938)
Fever	83.9% (960/1144)	8.1% (93/1144)	3.5% (40/1144)	3.6% (41/1144)	0.9% (10/1144)	0% (0/1144)
Undetermined	75.5% (1069/1416)	9.9% (140/1416)	9.3% (132/1416)	3.2% (46/1416)	2.0% (29/1416)	0% (0/1416)

Table 4. Percent (Number) of Antibiotic Days Children Spent of Antibiotics According to the Prescriber and Associated Illness Episode

Illness Associated With Antibiotic Intake	Physician/Nurse Days on Antibiotics, % (n/N)	Pharmacy Days on Antibiotics, % (n/N)	Self-Prescribed Days on Antibiotics, % (n/N)	Nurse Assistant Days on Antibiotics, % (n/N)	Neighbor/Family Days on Antibiotics, % (n/N)	Undetermined Days on Antibiotics, % (n/N)
All causes	83.5% (14 079/16 870)	7.5% (1268/16 870)	4.5% (761/16 870)	3.2% (544/16 870)	1.3% (212/16 870)	0% (6/16 870)
Acute lower respiratory infection	97.0% (516/532)	7.5% (16/532)	0% (0/532)	0% (0/532)	0% (0/532)	0% (0/532)
Dysentery	97.5% (310/318)	3.0% (2/318)	1.9% (6/318)	0% (0/318)	0% (0/318)	0% (0/318)
Diarrhea	81.4% (2827/3473)	0.6% (222/3472)	5.0% (174/3473)	4.7% (163/3473)	2.3% (81/3473)	0.2% (6/3473)
Fever	87.7% (4972/5669)	6.4% (368/5669)	2.4% (135/5669)	2.9 (165/5669)	0.5% (29/5669)	0% (0/5669)
Undetermined	79.3 (5454/6878)	6.5% (660/6878)	6.5% (446/6878)	3.1% (216/6878)	1.5% (102/6876)	0% (0/6878)

Of all children, 273 (90.1%) received at least 1 antibiotic during follow-up. Overall, by the end of follow-up, on average, a child had spent cumulatively 4.3% of their first 5 years of life on antibiotics. Amoxicillin was the most commonly prescribed antibiotic (2.08% of days of follow-up time), followed by erythromycin and trimethoprim-sulfamethoxazole (Table 1).

On average, subjects received a cumulative 3.63 antibiotic courses per year. Physicians and nurses prescribed 79.4% (2941/3702) of the courses received by all children in this cohort, equating to 2.88 antibiotic courses per child-year. The second most common antibiotic prescriber was pharmacies, who prescribed 8.1% (301/3702) of antibiotic courses or 0.3 antibiotic course per child-year, followed by self-prescriptions representing 6.8% (251/3702) of antibiotic courses (0.25 antibiotic courses per child-year), nurse technicians with 3.7% (136/3702) of antibiotic courses (0.13 antibiotic courses per child-year), and neighbors or family members with 1.9% (71/3702) of antibiotic courses (0.07 antibiotic courses per child-year) (Table 2).

Physicians and nurses were the principal prescribers for antibiotic courses prescribed for ALRI (102/105 courses) and dysentery (95/99 courses). For episodes of uncomplicated diarrhea, undifferentiated fever, and undetermined illnesses, physicians and nurses prescribed 76.2% (715/938), 83.9% (960/1144), and 75.5% (1069/1416) of the antibiotic courses, respectively (Table 3). Taken together, courses prescribed for

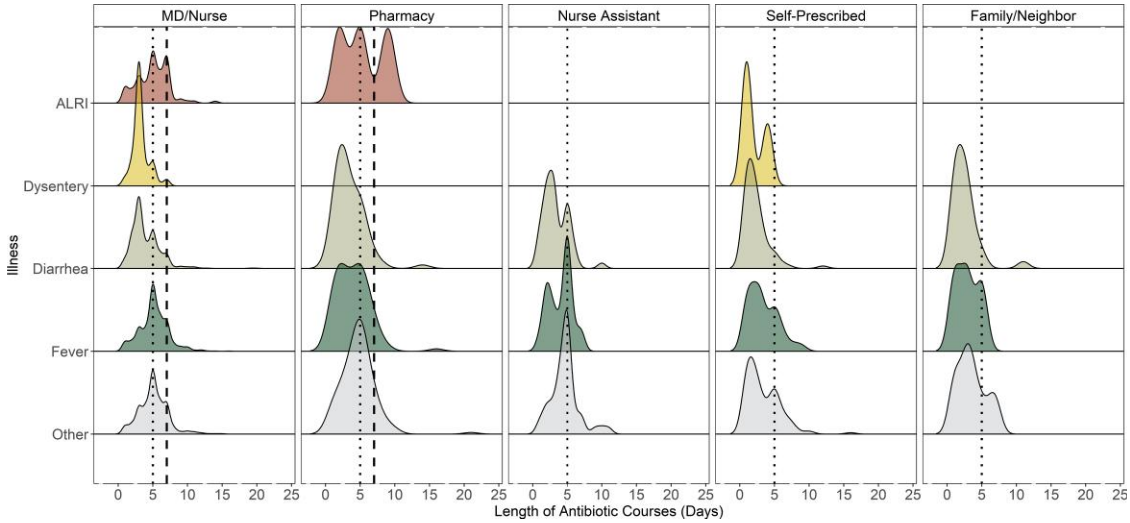

Figure 1. Probability distribution of the length of antibiotic courses (days) by illness and prescriber.

uncomplicated diarrhea and undifferentiated fever constituted 56% (2082/3702) of the total number of courses prescribed. Table 4 translates antibiotic courses into days on antibiotics associated for each specific illness and antibiotic prescriber. Specifically, 16 870 days on antibiotics were recorded for the entire cohort, representing 4.5% of total follow-up time.

Figure 1 shows density plots for the duration of antibiotic courses for each illness and prescriber. Of the 105 antibiotic courses prescribed for ALRI, 59.0% (62/105) were short courses and 34.4% (36/105) were of standard length. Of the 99 courses prescribed for episodes of dysentery, 76.8% (76/99) were of short length and 19.2% (19/99) were of standard length. Among courses associated with uncomplicated diarrhea, 59.6% (559/938) were short courses and 25.6% (240/938) were of standard length. Among courses associated with undifferentiated fever and undetermined illnesses, 25.0% (286/1144) and 26.6% (377/1416) were classified as short courses, and 39.9% (456/1144) and 40.9% (579/1416) were classified as standard courses, respectively.

The number of extended courses of antibiotics in comparison to standard and short courses of antibiotics (27.3% [1012/3702]) translated into 2223 extra days on antibiotics, or 13.2% (2223/16870) of the total number of days on which a child received an antibiotic. The number of extended and standard courses of antibiotics in comparison to short courses of antibiotics (63.3% [2342/3702], translated into 6530 extra days on antibiotics, or 38.7% of the total number on which a child received an antibiotic (Supplementary Tables 1 and 2.)

Additionally, among the antibiotic courses of extended length for ALRI, dysentery, diarrhea, and fever, physicians prescribed 85.7% (6/7), 100% (4/4), 89.9% (125/139), and 92.0% (370/402). These represented 5.9% (6/102) of the ALRI-associated courses, 4.2% (4/95) of the dysentery-associated courses, 17.0% (125/715) of the diarrhea-associated courses, and 38.5% (370/960) of the fever-associated courses prescribed by physicians or nurses.

Finally, the odds of being prescribed an antibiotic were strongly associated with the occurrence of an episode of ALRI (odds ratio [OR]: 15.11; 95% confidence interval [95% CI], 11.82–19.32; $P < .001$) and dysentery (OR: 26.47; 95% CI, 19.83–35.34); $P < .001$), after adjusting for age, sex, maternal education, and average household income. The equivalent associations with the occurrence of episodes of fever, without diarrhea, ALRI, or dysentery (OR: 6.04; 95% CI, 5.59–6.54; $P < .001$), as well as diarrhea without fever or ALRI dysentery (OR: 5.89; 95% CI, 5.31–6.53; $P < .001$) were observed (Table 5).

DISCUSSION

Most studies in low-resource areas address antibiotic prescriptions at the outpatient setting, where physicians and physician assistants are the predominant prescribers [21]. This study is one of the few that captures data that include the prescribers that expose children to antimicrobials and the overall diagnosed syndrome, providing highly granular data that have the potential to drive interventions that reduce antibiotic use at the community level. Within a cohort of children in a low-resource community of periurban Iquitos, Peru, on average a child had spent 4.3% of their first 5 years of life on antibiotics. This demonstrates that antibiotic use is intense when measured at the population level, with likely consequences being not only evolutionary pressure toward the development of resistant pathogens but ecologic restriction of the host microbiome.

Although it is often assumed that increased availability of antibiotics to the public creates a situation of unfettered use, few

Table 5. Associations Between Antibiotic Prescriptions and the Occurrence of Diarrhea, Fever, Acute Lower Respiratory Infections, and Dysentery Among Children Followed, Adjusted for Covariates

	OR (95% CI)	*P* Value
ALRI	15.11 (11.82–19.32)	<.001
Sex (female)	1.01 (.90–1.15)	.848
Age	0.99 (.98–.99)	<.001
Maternal education (primary completed)	1.10 (.96–1.24)	.164
Household income (USD)	0.99 (.99–1.00)	.845
Dysentery	26.47 (19.83–35.34)	<.001
Sex (female)	1.01 (.89–1.15)	.849
Age	0.99 (.98–.99)	<.001
Maternal education (primary completed)	1.09 (.96–1.24)	.170
Household income (USD)	0.99 (.99–1.00)	.856
Diarrhea[a]	5.89 (5.31–6.53)	<.001
Sex (female)	1.02 (.90–1.16)	.712
Age	0.99 (.98–.99)	<.001
Maternal education (primary completed)	1.09 (.96–1.24)	.152
Household income (USD)	0.99 (.99–1.00)	.519
Fever[b]	6.04 (5.59–6.54)	<.001
Sex (female)	1.02 (.90–1.15)	.731
Age	0.99 (.98–.99)	<.001
Maternal education (primary completed)	1.10 (.97–1.25)	.099
Household income (USD)	0.99 (.99–1.00)	.676

Abbreviation: ALRI, acute lower respiratory infection.

[a]Diarrhea without fever, ALRI, or dysentery.

[b]Fever without diarrhea, ALRI, or dysentery.

objective data support this assumption as universal [22]. In this cohort, early-life antibiotic use was common, with medical personnel as the main prescribers. Other prescribers had limited participation, similarly to previous findings in the Peruvian capital [23, 24]. This is likely a result of universal primary care in Peru and may not reflect the reality in other countries where access to primary care is less available. That said, this study was carried out in one of the most impoverished areas of Latin America and so does provide a valid representation of vulnerable populations in such contexts.

These results provide evidence that interventions that aim to reduce antibiotic prescriptions at the community level should be tailored toward doctors and nurses, who constitute an easier, accessible, and cost-effective target than the nonmedical population given that they already have some level of medical training and are easy to reach through professional networks. Additionally, at least 13% of days in which children were on antibiotics could have been prevented if the duration of courses were within the length recommended by national and international standards. Duration of antibiotic therapy is an attractive and feasible target for intervention that has the potential to decrease a considerable burden of antibiotic utilization [25] in settings where rapid diagnostics are likely inaccessible. Prolonged courses of antibiotics are at times given with the poorly evidenced rationale that therapy of insufficient duration to completely clear the infection will result in clinical relapse with a resistant pathogen. The application of this thinking has entrenched courses of therapy without critical evaluation over time. Recent evidence suggests that shorter courses for most common syndromes are equally effective [26, 27].

A survey performed in Lima including 1200 caregivers of children younger than age 5 years concluded that caregivers tended to respect a decision not to prescribe an antibiotic when it came from a physician, a decision that in combination with robust stewardship programs can reduce unnecessary antibiotic use [24]. That said, antibiotic prescriptions by nonmedical providers are still prevalent in this community, where over-the-counter antibiotics are attainable [28, 29]. As a result, including pharmacists in antibiotic stewardship programs should also be evaluated [30].

At least half of the antibiotic courses taken by children were attributed to a case of fever or uncomplicated diarrhea, showing that a considerable percent of courses could have been potentially prevented, given that these episodes are likely viral in nature and the intake of antibiotics is unlikely to have an impact on case resolution [31, 32]. Antibiotic prescriptions for cases of diarrhea are common in comparable settings, with up to 40% of diarrhea cases treated with an antibiotic [23]. However, this dataset is limited by the resolution regarding undetermined illnesses, and as a result appropriateness cannot be evaluated for this category. Additionally, we are not able to determine the fraction of those illness episodes that sought care but were not prescribed an antibiotic because we were unable to discern them from episodes that did not seek any type of care. Similarly, in previous studies, amoxicillin was the most commonly prescribed antibiotic, followed by trimethoprim-sulfamethoxazole, erythromycin, and ciprofloxacin [29, 33]. These are all listed by WHO as essential medicines, and their successful use for the treatment of severe cases of bacterial gastroenteritis is threatened by the emergence of antimicrobial resistance [2].

Establishing antibiotic stewardship at a global level is a critical requirement to control the emergence of highly resistant pathogens [34]. Appropriate auditing of prescriptions by medical personnel, as well as effective point-of-care practices such as rapid diagnostic tests, clinical decision support tools, and delayed prescriptions are possible and appropriate, especially in countries that provide universal healthcare to large portions of the population [34]. Although it is frequently presumed that antibiotic therapy is initiated by untrained personnel in situations in which these drugs are directly available to the public, empiric studies in this and similar contexts suggest that stewardship strategies may not need to differ in strategy as much as has been presumed. The meaningful inclusion of low- and middle-income countries into stewardship practice has the potential to add the majority of the world's population to improved practices to contain the emergence of antimicrobial resistance.

CONCLUSIONS

Physicians are the main antibiotic prescribers within a pediatric community-based cohort in Iquitos, Peru. Antibiotic use was common among the cohort, and highly associated with moderate to severe illness including acute respiratory disease and dysentery. However, during episodes of uncomplicated diarrhea and fever, it was also common for children to receive antibiotics. Antibiotic stewardship programs should be implemented at the primary care level and tailored toward the requirements of the community in need based on a baseline evaluation of main providers and use.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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