Antibiotic prescription from qualified sources for children with fever/cough: cross-sectional study from 59 low- and middle-income countries

Md Sabbir Hossain,[a,d,e] Md. Fakrul Islam,[a,d,e] Prosenjit Basak Arka,[a,d,e] Mahfuzer Rohman,[a,d,e] Talha Sheikh Ahmed,[b,e] Tanvir Ahammed,[a] Muhammad Abdul Baker Chowdhury,[a] and Md Jamal Uddin[a,c,*]

[a]Department of Statistics, Shahjalal University of Science and Technology, Sylhet 3114, Bangladesh
[b]Department of Geography and Environment, Shahjalal University of Science and Technology, Sylhet 3114, Bangladesh
[c]Department of General Educational and Development, Daffodil International University, Dhaka, Bangladesh

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Summary

Background Children in low and middle-income countries (LMICs) receive a staggering number of antibiotic prescriptions, many of which are inappropriate. We aimed to explore the proportion of antibiotic prescriptions from qualified sources of children under five who had a fever/cough in the two weeks prior to the survey in LMICs.

Methods We used data from cross-sectional studies of the latest Demographic and Health Survey (DHS) datasets (n = 43,166) in 59 LMICs covering Sub-Saharan Africa, North Africa-West Asia-Europe, Central Asia, South & Southeast Asia, Oceania, and Latin America & the Caribbean regions. The study was conducted from March 2, 2020 to October 15, 2022. We only included the latest available surveys by country, and children under five who had taken antibiotics for fever/cough were included in the study. Finally, the outcome variable was classified into two distinct categories: those who had taken antibiotics from qualified sources and those who did not.

Findings About three in four children (74.0%) received antibiotics from qualified sources. Tanzania (22.4%) and Malawi (99.9%) had the lowest and highest percentages of antibiotic prescriptions by qualified sources, respectively. Oceania had the highest percentage of qualified antibiotic prescriptions with 88.9% and Central Asia had the lowest percentage with 56.3%.

Interpretation As unqualified sources of antibiotics for fever/cough in children under five were alarmingly high in some of the LMICs, the study emphasises the importance of nationwide efforts to regulate antibiotics prescriptions.

Funding None.

Keywords: Antibiotics; LMICs; Qualified source; Standard DHS; Under-five children

Introduction

Antibiotics have been incredibly effective in enhancing health outcomes for children under five. Together with advancements in nutrition, clean water, sanitation, and vaccine coverage, antibiotics have contributed to a global decrease in children under five mortalities from 216 deaths per 1000 live births in 1950 to 39 in 2017 and a rise in male life expectancy from 48 years to 71 during the same period.[1,2]

However, antimicrobial resistance (AMR) is on the rise globally, posing a danger to the beneficial effects of antibiotics on health.[3,4] It is a critical challenge to the successful treatment of an ever-increasing variety of diseases caused by viruses, bacteria, parasites, and fungi, according to a World Health Organization (WHO) global report.[5] Therefore, it is urgent to address AMR, which kills 700,000 people annually worldwide.[6] In addition to its impact on public health, AMR has also caused significant financial strain in low and middle-income countries (LMICs). Specifically, antimicrobial agents account for substantial healthcare expenses in developing countries, which may incur up to

*Corresponding author. Department of Statistics, Shahjalal University of Science and Technology, Sylhet, Bangladesh.
E-mail address: jamal-sta@sust.edu (M.J. Uddin).
[d]Equal contributions.
[e]The degree will be completed in December 2023.

Research in context

Evidence before this study
The terms “child”, “children”, “antibiotic”, “antimicrobial”, “qualified”, “unqualified”, “low-income”, “developing”, “low income”, “low and middle income”, “Africa”, “Latin America”, “Asia”, “prescription” were used to search Google Scholar and PubMed for articles published between January 1, 2000 and March 1, 2022. There is no research on whether or not the antibiotics provided to young children in LMICs come from qualified sources.

Added value of this study
This is the first investigation into qualified sources of antibiotics for fever/cough in children under five. Our study included 59 LMICs, which results in a generalized result for antibiotic prescriptions from qualified sources. According to our research, eleven LMICs—Bangladesh, Chad, Comoros, Congo, Congo Democratic Republic, Côte d'Ivoire, Gabon, Kyrgyz Republic, Tajikistan, Tanzania, and Yemen—received more than 40% of their antibiotics from unqualified sources.

Implications of all the available evidence
Our research indicates that a significant number of antibiotics for fever/cough were coming from unqualified sources in eleven different LMICs. Also, getting antibiotics for fever/cough from unqualified sources was very common in the Central Asian region. The study sheds light on where children under five in LMICs get their prescriptions for antibiotics when they have a fever/cough. In order to prevent pharmacies from dispensing antibiotics recommended by unqualified sources, our study recommends implementing a more robust health infrastructure as well as various checks and balances.

40% of total healthcare costs. For example, antimicrobial agents consume 25–50% of India's, Bangladesh's, Thailand's, and Tanzania's government pharmaceutical expenditures.[7] Antibiotic misuse and the emergence of AMR are inextricably connected.

There may be a link between primary care doctors' antibiotic prescriptions and AMR.[8] Antibiotic usage was high in rural areas, especially in illnesses with a primarily viral aetiology, such as diarrhoea or URTI.[8] The use of antibiotics has revealed that parents' lower socioeconomic class and education level may be major variables in their antibiotic misuse.[9]

Children in LMICs are administered an incredible number of antibiotics between birth and the age of five. The rate of antibiotic use in LMICs increased 39% between 2000 and 2015, while the amount of antibiotics consumed, measured in defined daily doses (DDD), increased 65% (21.1–34.8 billion DDDs) (11.3–15.7 DDDs per 1000 inhabitants per day).[10] According to a study, around 57% of these doses appear to be inappropriate.[11] Although data on antibiotic usage and the incidence of AMR in LMICs is more limited than in high-income countries, the current evidence shows that AMR is more prevalent in LMICs than in high-income countries.[12] One of the factors that may contribute to this situation is the supply of antibiotics from unqualified sources, which can result in the overconsumption of antibiotics and unfinished doses, leading to a significant number of deaths in children.

Antimicrobial agents are sold without a prescription or medical supervision in many parts of the world. For example, according to a study in Thailand, antibiotics purchased through unqualified sources can account for a significant portion of antibiotics use.[13] However, antimicrobial efficacy initiatives have mostly targeted hospitals or providers, omitting non-prescription antimicrobial usage.[14] Healthcare professionals, especially those with little to no training in AMR and antibiotic use and those working in rural regions, demonstrated low awareness of the effects of antibiotics and AMR.

All sorts of healthcare providers should receive educational messages on the wise use of antibiotics and how they function as part of specific and targeted interventions to combat AMR in LMICs.[15] A systematic review revealed that AMR and hospital-acquired infections can be reduced by interventions to prevent excessive antibiotic prescribing to hospital inpatients, while efforts to boost effective prescribing can improve clinical outcomes.[16]

To the best of our knowledge, there is no study on whether the antibiotics prescribed for children under five in LMICs originated from qualified sources or not. Accurate information about the sources of antibiotic prescription is crucial as prescriptions from unqualified sources burden LMICs with massive costs in the healthcare sector. Therefore, our study shed light on whether antibiotics are prescribed by qualified sources or not. Moreover, it will help policymakers and planners in LMICs take convenient and efficient steps regarding this crucial matter.

Methods

Data source & study design

We used data from cross-sectional studies of the latest standard Demographic and Health Survey (DHS) conducted in LMICs, funded by the U.S. Agency for International Development (USAID). DHS is a global survey that is conducted every three to five years in LMICs under the same protocol. The DHS survey includes women between the ages of 15 and 49 and children under five who reside in residential households. In some countries DHS includes male household members. The study time spanned from March 2, 2020 to October 15, 2022.

A two-stage stratified cluster sampling method is used in the survey. Selecting locations or clusters was the initial stage. The second stage involves systematically selecting households from each cluster or Enumeration Area (EA). The DHS program collects data for children under five on vaccination, childhood illness and newborn care information from their mother. To enable cross-country comparison, DHS surveys adhere to a set of standard operating protocols that include sampling, questionnaires, data collecting, cleaning, coding, and analysis. Oral and written consents were provided by women. DHS receives ethical approval for all surveys from the institutional review boards of ICF International and the ethics regulatory authorities of the nations in which the research is conducted. The detailed guidelines can be found at https://dhsprogram.com/.

Data harmonization

We downloaded the latest standard DHS data of 92 LMICs from the website https://dhsprogram.com/. Since our study involves only children under five, we used to "Children Recode (KR)" datasets to perform our analyses. 59 LMICs (Afghanistan, Albania, Angola, Bangladesh, Benin, Burkina Faso, Burundi, Cambodia, Cameroon, Chad, Comoros, Congo, Congo Democratic Republic, Cote d'Ivoire, Dominican Republic, Egypt, Eswatini, Ethiopia, Gabon, Gambia, Ghana, Guatemala, Guinea, Guyana, Haiti, Honduras, India, Indonesia, Jordan, Kenya, Kyrgyz Republic, Lesotho, Madagascar, Malawi, Maldives, Mali, Mauritania, Morocco, Mozambique, Myanmar, Namibia, Nepal, Nigeria, Papua New Guinea, Pakistan, Philippines, Rwanda, Sao Tome and Principe, Senegal, Sierra Leone, South Africa, Tajikistan, Tanzania, Timor-Leste, Togo, Uganda, Yemen, Zambia, Zimbabwe) were finally included from a possible of 92 countries in our study. These countries were chosen as they met our inclusion criteria and had up-to-date standard DHS data. For example, thirteen countries with Standard DHS datasets before 2000 (Botswana, Brazil, Ecuador, El Salvador, Kazakhstan, Mexico, Paraguay, Nigeria Ondo state, Sudan, Trinidad and Tobago, Uzbekistan, Thailand, and Tunisia) were excluded from the study as they may not represent the current state of antibiotic consumption. Moreover, eight countries (Sri Lanka, Samoa, Cape Verde, Eritrea, Turkmenistan, Lao People's Democratic Republic, and Equatorial Guinea) were excluded due to their unavailability in the public domain. In addition, thirteen countries (Moldova, Nicaragua, Niger, Peru, Liberia, Armenia, Azerbaijan, Bolivia, Central African Republic, Ukraine, Vietnam, Turkey, and Colombia) were further eliminated because of insufficient data and relevant variables. The extent of non-response rate in each of the above countries is not reported. This is because, in some countries, the DHS survey reports are either publicly unavailable or not in English.

To analyse survey datasets some issues such as unequal unit selection probabilities should be considered. Sample weights help to eliminate bias that may arise from disproportionate sampling and impacts of non-response and are important in calculating standard errors. Thus, excluding weights from the study sometimes results in significantly biassed estimates.

In STATA, singleton was introduced to handle a single PSU in a stratum. Single PSU in stratum can occur because of various reasons such as missing data. This leads to numerous problems in analysing the data such as not being able to calculate standard errors. To handle singleton PSUs in each stratum, we evaluated three methods: singleton (certainty) where we treated every singleton unit as certainty units, singleton (scaled) where for each stratum we used the average of the variances from the strata with multiple sampling units as a scaling factor for singleton (certainty), and singleton (centred) where we centred the singleton PSUs at the grand mean. Of these three methods, we used singleton (scaled) method for our analysis. All levels of categorical explanatory variables were defined in a suitable manner for interpretation and ease of analysis. After extracting the study variables in each country dataset, we pooled them into one data set.[17]

Outcome variable

The outcome variable "Antibiotic Taken for Fever/Cough from Qualified Sources" is a dichotomous variable classified as "YES = 1/NO = 0." We enquired if the children recently had a fever/cough. If the response is yes, we checked to see if they have had any medical treatment using antibiotics. Finally, we investigated whether the prescriptions were provided by qualified sources or not [Fig. 1]. We classified any government hospitals, private hospitals, clinics, NGOs, and public health sectors as qualified sources, whereas pharmacies, shops, churches, traditional practitioners, markets, drug sellers, friends/relatives, supermarkets, shops, and others were categorised as non-qualified. Although pharmacists are experts in medicine dispensing, they are not authorised to prescribe antibiotics in LMICs.[18,19] Thus we categorised 'pharmacy' as unqualified sources of antibiotics.

Explanatory variables

Two types of explanatory variables were obtained from the standard DHS: level one (individual-level variables) and level two (community-level variables). Level one comprises the number of children under five, age in years, their sex, body mass index (BMI) of children under five, type of place of residence, wealth index, respondents' occupation, husband or partner's occupation, children having any type of vaccination (DHS survey only includes whether children ever received any type of vaccination), months of breastfeeding, delivery

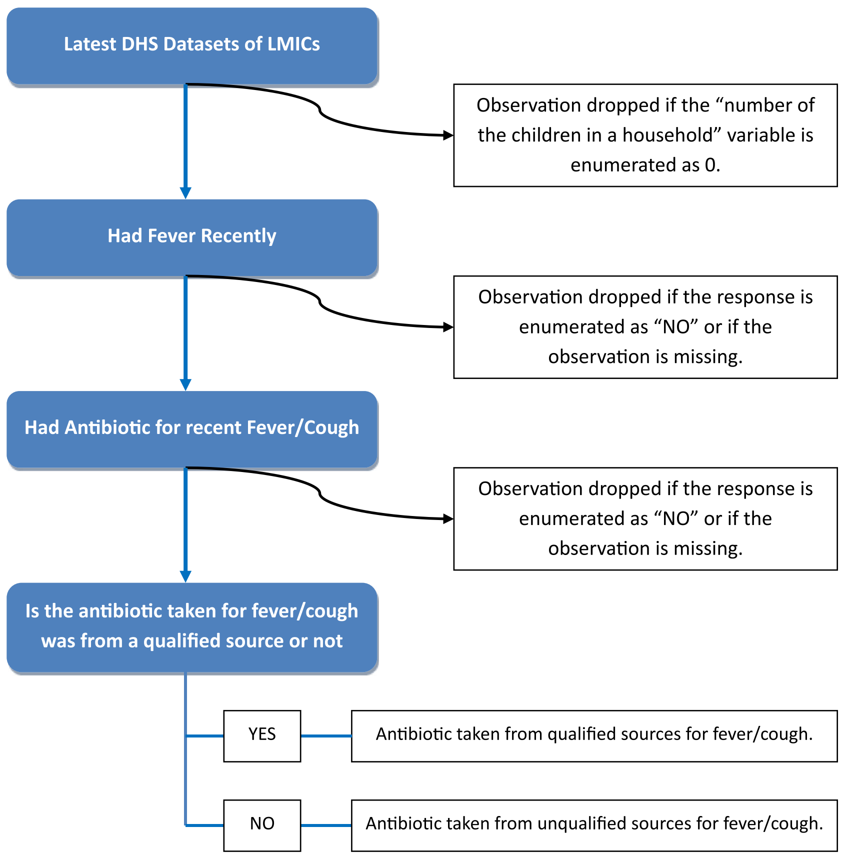

Fig. 1: **Outcome extracting criteria**.

by caesarean section. Residence and country are variables at level two. For analysis and interpretation, these variables were recoded to make them relevant. Every variable was coded a priori by the available data and the most plausible causal pathways. Table 1 contains a detailed description of each variable.

Statistical analysis

We calculated various descriptive statistics of qualified antibiotic prescriptions with respect to countries, continents, economic status, top and bottom ten countries in antibiotic consumption. All of the reported findings in tables and figures are based on weighted estimates to reflect the estimates of national figures, apart from the first paragraph of the 'Results' section where the actual overall numbers were summarised. All descriptive findings were accompanied with corresponding bar diagrams. The geospatial analysis was conducted through ArcGIS version 10.7.[20] All statistical analyses were conducted in STATA version 14.[21] All the graphs were produced by Microsoft Excel.

STROBE Statement—Checklist, outlining items to be included in reports of cross-sectional studies, was followed in this study [Supplementary Table S1].

Role of the funding source

There was no funding source for this study. We used publicly available datasets from DHS website, and all authors had full access to all the data in the study and accept responsibility for the decision to submit for publication. More than one author has verified the statistical analysis and results of the study and takes the full responsibility of the results.

Results

All of the findings reported below are based on the weighted estimates to reflect the population except the first paragraph of the country description.

Country description

We identified 43,166 children under five who had taken antibiotics for fever/cough two weeks prior to the survey. Then, we divided the children into two groups: children who obtained the antibiotic from a qualified source (74.0%) and those who did not. Among them 22,649 (52.6%) were males. The percentages of qualified antibiotic prescriptions for males and females were 74.7% and 73.4%, respectively.

Variables	Code at DHS dataset	Categories in DHS	Recoding procedure
Level one variables (Individual level variables)			
Number of children under 5	v137	One	1 = "one"
		Two	2 = "two"
		Three	3 = "three"
		Four	4 = "four"
		Five or above	5 = "five or above".
Age of the child (In years)	hw1	One year old	1 = "min/12 months"
		Two years old	2 = "13/24 months"
		Three years old	3 = "25/36 months"
		Four years old	4 = "37/48 months"
		Five years old	5 = "49/60 months".
Sex of the child	b4	Male	1 = "male"
		Female	2 = "female"
Body mass index (BMI) of children under five	This was deduced by code from the dataset.	1	1 = "min–9.9"
		2	2 = "9.9–14.9"
		3	3 = "14.9–18.5"
		4	4 = "18.5–24.9"
		5	5 = "24.9–max".
Wealth index	v190	Poorest	1 = "poorest"
		Poorer	2 = "poorer"
		Middle	3 = "middle"
		Richer	4 = "richer"
		Richest	5 = "richest"
Respondents' occupation (grouped)	v705	Did not work	0 = "Did not work"
		Agriculture	1 = "Agriculture"
		Manual labour	2 = "Manual labour"
		Professional/technical/managerial	3 = "Professional/technical/managerial"
		Others	4 = "Others"
Partner/husband's occupation (grouped)	v717	Did not work	0 = "Did not work"
		Agriculture	1 = "Agriculture"
		Manual labour	2 = "Manual labour"
		Professional/technical/managerial	3 = "Professional/technical/managerial"
		Others	4 = "Others"
Had fever in last two weeks	h22	Yes	1 = "Yes"
		No	0 = "No"
Antibiotic taken for fever	This was deducted by code from the dataset.	Yes	1 = "Yes"
		No	0 = "No"
Months of breastfeeding	m5	One year breastfed	1 = "min/12 months"
		Two years breastfed	2 = "13/24 months"
		Three years breastfed	3 = "25/36 months"
		Four years breastfed	4 = "37/48 months"
		Five years breastfed	5 = "49/60 months"
		Ever breastfed, not currently breastfed	93 = "ever not currently breastfed"
		Never breastfed	94 = "never breastfed"
		Inconsistent	97 = "inconsistent"
Delivery by caesarean section	m17	No	1 = "Yes"
		Yes	0 = "No"
Ever had vaccination	h10	No	1 = "Yes"
		Yes	0 = "No"

(Table 1 continues on next page)

Variables	Code at DHS dataset	Categories in DHS	Recoding procedure
(Continued from previous page)			
Level two variables (Community variables)			
Type of place of residence	v025	Urban	1 = "Urban"
		Rural	2 = "Rural"
Country code	v000	This cell needs a hand	
Dependent variables			
Antibiotics prescribed for fever by qualified doctors	This was deducted by code from the dataset.	Yes	1 = "Yes"
		No	0 = "No"
Random effect variables			
Sampling weight	v005	For weighting the observation	
Primary sampling unit (PSU)	v021	For sample selection	
Strata	v022	For stratification	

Table 1: **Variables recoding procedures.**

Among the selected countries, Cameroon (0.3%), Nigeria (4.3%), Mauritania (6.1%), Cambodia (6.8%), Bangladesh (7.0%), Mozambique (7.6%), Benin (15.3%), Mali (16.9%), Tanzania (18.2%), and Eswatini (19.0%) were the bottom ten in terms of consuming antibiotics for fever/cough [Table 2]. The above bottom ten countries in consuming antibiotics received 62.0% of their antibiotics from qualified sources [Fig. 2]. Moreover, Congo (68.7%), Egypt (65.5%), Tajikistan (61.8%), Honduras (52.1%), Gabon (51.1%), Albania (50.5%), Yemen (49.3%), Sao Tome and Principe (48.0%), Afghanistan (47.6%), and Namibia (46.3%) were the top ten in terms of consuming antibiotics [Table 2]. The above top ten countries in consuming antibiotics received 67.1% of their antibiotics from qualified sources [Fig. 2].

The countries that have the lowest percentage of antibiotic prescribed by qualified sources were Tanzania (22.4%), Bangladesh (23.7%), Congo Democratic Republic (46.2%), Congo (47.1%), Chad (47.9%), Yemen (52.1), Tajikistan (55.4), Comoros (56.7%), Côte d'Ivoire (58.1%), and Gabon (58.1%); the countries had the highest percentage of antibiotic prescribed by qualified sources were to Malawi (99.9%), Mozambique (96.3%), Cambodia (94.7%), Zambia (92.2%), Eswatini (90.8%), Papua New Guinea (89.9%), Burkina Faso (89.6%), Indonesia (89.6%), Nigeria (88.8%) and Maldives (88.5%) [Table 2] [Fig. 3].

Descriptive statistics of socio-demographic variables

Table 3 shows the relationship between selected explanatory variables and antibiotics prescribed for fever/cough by qualified sources. In general, we found no sub-groups to be especially high or low risk-groups for taking antibiotics from qualified sources. Children living in rural areas received 75.0% of antibiotics from qualified sources, compared to urban areas with 72.2%. 78.8% of children whose parents received higher education went to qualified sources for antibiotics. However, there were 5.3% missing responses in this variable. The percentage of antibiotics received from qualified sources seems to decline as the number of children under five in the household increases (One; 76.8%, two; 73.1%, three; 69.1%, four; 69.7%). Conversely, the percentage increases with the year children under five were breastfed (One Year; 76.3%, Two Years; 77.2%, Three Years; 78.7%). However, the percentage of missing in this variable was 5.2%. Children who were delivered by caesarean sections received antibiotics from qualified sources 78.0% of the time. The percentage of missing in this variable was 0.4%.

The percentage of antibiotics taken for fever/cough from qualified sources for children aged one year, two years, three years, four years, and five years are 75.7%, 73.8%, 73.4%, 72.0%, and 71.4%, respectively. However, 32.3% of the variable was missing. According to their mothers' occupations—agricultural, manual labour, professional/technical/managerial, others, and mothers who did not work—children under the age of five received 72.2%, 72.7%, 74.7%, 76.0%, and 70.7% of their antibiotics from qualified sources, respectively. The missing percentage of this variable was 16.2%. On the other hand, the percentage of antibiotics taken from qualified sources for children under five on the basis of their mothers' partner/husband's occupation were 76.3% (agricultural), 71.7% (manual labour), 71.7% (professional/technical/managerial), 72.8% (others) and 72.7% whose mothers' partner did not work. However, there were 22.2% missing response in this variable. The percentage of children taking antibiotics for fever/cough from qualified sources in terms of their BMI are 74.5% for <9.9, 74.2% for 9.9–14.9, 72.9% for 14–18.5, 75.3% for 18.5–24.9 and 72.1% for >24.9 of BMI index. In this variable, there were 36.1% missing responses. According to the wealth index of child's family, the percentage of taking antibiotics for fever/cough is 73.7% for

Country	Had fever recently, weighted N (%)	Antibiotic taken for fever, weighted N (%)	Antibiotics prescribed from qualified sources, weighted N (%)	Antibiotics prescribed from unqualified sources, weighted N (%)
Afghanistan	8682 (29.1)	4040 (47.6)	2977 (74.1)	1043 (26.0)
Albania	160.6 (6.4)	81.1 (50.5)	68.1 (84.0)	13.0 (16.1)
Angola	1829 (14.9)	550.1 (30.1)	462.9 (84.2)	87.2 (15.8)
Bangladesh	2697 (37.3)	187.3 (7.0)	44.3 (23.7)	143 (76.3)
Benin	2437 (19.6)	372.9 (15.3)	243.7 (65.4)	129.1 (34.6)
Burkina Faso	2868 (20.8)	873.5 (30.7)	781.8 (89.6)	90.9 (10.4)
Burundi	5033 (39.6)	1118 (22.2)	940.8 (84.2)	177.2 (15.9)
Cambodia	1953 (28.2)	132.5 (6.8)	125.5 (94.7)	7.0 (5.3)
Cameroon	1402 (15.6)	4.7 (0.3)	4.0 (86.4)	0.6 (13.6)
Chad	3949 (24.0)	845.1 (22.0)	400.5 (47.9)	435.6 (52.1)
Comoros	654.8 (22.0)	170.4 (26.7)	96.6 (56.7)	73.8 (43.3)
Congo	1840 (25.2)	1257 (68.7)	591.6 (47.1)	664.1 (52.9)
Congo Democratic Republic	4960 (29.9)	1480 (30.2)	681.5 (46.2)	792.4 (53.8)
Cote d'Ivoire	1584 (24.3)	439 (28.4)	249.2 (58.1)	179.7 (41.9)
Dominican Republic	747.7 (22.6)	248.9 (33.4)	195.5 (78.5)	53.4 (21.5)
Egypt	3870 (26.3)	2531 (65.5)	1985 (78.4)	546.4 (21.6)
Eswatini	676 (29.5)	111.8 (19.0)	101.5 (90.8)	10.3 (9.2)
Ethiopia	1470 (14.4)	389.1 (26.5)	304.6 (78.3)	84.5 (21.7)
Gabon	1120 (25.2)	564.1 (51.1)	326.3 (58.1)	235.2 (41.9)
Gambia	1102 (15.6)	433.4 (39.4)	307.8 (71.0)	125.7 (29.0)
Ghana	740.6 (14.2)	187.1 (25.3)	140.3 (75.0)	46.8 (25.0)
Guatemala	2835 (23.8)	1077 (38.0)	805.8 (74.8)	271.1 (25.2)
Guinea	1209 (17.3)	232.1 (19.2)	165 (71.1)	67.1 (28.9)
Guyana	359.3 (20.5)	77.6 (22.1)	61 (78.6)	16.6 (21.4)
Haiti	1789 (32.0)	546.2 (30.5)	405.1 (74.2)	141.1 (25.8)
Honduras	2235 (23.5)	1160 (52.1)	855.3 (73.8)	303.6 (26.2)
India	28,000 (13.2)	6858 (24.5)	5735 (83.6)	1123 (16.4)
Indonesia	5015 (31.5)	1427 (28.6)	1278 (89.6)	148.7 (10.4)
Jordan	1162 (12.9)	459.1 (39.5)	338.5 (73.7)	120.6 (26.3)
Kenya	4478 (24.9)	1927 (43.6)	1523 (79.5)	391.7 (20.5)
Kyrgyz Republic	203.7 (5.3)	88 (45.3)	52.7 (59.8)	35.4 (40.2)
Lesotho	398.7 (15.6)	100.6 (25.3)	74.7 (74.3)	25.9 (25.7)
Madagascar	1098 (9.4)	430.1 (40.9)	274.8 (64.0)	154.9 (36.0)
Malawi	4703 (29.2)	1134 (24.1)	916.8 (99.9)	0.8 (0.1)
Maldives	655.7 (24.6)	285.4 (43.5)	252.6 (88.5)	32.8 (11.5)
Mali	1507 (16.0)	254.4 (16.9)	179.2 (70.5)	75.2 (29.5)
Mauritania	1810 (16.6)	111.2 (6.1)	91.5 (82.3)	19.7 (17.7)
Morocco	1538 (27.3)	427 (27.8)	297.8 (69.8)	129.2 (30.3)
Mozambique	1439 (13.6)	109.6 (7.6)	105.5 (96.3)	4.1 (3.7)
Myanmar	636.3 (15.9)	199.7 (31.5)	149.4 (74.8)	50.3 (25.2)
Namibia	1026 (26.7)	460.3 (46.3)	312.6 (67.9)	147.7 (32.1)
Nepal	986.5 (21.6)	345.5 (35.0)	216.3 (62.6)	129.3 (37.4)
Nigeria	1739 (14.5)	73.5 (4.3)	65.33 (88.8)	8.2 (11.2)
Pakistan	3614 (37.7)	1416 (39.2)	1142 (80.6)	274.5 (19.4)
Papua New Guinea	1680 (20.1)	308.9 (19.4)	277.6 (89.9)	31.1 (10.1)
Philippines	1592 (16.8)	352.7 (22.2)	249.3 (70.7)	103.5 (29.3)
Rwanda	1472 (18.8)	583.4 (39.6)	482.2 (82.7)	101.2 (17.4)
Sao Tome and Principe	296.7 (17.4)	135.9 (48.0)	116.7 (85.9)	19.2 (14.1)
Senegal	2433 (23.2)	636.2 (26.2)	520 (81.7)	116.2 (18.3)
Sierra Leone	1443 (17.0)	363.8 (25.2)	278.5 (76.5)	85.4 (23.5)
South Africa	618.1 (21.2)	180.5 (29.2)	119.5 (66.2)	61.0 (33.8)
Tajikistan	572.5 (9.3)	353.6 (61.8)	196 (55.4)	157.6 (44.6)
Tanzania	1651 (18.3)	299.8 (18.2)	67.1 (22.4)	232.7 (77.6)
Timor-Leste	905.7 (13.2)	206.7 (22.8)	149.3 (72.3)	57.3 (27.7)
Togo	1345 (22.0)	413.1 (30.9)	291.6 (70.7)	120.6 (29.3)

(Table 2 continues on next page)

Country	Had fever recently, weighted N (%)	Antibiotic taken for fever, weighted N (%)	Antibiotics prescribed from qualified sources, weighted N (%)	Antibiotics prescribed from unqualified sources, weighted N (%)
(Continued from previous page)				
Uganda	4689 (34.1)	1360 (29.0)	1029 (75.6)	331.2 (24.4)
Yemen	4774 (32.0)	2290 (49.3)	1186 (52.1)	1091 (47.9)
Zambia	1460 (16.2)	499.1 (34.2)	460.2 (92.2)	39 (7.8)
Zimbabwe	789.1 (14.0)	268.5 (34.0)	218.5 (81.4)	50 (18.6)

Due to missing information about sources of antibiotic consumption, the sum of qualified and unqualified sources does not sum up to 100% in some countries.[22]

***Table 2:* Weighted descriptive statistics of antibiotics for fever/cough from qualified and unqualified sources in 59 LMICs.**

poorest, 73.2% for poorer, 74.1% for middle, 75.5% for richer and 73.7% for richest. For children who had vaccination at least once, the percentage who had taken antibiotics for fever/cough from qualified sources was 66.6%. In comparison, for children who never had vaccination the percentage who had taken antibiotics from qualified sources was 63.1%. However, there was 72.6% missing for this variable.

Stratified analysis

Country-wise comparison

In the least ten countries in terms of antibiotics consumption in LMICs, 62.0% of children with fever/cough received antibiotics from qualified sources. In contrast, in the highest ten countries, 67.1% of children with fever received antibiotics from qualified sources.

Continent wise comparison

From Fig. 4, comparing the continents, Oceania had the highest percentage of taking antibiotics from qualified sources (88.9%) whereas Central Asia had the lowest percentage (56.3%) of all continents. The other continents have the percentages of taking antibiotics from qualified sources as follows: Sub-Saharan Africa (71.4%), North Africa-West Asia-Europe 67.1%, South & Southeast Asia (79.8%) and Latin America & Caribbean (74.7%).

Country economic status

From Fig. 5, comparing the countries' socioeconomic status, the lower-middle-income countries had the highest rate (76.5%) of taking antibiotics from qualified sources, followed by upper-middle-income countries (72.2%) and lower-income countries (70.9%).

Discussion

Antibiotic consumption in children under five has been well reported in LMICs.[23] Antibiotic consumption comes with considerable health[24] and economic[7] burdens for LMICs. The sources from which people receive these antibiotics are of utmost importance as inappropriate use can lead to AMR.[25]

Our findings have revealed that antibiotic consumption for fever/cough among children is quite high across LMICs, which is in line with a previous study.[23] Among the children receiving antibiotics, we found that one in four children receiving antibiotics from unqualified sources. Another study has also found similar percentages.[26] Between the top ten and bottom ten LMICs in antibiotic usage, there appears to be a 5-percentage point variation (62% in bottom ten as opposed to 67.1% in top ten countries) in how those antibiotics were consumed. We have found that over 40% of antibiotics have been received from unqualified

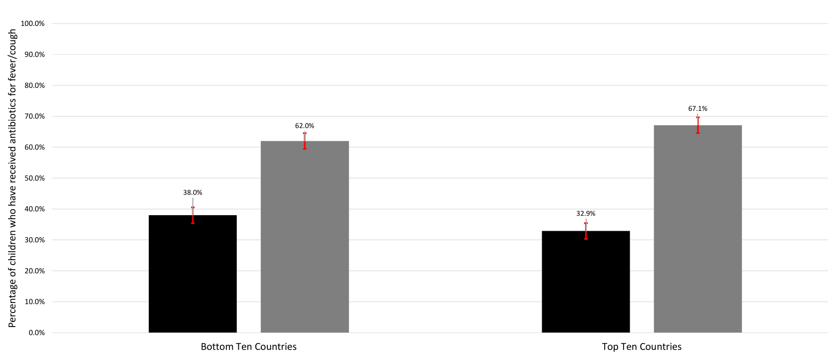

***Fig. 2:* Comparison between countries with the highest and lowest weighted antibiotics consumption rate.** Legend: Here, the black colour represents the antibiotics from unqualified sources on the other hand the grey colour represents the antibiotics from qualified sources.

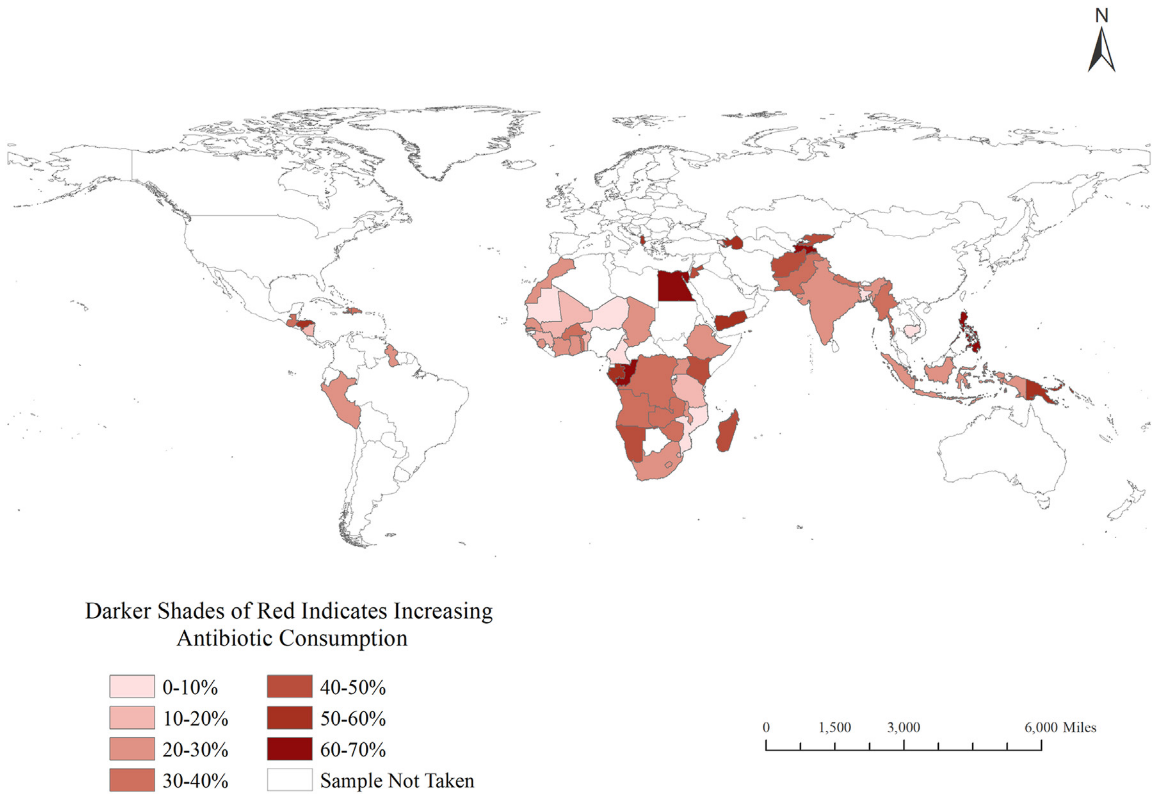

Fig. 3: **The weighted percentage of children under five who had taken antibiotics from unqualified sources for fever/cough in lower and middle-income countries.** Legend: Here, the darker shades of red indicating unqualified sources of antibiotics.

sources in eleven LMICs (Bangladesh, Chad, Comoros, Congo, Congo Democratic Republic, Côte d'Ivoire, Gabon, Kyrgyz Republic, Tajikistan, Tanzania, and Yemen). The percentages are particularly alarming for Tanzania and Bangladesh, with 77.6% and 76.3% prescriptions from unqualified sources, respectively. Among the countries in our study, Egypt, Albania, Gabon, Honduras and Tajikistan have very high (more than 50%) antibiotic consumption rate in children for fever/cough. Although these countries have a relatively high rate of prescription from qualified sources, the high consumption rate is detrimental to the health of the affected children.[27] On the other hand, although Bangladesh has 76% of unqualified sources of antibiotics for fever/cough, only 7% of the children in Bangladesh received antibiotics at all for fever/cough. Therefore, despite having a relatively low rate of unqualified sources of antibiotics, the aforementioned five countries are in a worse position than countries such as Bangladesh.

A number of the countries (e.g., Uganda, Bangladesh etc.) in our study have inadequate access to medical treatment. This may prompt them to seek treatment from untrained providers like drug sellers or conventional healers.[28–30] From the perspective of Bangladesh, there is a lack of trained healthcare professionals in Bangladesh, especially in rural regions. As a result, they could turn to unqualified healthcare providers like drug sellers or conventional healers. According to a study in Bangladesh, there is a high prevalence of using unqualified healthcare providers since there is little access to qualified medical professionals.[31]

Healthcare is quite expensive in many LMICs, which prompts individuals to look for less expensive options.[32] For example, Bangladesh's medical expenses can be considerable, especially for those with limited resources. According to a study done in metropolitan Bangladesh, pharmacies sell antibiotics for less money than qualified healthcare professionals.[31,33] Antibiotics can be more affordable from unqualified drug sellers than from qualified healthcare professionals. For instance, a study in Kyrgyzstan demonstrated that pharmacies sell antibiotics for less prices than qualified healthcare professionals.[34] According to another study conducted in Tanzania, rural populations frequently turn to traditional healers since they have little access to modern medical care.[35]

The risks of improper use of antibiotics, such as the development of antibiotic resistance, may not be well recognised among LMICs. This may result in obtaining

Variables	Category	Qualified, weighted N (%)	Unqualified, weighted N (%)	Missing percentage
Child's age	One year old	5274 (75.7)	1691 (24.3)	32.3
	Two years old	5386 (73.8)	1913 (26.2)	
	Three years old	4458 (73.4)	1615 (26.6)	
	Four years old	3630 (72.0)	1409 (28.0)	
	Five years old	2742 (71.4)	1100 (28.6)	
Sex of the child	Male	16,911.9 (74.7)	5740 (25.3)	0
	Female	15,054.8 (73.4)	5467 (26.6)	
Type of place of residence	Urban	10,686.8 (72.2)	4121 (27.8)	0
	Rural	21,280.7 (75.0)	7086 (25.0)	
Mother's highest educational level	No education	8319 (74.3)	2876 (25.7)	5.3
	Primary	8630 (74.1)	3014 (25.9)	
	Secondary	11,141.2 (76.1)	3499 (23.9)	
	Higher	2691 (78.8)	726.1 (21.3)	
Number of children under 5 in the household	One	13,369.1 (76.8)	4056 (23.3)	0
	Two	12,361.9 (73.5)	4457 (26.5)	
	Three	4143 (69.1)	1852 (30.9)	
	Four	1137 (69.7)	494.5 (30.3)	
	Five or above	913.7 (72.4)	348.5 (27.6)	
Partner's/husband's occupation (grouped)	Did not work	678.8 (76.3)	210.8 (23.7)	22.2
	Agriculture	6859 (71.7)	2710 (28.3)	
	Manual labour	7312 (71.7)	2882 (28.3)	
	Professional/technical/managerial	3058 (72.8)	1145 (27.3)	
	Others	6361 (72.7)	2386 (27.3)	
Respondents occupation (grouped)	Did not work	13,253.5 (72.2)	5093 (27.8)	16.2
	Agriculture	5155 (72.7)	1937 (27.3)	
	Manual labour	1654 (74.7)	561.2 (25.3)	
	Professional/technical/managerial	1414 (76.0)	446.8 (24.3)	
	Others	4721 (70.7)	1954 (29.3)	
Wealth index combined	Poorest	6619 (73.70	2365 (26.3)	0
	Poorer	6398 (73.2)	2343 (26.8)	
	Middle	6571 (74.1)	2296 (25.9)	
	Richer	6687 (75.5)	2174 (24.5)	
	Richest	5692 (73.7)	2029 (26.3)	
Body mass index (BMI) of children under five	1	157.2 (74.5)	53.7 (25.5)	36.1
	2	6981 (74.2)	2431 (25.8)	
	3	11,184.3 (72.9)	4173 (27.2)	
	4	1805 (75.3)	592.1 (24.7)	
	5	152.7 (72.1)	59.1 (27.9)	
Delivery by caesarean section	No	26,742.6 (73.1)	9841 (26.9)	0.4
	Yes	5118 (80.0)	1281 (20.0)	
Months of breastfeeding	One year breastfed	8178 (76.3)	2534 (23.7)	5.2
	Two years breastfed	6675 (77.2)	1973 (22.8)	
	Three years breastfed	1706 (78.7)	462.9 (21.3)	
	Four years breastfed	409.8 (77.0)	122.1 (23.0)	
	Five years breastfed	157 (77.1)	46.7 (22.9)	
	Ever breastfed, not currently breastfed	12,123.8 (70.3)	5122 (29.7)	
	Never breastfed	990.1 (69.8)	429 (30.2)	
	Inconsistent	4.6 (90.1)	0.5 (9.9)	
Ever had vaccination	No	779.5 (63.1)	455.4 (36.9)	72.6
	Yes	7056 (66.6)	3543 (33.4)	

Table 3: **Weighted descriptive statistics of socio-economic variables associated with prescriptions from qualified and unqualified sources.**

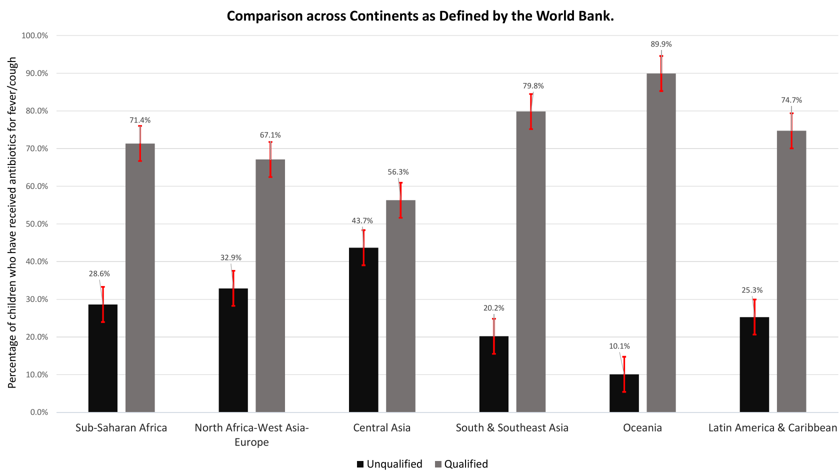

Fig. 4: **Comparison of weighted percentage of antibiotics sources across continents as defined by the World Bank.** Legend: Here, the black colour represents the antibiotics from unqualified sources on the other hand the grey colour represents the antibiotics from qualified sources.

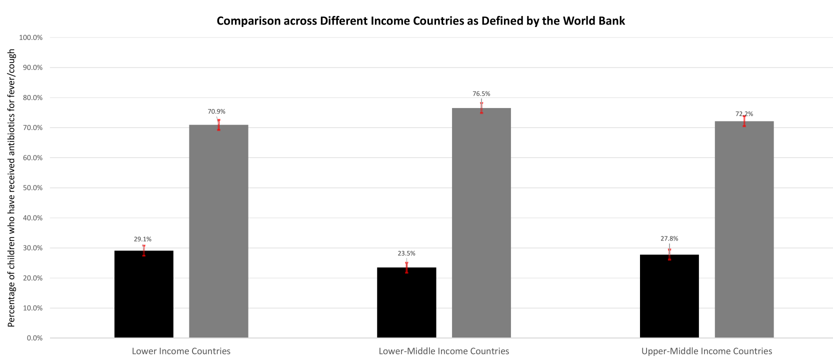

Fig. 5: **Comparison of weighted percentage of antibiotics sources across different income countries as defined by the World Bank.** Legend: Here, the black colour represents the antibiotics from unqualified sources, on the other hand the grey colour represents the antibiotics from qualified sources.

antibiotics from unqualified sources and using them inappropriately. For instance, a study in the Congo revealed that both patients and healthcare professionals were unaware of antibiotic resistance, and that over 70% of medicines were supplied incorrectly.[35–37]

The proportion of antibiotics received for fever/cough from qualified sources is influenced by a variety of socioeconomic variables. Children in rural areas have typically been receiving more prescriptions from qualified sources (about 3 percentage point) for antibiotics than those in urban areas. This is however not consistent across the LMICs. For example, in six countries (e.g., Chad, Congo Democratic Republic, Cote d'Ivoire, Eswatini, Haiti and Morocco), the percentage of prescriptions from qualified sources have been high in urban areas rather than in rural ones. There are a few reasons why antibiotic prescriptions by qualified sources are low in urban areas. Firstly, since people in urban areas are more educated and have basic knowledge about antibiotics for common childhood diseases,[37,38] they buy antibiotics for their children without any doctor's consultation. Secondly, the abundance of pharmacies in urban areas compared to rural areas[39] also leads to unqualified purchases of antibiotics. Finally, excessive queuing lines in urban government hospitals is also a contributing factor in people not going to government health workers for common and repetitive childhood diseases.[40]

Our findings indicate that the percentage of taking antibiotics from qualified sources drops as children grow older. Similar result was also shown in a study in China.[41] We have further observed a decreasing pattern in prescriptions from qualified sources for antibiotics with the increase in the number of children in a household. When there have been correspondingly two, three, and four children, the proportion of receiving an antibiotic prescription from qualified sources decreased compared to one child. There could be a few reasons for the preceding results. Firstly, households with more than one child are more experienced in dealing with common childhood diseases, so they are more prone to use their experiences to buy antibiotics without a prescription rather than visiting a qualified doctor.[42–44] Secondly, the number of children can weigh down economically on every household. As a result, households with more than one child look for cheaper and convenient sources for antibiotics and thus opt for unqualified sources.[45]

We found that the percentage of taking antibiotics from qualified sources for children increases with the mothers' education level. Several studies also suggest that parents' higher education level significantly reduces taking antibiotics from unqualified sources.[46,47]

On the other hand, we have seen an upward trajectory in prescriptions from qualified sources with the increase in the years of breastfeeding. When children have been breastfed for correspondingly two, three, and four years, the proportion of receiving an antibiotic prescription from qualified sources increased considerably compared to those who never did. Mothers who have breastfed their child for a long time tend to take antibiotic prescriptions from a qualified source for the child more than others who breastfed for a short time or never did.

The children whose mothers had caesarean sections have received reasonably more (about 6 percentage point) prescriptions from qualified sources for antibiotics than those who did not. The primary reason is mothers who have had caesarean sections frequently require long-term care from qualified doctors and are more familiar with antibiotics. In such cases, children tend to receive more antibiotics from unqualified sources.[42,43,48]

Our study suggests that children in Malawi, Mozambique, Cambodia, Zambia, Eswatini, Papua New Guinea, Burkina Faso, Indonesia, Nigeria, and the Maldives have received a considerably high number of antibiotics for fever/cough from qualified sources. Of the six regions in which we divided our countries, Central Asia has the lowest percentage of antibiotics taken for fever/cough from qualified sources. Oceania, on the other hand, has the highest. Similar results have also been observed in a previous study.[49] Lower-middle-income countries have the highest percentage of taking antibiotics from qualified sources compared to upper-middle-income and lower-income countries. Children in LMICs receive antibiotics from qualified sources more (about 3 percentage point) than lower-income countries.

Our study finds that antibiotic taking from unqualified sources is alarmingly high in some of the LMICs (Bangladesh, Chad, Comoros, Congo, Congo Democratic Republic, Côte d'Ivoire, Gabon, Kyrgyz Republic, Tajikistan, Tanzania, and Yemen). There is a need to strengthen the enforcement of laws and regulations to prevent the sale and distribution of antibiotics from unqualified sources in these countries. Additionally, there should be a greater focus on urban areas, where the proportion of antibiotics obtained from unqualified sources is higher than in rural areas. Targeted interventions, such as health education campaigns, free healthcare services, and improved access to qualified sources of antibiotics, should be implemented to support vulnerable populations, including households with multiple children and children with uneducated mothers. It is also essential to raise public awareness and understanding of appropriate antibiotic use through community outreach initiatives, public health campaigns, and school-based education programs. Finally, promoting rational antibiotic use by healthcare professionals, reducing over-the-counter access to antibiotics, and promoting alternative treatments can help reduce the demand for antibiotics from unqualified sources.

To our knowledge, this is the first study conducted on qualified sources of antibiotics for fever/cough in children under five. Using geospatial analysis, we provided a comprehensive picture of prescriptions from qualified sources in LMICs. Our study incorporates a large number of LMICs which gives a generalised result for prescriptions from qualified sources of antibiotics.

Our analysis has several limitations. Firstly, several countries were unavailable in the DHS website. Secondly, in the available datasets, some countries did not include some of our variables of interest. Thirdly, some DHS datasets had very low observations which led to some unexpected results. Fourthly, we observed that a few of our variables had large number of missing values which may affect the robustness of the estimates. For example, several socio-demographic variables (child's age, BMI of children under five and ever had vaccination) had around 30% missing values. The variable "Ever had vaccination", especially, had 72% missing but we kept the variable in our study as we believe this may be a contributing variable to the awareness and availability of qualified sources of antibiotics. The extent of these missing values could provide some ambiguity in interpreting the results of these variables. Further study can be done by imputing missing values to improve the estimates. Finally, we only examined the unqualified sources of antibiotics for one childhood disease: fever/cough. Further study is needed to illustrate a complete scenario of prescription patterns of antibiotics for other common childhood diseases such as diarrhoea, Acute Respiratory Infection (ARI), etc.

Our study shows that eleven countries were receiving a high amount of antibiotics for fever/cough from unqualified sources. The region of central Asia was also extremely prone to receiving antibiotics for fever from unqualified sources. Several variables contribute to the proportion of children under five who had received antibiotics for fever/cough from qualified sources which are the type of place of residence, the number of children under five in the household, years of breastfeeding, and mothers who had caesarean sections. The study puts the spotlight on the sources of antibiotic prescriptions for fever/cough in children under five in LMICs. Our study calls for more robust health infrastructures and implementing various checks and balances for pharmacies not to provide antibiotics suggested by unqualified sources. The researchers hope this study will draw the attention of the relevant authorities to this appalling situation and recommend providing need-oriented support services at an individual level. Finally, the executives who make public health policies must acknowledge the circumstances and take the necessary steps at the national level.

Contributors
MSH, MFI, PBA, and MR cleaned, compiled, analysed the dataset, and wrote the original draft. TSA performed geospatial analysis. TA and MABC gave feedback on data analysis and manuscript structure, reviewed, and edited the first draft. MJU conceptualised, commented, and supervised the study. All authors have verified the underlying data, the statistical analysis, and the results of the study and take full responsibility for the results. All authors had full access to all the data in the study, reviewed the study numerous times, and accept responsibility for the decision to submit it for publication.

Data sharing statement
The data are available on request to the corresponding author.

Declaration of interests
There is no conflict of interest.

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Appendix A. Supplementary data
Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2023.102055.

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