

Trends in reported antibiotic use among children under 5 years of age with fever, diarrhoea, or cough with fast or difficult breathing across low-income and middle-income countries in 2005–17: a systematic analysis of 132 national surveys from 73 countries



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Summary

Background Global assessments of antibiotic consumption have relied on pharmaceutical sales data that do not measure individual-level use, and are often unreliable or unavailable for low-income and middle-income countries (LMICs). To help fill this evidence gap, we compiled data from national surveys in LMICs in 2005–17 reporting antibiotic use for sick children under the age of 5 years.

Methods Based on 132 Demographic and Health Surveys and Multiple Indicator Cluster Surveys from 73 LMICs, we analysed trends in reported antibiotic use among children under 5 years of age with fever, diarrhoea, or cough with fast or difficult breathing by WHO region, World Bank income classification, and symptom complaint. A logit transformation was used to estimate the outcome using a linear Bayesian regression model. The model included country-level socioeconomic, disease incidence, and health system covariates to generate estimates for country-years with missing values.

Findings Across LMICs, reported antibiotic use among sick children under 5 years of age increased from 36·8% (uncertainty interval [UI] 28·8–44·7) in 2005 to 43·1% (33·2–50·5) in 2017. Low-income countries had the greatest relative increase; in these countries, reported antibiotic use for sick children under 5 years of age rose 34% during the study period, from 29·6% (21·2–41·1) in 2005 to 39·5% (32·9–47·6) in 2017, although it remained the lowest of any income group throughout the study period.

Interpretation We found a limited but steady increase in reported antibiotic use for sick children under 5 years of age across LMICs in 2005–17, although overlapping UIs complicate interpretation. The increase was largely driven by gains in low-income countries. Our study expands the evidence base from LMICs, where strengthening antibiotic consumption and resistance surveillance is a global health priority.

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Introduction

Antimicrobial resistance is a leading global health challenge that threatens our ability to treat common infections and to do a wide range of medical procedures often associated with infectious complications. The direct and indirect effects of antimicrobial resistance will mostly be felt in low-income and middle-income countries (LMICs), because of their higher burden of infectious diseases and weaker health systems that are not adequately equipped to care for patients with drug-resistant infections.¹

Antibiotic consumption is an important and modifiable driver of antibiotic resistance development. The optimisation of antibiotic use has therefore been prioritised in the WHO Global Action Plan on

Antimicrobial Resistance.² However, the lack of data on antibiotic consumption, particularly from the poorest countries, has been an obstacle to achieving this objective.³ LMICs are at particular risk of high rates of antibiotic resistance development and spread given their high burden of infectious diseases, widespread lack of basic hygiene facilities, over-the-counter sales of antibiotics, informal sales outlets for medicines, and substandard or falsified drugs.⁴ For some of these same reasons, quantifying antibiotic use in resource-poor settings is particularly challenging, and the lack of reliable data on global antibiotic consumption from LMICs persists.³

Previous assessments of global antibiotic consumption have focused on high-income countries, with limited

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Research in context

Evidence before this study

We searched Scopus and PubMed for research articles of global antibiotic consumption assessments, including those that took place in low-income and middle-income countries (LMICs), published in any language between Jan 1, 2000, and Feb 15, 2020, using the search string: ((antibiotic*[Title] or antimicrob*[Title]) AND (consumption[Title] OR use[Title] OR exposure[Title]) AND (global[Title] OR developing countr*[Title] OR low-income[Title] OR middle-income[Title])). Six studies were identified in this search: four assessed global antibiotic consumption and trends using pharmaceutical sales data, one was a systematic review of smaller-scale research from low-income countries, and one was an assessment of antibiotic exposure in children visiting health facilities in eight LMICs in 2006–16. Among the four studies that assessed global antibiotic consumption, one assessed antibiotic consumption without analysis of trends over time, while the other three studies analysed trends over time on the basis of different countries, drug formulations, or time periods. These three studies showed increasing antibiotic consumption based on analysis of available pharmaceutical sales data for different countries, drug formulations, or time periods. The authors attributed the global increases to rising antibiotic consumption in LMICs. However, pharmaceutical sales data do not measure individual-level antibiotic use, nor are these data available or reliable for all countries, particularly low-income and lower-middle-income countries. Indeed, the three studies that analysed global antibiotic consumption trends over time relied heavily on data from high-income and upper-middle-income countries, while low-income and lower-middle-income countries were under-represented.

Added value of this study

We systematically compiled and analysed data on reported antibiotic use among children under 5 years of age with fever, diarrhoea, or cough with fast or difficult breathing symptoms from 132 Demographic and Health Surveys and Multiple

Indicator Cluster Surveys that took place in 73 LMICs between 2005 and 2017. Across LMICs, the proportion of reported antibiotic use among sick children under 5 years of age increased from 36.8% (uncertainty interval [UI] 28.8–44.7) in 2005 to 43.1% (33.2–50.5) in 2017, although results should be interpreted with caution because of overlapping UIs. Our results further show that the greatest increase among LMICs occurred in low-income countries, where there was an estimated 34% relative increase in antibiotic consumption from 29.6% (21.2–41.1) in 2005 to 39.5% (32.9–47.6) in 2017. Despite this increase, low-income countries had the lowest reported antibiotic use among sick children under the age of 5 years of any income group in each year throughout the study period.

Implications of all the available evidence

Our investigation substantially expands the evidence base for global patterns of antibiotic use from low-income and lower-middle-income countries that were under-represented in previous studies. Our findings are consistent with previous assessments that used pharmaceutical sales data to show rising global antibiotic consumption attributed to increases among LMICs. Building on these previous studies, we present new evidence indicating that low-income countries within LMICs have had the greatest increases in reported antibiotic use for sick children under 5 years of age since 2005. Nevertheless, despite these increases, low-income countries continued to have the lowest antibiotic use of any income group in each year throughout the study period. Our study used standardised, large-scale national surveys primarily targeted to low-income and lower-middle-income countries to help fill a crucial evidence gap from LMICs in this priority global health area. Such assessments should be viewed as complementary to longer-term initiatives that aim to strengthen routine systems for monitoring antimicrobial consumption and resistance patterns in LMICs, which have received heightened attention and investments in recent years.

evidence from LMICs and particularly low-income and lower-middle-income countries.^{5–10} The assessments have primarily relied on pharmaceutical wholesale data,^{5–8} which are useful in estimating population-level exposure to medicines, but do not directly measure individual-level usage or variations in antibiotic use by key socioeconomic or demographic characteristics. Furthermore, pharmaceutical sales data are often incomplete or unreliable in many LMICs, and might cover different populations or have varying representativeness between countries and over time. The data might also not correspond directly to the number of antibiotic courses eventually purchased or consumed by individuals.³ Taken together, these issues affect the availability and comparability of antibiotic consumption data across countries and over time, particularly for LMICs. Additionally, young children are more frequent users of antibiotics because of their greater

burden of infectious diseases and associated mortality risks compared with older children and adults, so focusing on patterns of paediatric antibiotic use in global assessments is of particular importance.^{5,8}

Acknowledging this evidence gap regarding antibiotic use in LMICs, a recent study assessed antibiotic exposure among children who visited health facilities in eight LMICs in 2006–16.¹¹ The authors found that about two-thirds of children attending health facilities received antibiotics, and that on average, the children received 24.5 antibiotic prescriptions by the age of 5 years. To add to this evidence, we systematically compiled data from standardised national household surveys that have been routinely and comparably conducted across multiple LMICs since the late 1990s. This study aimed to use these datasets to analyse trends in the proportion of reported antibiotic use among

children under 5 years of age across LMICs between 2005–17 by WHO region, World Bank income classification, and symptom complaint.

Methods

Search strategy and selection criteria

Demographic and Health Surveys and Multiple Indicator Cluster Surveys are cross-sectional cluster surveys based on nationally representative samples of households that have been comparably carried out every 3–5 years in LMICs over the past few decades. Since their inception in 1984, Demographic and Health Surveys have primarily been funded by the United States Agency for International Development, with technical support from the Demographic and Health Surveys Program and National Statistical Offices. Multiple Indicator Cluster Surveys have received financial and technical support from UNICEF since these surveys were first implemented in 1995. Both survey programmes use similar standardised methods and questionnaires to collect harmonised information on a wide range of key demographic and health issues relevant to LMICs. This includes information on common illness symptoms experienced by young children in the 2 weeks prior to the survey interview, as reported by female caregivers, and the medicines (including antibiotics) they were reportedly given to treat their conditions. Survey methods including procedures for obtaining ethical approval and participant consent are described in detail on the Demographic and Health Survey and Multiple Indicator Cluster Survey websites.

For this systematic analysis, Demographic and Health Surveys and Multiple Indicator Cluster Surveys which had been carried out since 2000 were systematically screened for inclusion in the study, which was guided by the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) guidelines. All datasets since 2000 that were publicly available as of Aug 15, 2018, were directly downloaded from the Demographic and Health Survey and Multiple Indicator Cluster Survey websites. Demographic and Health Surveys and Multiple Indicator Cluster Surveys were included if the final dataset was publicly available by Aug 15, 2018, the survey took place in a country classified as low-income, lower-middle-income, or upper-middle-income during the study period (according to the World Bank income classification of countries for each year in the study period),¹² and the questionnaire collected information to measure the primary outcome.

Data analysis

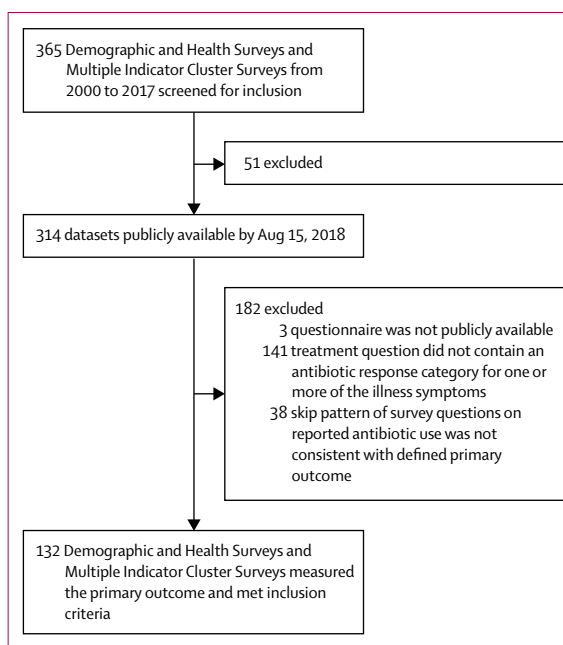
The primary outcome was defined as the proportion of children under the age of 5 years with reported symptoms of fever, diarrhoea, or cough with fast or difficult breathing in the 2 weeks before the survey interview who were reportedly given antibiotics to treat the condition. In this study, we refer to this outcome as reported antibiotic use for sick children under the age of 5 years.

During the survey interview, women 15–49 years of age living in each surveyed household were asked a series of questions about their children under 5 years of age, including questions about specific illness symptoms experienced by the child in the previous 2 weeks. If the child was reported to have fever, diarrhoea, or cough with fast or difficult breathing, the caregiver was asked if care was sought for each of these reported symptoms separately, and if yes, from where care was sought. The caregiver was also asked if any medicines (including antibiotics) were given to treat each of these reported symptoms. This treatment question was asked separately for each symptom. The caregiver was not prompted about specific medicines and multiple responses were allowed. The interviewer only recorded if an antibiotic (either pill, syrup, or injection) was given to treat each reported symptom. No further information was typically recorded about antibiotic type, dosage, or completion of the treatment course although a few surveys included specific antibiotic types as response categories. A positive outcome was defined as any antibiotic (antibiotic pill, syrup, injection, or specific antibiotic type) that was reportedly given to a child under 5 years of age to treat fever, diarrhoea, or cough with fast or difficult breathing symptoms, which the children were reported to have experienced in the 2 weeks before the survey interview.

A standard statistical approach^{13,14} was used to account for uncertainty around estimates for missing country-years. Specifically, hierarchical designs (region, country, and income groups) were used to model the proportion of reported antibiotic use among sick children under the age of 5 years. A logit transformation was employed to estimate

For more on the **Demographic and Health Surveys Program** see <https://dhsprogram.com/>

For more on **Multiple Indicator Cluster Surveys** see <https://mics.unicef.org>



For the **PRISMA guidelines** see <http://www.prisma-statement.org/>

Figure 1: Flow diagram of national survey data screened for study inclusion

	Survey data points (n=132)	Children under 5 years of age surveyed (n=1 507 521)	Low-income and middle-income countries in region or classification (n=140)	LMICs with at least one survey data point (n=73)	LMICs with at least two survey data points (n=38)
WHO region					
African LMICs	68 (51.5%)	694 778 (46.1%)	45 (32.1%)	37 (50.7%)	21 (55.3%)
Americas LMICs	22 (16.7%)	196 567 (13.0%)	26 (18.6%)	11 (15.1%)	6 (15.8%)
Eastern Mediterranean LMICs	9 (6.8%)	130 392 (8.6%)	17 (12.1%)	5 (6.8%)	3 (7.9%)
European LMICs	12 (9.1%)	30 878 (2.0%)	20 (14.3%)	9 (12.3%)	2 (5.3%)
South-East Asia LMICs	15 (11.4%)	411 377 (27.3%)	11 (7.9%)	8 (11.0%)	4 (10.5%)
Western Pacific LMICs	6 (4.5%)	43 529 (2.9%)	21 (15.0%)	3 (4.1%)	2 (5.3%)
World Bank income classification					
Low income	53 (40.2%)	540 621 (35.9%)	37 (26.4%)	28 (38.4%)	14 (36.8%)
Lower-middle income	47 (35.6%)	739 134 (49.0%)	52 (37.1%)	26 (35.6%)	17 (44.7%)
Upper-middle income	32 (24.2%)	227 766 (15.1%)	51 (36.4%)	19 (26.0%)	7 (18.4%)

Data are n (%). LMICs=low-income and middle-income countries.

Table: National survey data inputs to statistical model

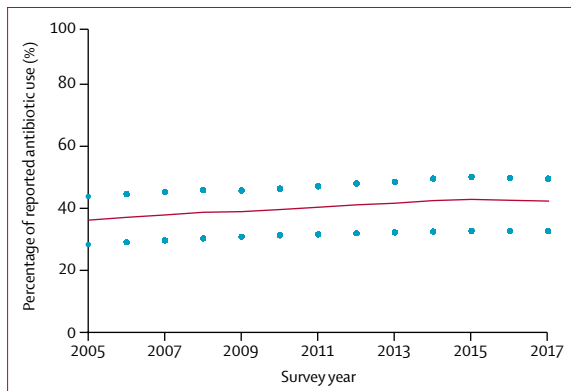


Figure 2: Trends in reported antibiotic use among sick children under 5 years of age across LMICs in 2005-17
The red line represents average antibiotic use across LMICs. The dots represent uncertainty intervals. LMICs=low-income and middle-income countries.

the outcome for all countries and all years between 2005 and 2017 using a linear Bayesian regression model.

Table 1 summarises survey data inputs to the statistical model by WHO region and all Demographic and Health Surveys and Multiple Indicator Cluster Survey inputs by country and year are presented in supplementary materials (appendix pp 1-3). To generate estimates for country-years with no survey data, the final model included country-level socioeconomic, disease incidence, and health system covariates that were selected on the basis of data availability for all countries and years during the study period, as well as on the basis of empirical evidence of their associations with antibiotic use for sick children under 5 years of age in LMICs.^{15,16} These covariates included: (1) Human Development Index value;¹⁷ (2) national population of children under the age of 5 years;¹⁸ (3) national incidence rates of malaria and respiratory and diarrhoeal infections for children aged 0-4 years;¹⁹ and

(4) national public and private health spending per capita (in international dollars).²⁰

We used Markov chain Monte Carlo to simulate the posterior distribution, which generated predictions for all country-years from the estimated model parameters. A burn-in period of 2500 samples and three chains (each with a sample size of 10 000) was used. Non-informative priors were employed in this analysis. Country-level values for the proportion of reported antibiotic use among sick children under 5 years of age were weighted to regional or country income groupings using national population estimates for children in this age group. To reflect uncertainty around estimates for countries without data, random intercepts and slopes for these countries were simulated from the posterior means and covariance of country intercepts and slopes for countries with data. Uncertainty intervals (UIs) were generated using weighted second and 98th percentiles of the posterior samples based on a total of 30 000 posterior draws. Each country was classified according to its WHO regional grouping and World Bank income classification in each year during the study period, which was allowed to shift over time during the regression modelling process. For the analysis by symptom complaint, we applied the same statistical approach to the subset of observations with diarrhoea alone, fever alone, or cough with fast or difficult breathing symptoms alone. Stata (version 15.1; StataCorp, College Station, TX, USA) was used for this analysis.

Role of the funding source

The funders of the study had no role in the study design, data collection, data analysis, data interpretation, manuscript preparation, writing of the report, or decision to publish. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

See [Online](#) for appendix

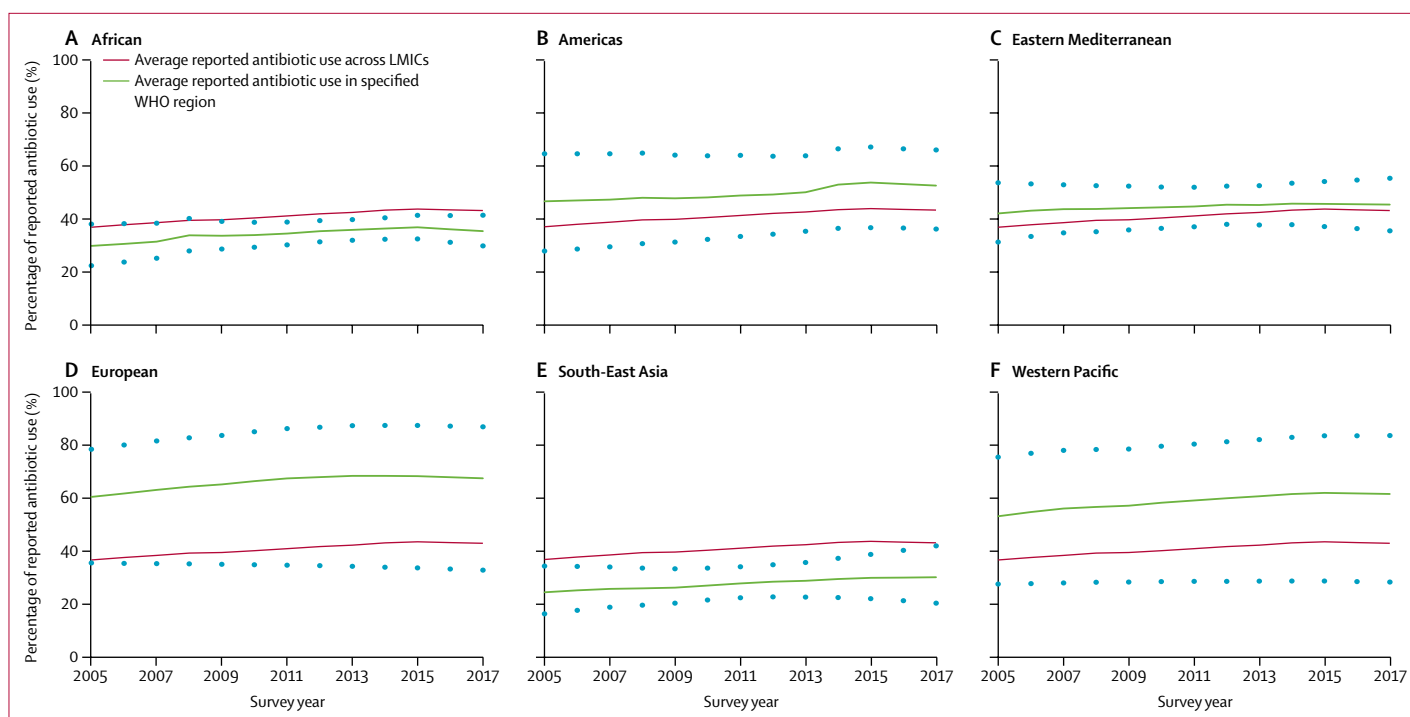


Figure 3: Trends in reported antibiotic use among sick children under 5 years of age across LMICs in 2005–17 by WHO regional groupings

(A) African region. (B) Americas region. (C) Eastern Mediterranean region. (D) European region. (E) South-East Asia region. (F) Western Pacific region. The red line represents average antibiotic use across LMICs. The dots represent uncertainty intervals. LMICs=low-income and middle-income countries.

Results

We screened 365 Demographic and Health Surveys and Multiple Indicator Cluster Surveys that were carried out in LMICs since 2000 for inclusion in our study (figure 1). Among these 365 surveys, 314 datasets were publicly available for research purposes as of Aug 15, 2018. Of the 314 datasets, 132 surveys from 73 LMICs in 2005–17 measured the primary outcome to meet inclusion criteria for the study.

The final dataset included 1507521 children under 5 years of age, with 443272 reported to have had either fever, diarrhoea, or cough with fast or difficult breathing symptoms in the 2 weeks before the survey interview. LMICs in the WHO African region accounted for 68 (51.5%) of 132 total survey data points and 694778 (46.1%) of 1507521 observations in children under 5 years of age, forming the main inputs to the statistical model (table). Low-income and lower-middle-income countries accounted for 100 (75.8%) of total survey data points and 1279755 (84.9%) of 1507521 observations in children under 5 years of age.

Across LMICs, we estimated that reported antibiotic use among sick children under 5 years of age increased from 36.8% (UI 28.8–44.7) in 2005 to 43.1% (33.2–50.5) in 2017, although results from our analyses should be interpreted with caution because of wide and overlapping UIs (figure 2).

LMICs in the Europe and Western Pacific WHO regions had the highest reported antibiotic use among

sick children under 5 years of age in 2017, with 67.7% (UI 33.0–87.1) in the European region and 61.7% (28.5–83.8) in the Western Pacific region (figure 3). LMICs in the Africa and South-East Asia regions had the lowest reported antibiotic use in 2017, with 35.4% (29.8–41.4) in Africa and 30.1% (20.3–42.0) in South-East Asia. Despite their lower antibiotic use relative to other WHO regions, Africa and South-East Asia had the greatest relative increase in antibiotic use since 2005. Specifically, in Africa, reported antibiotic use among sick children under 5 years of age rose 19% during the study period from 29.8% (22.3–38.0) in 2005 to 35.4% (29.8–41.4) in 2017. Similarly, in South-East Asia, there was a 23% relative increase in reported antibiotic use for sick children under 5 years of age, from 24.5% (16.3–34.3) in 2005 to 30.1% (20.3–42.0%) in 2017.

Low-income and lower-middle-income countries had the lowest reported antibiotic use among sick children under 5 years of age in 2017, with 39.5% (32.9–47.6) in low-income countries and 41.7% (33.7–48.7) in lower-middle-income countries. Upper-middle-income countries had the highest reported antibiotic use with 59.2% (35.3–76.3; figure 4). In low-income countries, reported antibiotic use for sick children under 5 years of age rose 34% during the study period, from 29.6% (21.2–41.1) in 2005 to 39.5% (32.9–47.6) in 2017. By contrast, the change in reported antibiotic use during the study period in lower-middle-income and upper-middle-income countries was minimal,

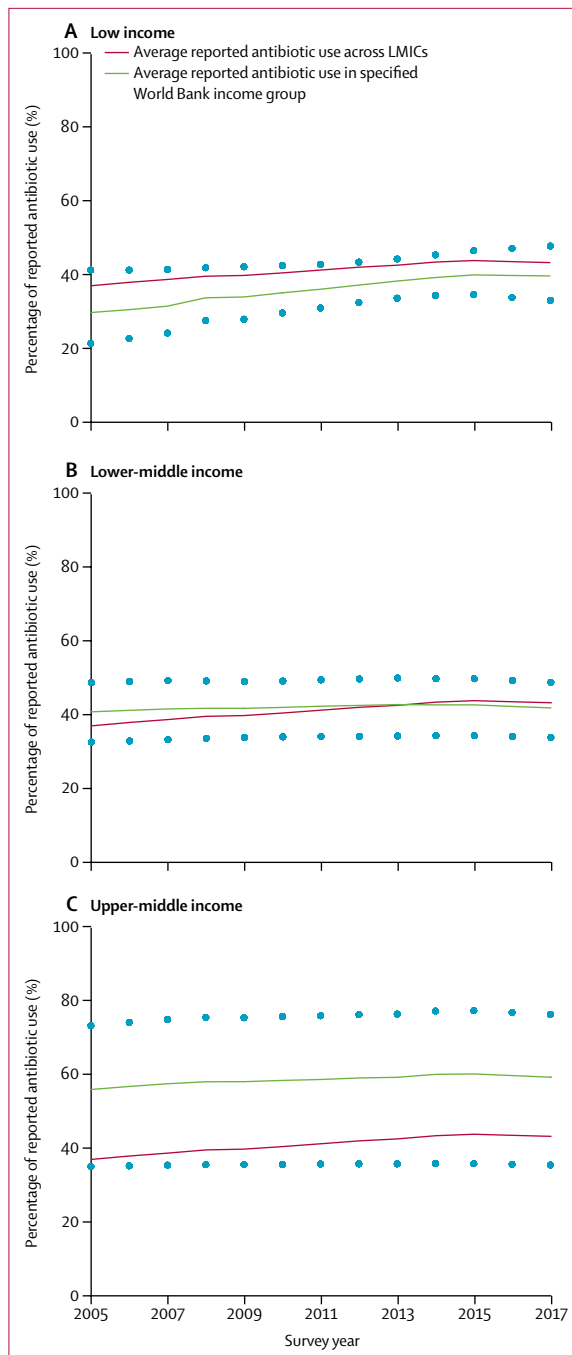


Figure 4: Trends in reported antibiotic use among sick children under 5 years of age across LMICs in 2005–17 by World Bank income classifications (A) Low-income countries. (B) Lower-middle-income countries. (C) Upper-middle-income countries. The red line represents average antibiotic use across LMICs. The dots represent uncertainty intervals. LMICs=low-income and middle-income countries.

from 40.7% (32.4–48.6) in 2005 to 41.7% (33.7–48.7) in 2017 in lower-middle-income countries, and from 55.9% (34.9–73.2) in 2005 to 59.2% (35.3–76.3) in 2017 in upper-middle-income countries.

Among different symptom combinations across LMICs, reported antibiotic use among sick children under 5 years of age was lowest if diarrhoea symptoms alone were reported, compared with other symptoms reported alone. Across LMICs, 33.4% (9.3–69.0) of sick children under 5 years of age with diarrhoea alone (and no other reported symptoms) received antibiotics to treat the condition in 2017, compared with 43.7% (12.2–82.6) if fever symptoms alone were reported, and 49.6% (14.3–84.5) if cough with fast or difficult breathing symptoms alone were reported (figure 5). Reported antibiotic use among sick children under 5 years of age was consistently highest in upper-middle-income countries at 39.7% (12.1–72.7) for diarrhoea alone, 55.1% (22.7–83.4) for fever alone, and 61.0% (29.1–84.1) for cough with fast or difficult breathing alone.

Despite wide and overlapping UIs, our estimates suggest that reported antibiotic use among sick children under 5 years of age with diarrhoea alone in LMICs remained relatively unchanged during the study period, from 34.7% (9.3–70.6) in 2005 to 33.4% (9.3–69.0) in 2017. By contrast, reported antibiotic use among sick children under 5 years of age with fever alone rose 13% across LMICs, from 38.8% (9.0–79.2) in 2005 to 43.7% (12.2–82.6) in 2017. Similarly, reported antibiotic use among sick children under 5 years of age who had cough with fast or difficult breathing symptoms alone increased 20% across LMICs, from 41.4% (7.6–80.3) in 2005 to 49.6% (14.3–84.5) in 2017. Estimates also suggest that the increase across LMICs was driven by rising use in low-income countries, where reported antibiotic use among sick children under 5 years of age rose 34% for fever symptoms alone (from 30.1% [7.3–74.6] in 2005 to 40.3% [11.3–87.3%] in 2017), and 37% for cough with fast or difficult breathing symptoms alone (from 33.9% [5.6–78.7] in 2005 to 46.4% [11.3–89.1%] in 2017).

Discussion

Overall, study findings indicate a limited but steady increase in the proportion of reported antibiotic use among sick children under 5 years of age across LMICs between 2005 and 2017. Modelled estimates further suggest that this increase was largely driven by low-income countries, where there was a 34% relative increase in reported antibiotic use for sick children under 5 years of age during the study period. Nevertheless, low-income countries (particularly in Africa and South-East Asia) continued to have the lowest reported antibiotic use among sick children under 5 years of age every year between 2005 and 2017, compared with other income and regional groups. However, results from our investigation should be interpreted with caution because of wide and overlapping UIs.

We found that, on average, around four in ten sick children under the age of 5 years across LMICs were reported to receive antibiotics to treat their condition in 2017. The highest reported antibiotic use for sick children

under 5 years was found in upper-middle-income countries as well as LMICs in the Europe and Western Pacific regions, where antibiotic use was approximately twice as high as in low-income countries and LMICs in Africa and South-East Asia.

Our findings add to existing evidence on childhood antibiotic exposure in LMICs,¹¹ although results cannot be directly compared because of differences in methodology and range of countries covered. Furthermore, whereas our study was based on household surveys, the earlier analysis was focused on children presenting to health facilities. We note, however, that the 36·8–43·1% antibiotic use seen in our study between 2005 and 2017 is lower than the average of 62·7% in the previous analysis.¹¹ Although this difference in results could simply be due to differences between the studies as outlined, it could also reflect that the proportion of antibiotic use in the community is on the average, lower than that seen at health facilities. This is not unexpected, as many episodes of illness in the community go untreated, and only a fraction (often perceived as more serious) end up presenting to a health facility and hence are more likely to receive antibiotics.

Since we do not know the underlying aetiologies of reported symptoms, we cannot draw conclusions about antibiotic misuse or overuse based on our results. Yet it is well recognised that millions of people do not have access to antibiotics and other life-saving medicines in LMICs, particularly in low-income countries and LMICs in Africa and South-East Asia.⁴ These are the same income groups and regions where our results also showed the lowest reported antibiotic use for sick children under 5 years of age. Our findings could therefore potentially reinforce evidence that access issues remain in these poorest settings where health systems are typically weakest.⁴

It has been increasingly recognised that the access-excess divide in antibiotic use is more complicated than simply between rich and poor countries,²¹ and there may be important socioeconomic or other differences in antibiotic use within LMICs that delineate an access-excess divide.^{4,21} For example, it is notable that in our analysis approximately a third of children under 5 years of age with diarrhoea alone received antibiotics, despite their lack of indication for most diarrhoeal infections.²² This suggests probable excess use of antibiotics for childhood diarrhoeal conditions in LMICs, which merits further investigation. Similarly, we found higher reported antibiotic use for sick children under 5 years of age in LMICs than recent aetiology studies would suggest is warranted,^{23–25} particularly in upper-middle-income countries. In low-income and lower-middle-income countries where weak health systems and inadequate diagnostic capacity are commonplace, WHO Integrated Management of Childhood Illness guidelines are designed to maximise sensitivity at the expense of specificity so that more children than necessary are likely to receive antibiotics.²⁶ Qualitative studies further

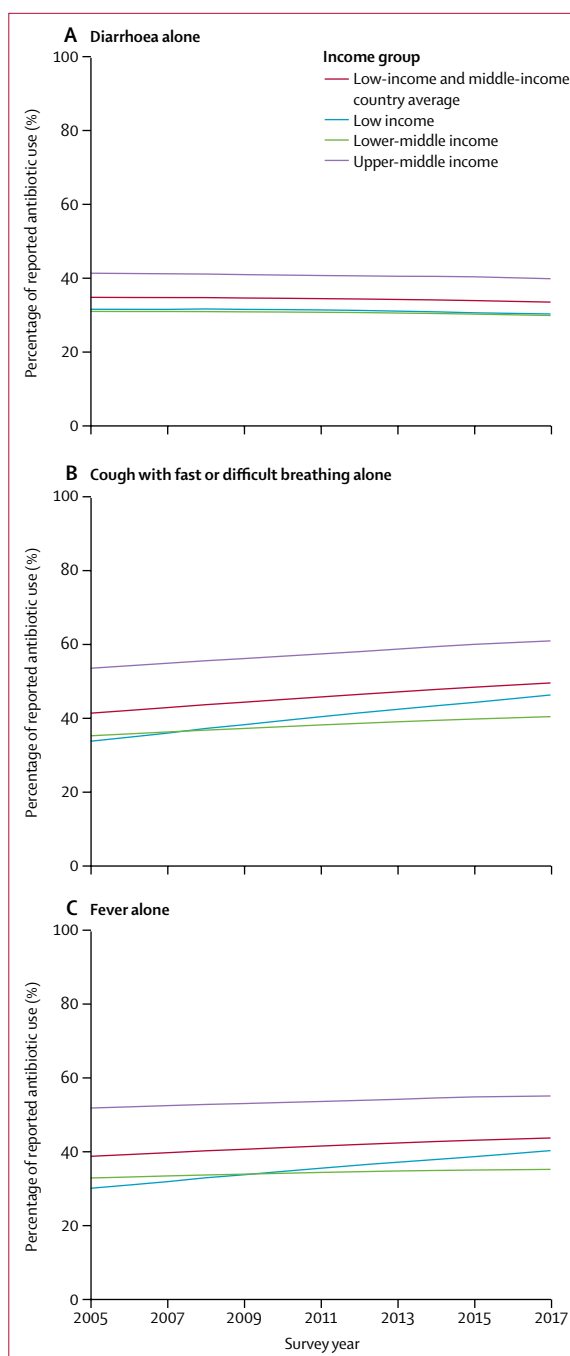


Figure 5: Trends in reported antibiotic use among sick children under 5 years of age with illness symptoms across LMICs in 2005–17 by reported symptom complaint

LMICs=low-income and middle-income countries.

suggest that health workers and caregivers are understandably prone to over-treating sick children in settings with weak health systems, inadequate diagnostics, and higher burdens of infectious diseases, where they fear missing a life-threatening diagnosis or where children may not return if symptoms worsen.²⁷ Additionally, in the

poorest settings, the first source of care often visited for sick children is typically a private drug shop where inappropriate dispensing of antibiotics is prevalent.²⁸ Indeed, current misdirected antibiotic treatment practices and poor quality care for sick children will likely continue in resource-poor settings without intensified efforts to extend the reach and quality of formal health systems.

Our results are consistent with findings from previous assessments of global antibiotic consumption, that primarily relied on pharmaceutical sales data to estimate daily antibiotic doses consumed per capita.⁵⁻⁷ These studies found increasing global antibiotic consumption during the study periods, that was attributed to rising consumption in LMICs. The increases in consumption in LMICs have been attributed to per capita GDP growth rates,⁶ but could potentially also reflect improvements in access to antibiotics in LMICs through integrated community case management interventions,^{28,29} or other initiatives to extend the reach and quality of health services. In one study, increases in antibiotic consumption across LMICs were attributed largely to Brazil, Russia, India, China, and South Africa.⁷ Of these, only India was included in our analysis, and our study incorporated data from a substantially expanded set of low-income and lower-middle income countries that were markedly under-represented in previous global assessments. This represents an important contribution to the evidence base on antibiotic use patterns from the poorest countries. Future analyses should use these same national surveys to further examine socioeconomic and demographic differences in antibiotic use for sick children under 5 years of age within LMICs, which has previously not been possible given the primary reliance on pharmaceutical sales data in global antibiotic consumption assessments to date.

Finally, assessments of antibiotic consumption and usage based on pharmaceutical sales data or national surveys should be viewed as complementary efforts to longer-term initiatives that aim to strengthen routine systems for monitoring antimicrobial consumption and resistance patterns in LMICs. To this end, in 2015 the Global Antimicrobial Resistance Surveillance System³⁰ was specifically developed to monitor resistance patterns, and antimicrobial consumption data have been recently incorporated into the system for improved coordination in these data collection mechanisms. WHO has also initiated a global surveillance system for monitoring antimicrobial consumption in 20 countries, including capacity building in 57 LMICs to develop standardised national antimicrobial consumption surveillance systems.³¹ Recent investments in these efforts hold promise to further strengthen surveillance of antimicrobial consumption and resistance in LMICs, which is crucial for filling major evidence gaps in this priority global health area.

Important data limitations in this study should be highlighted. First, Demographic and Health Surveys and Multiple Indicator Cluster Surveys do not typically

provide information on antibiotic type, dosage, or completion of the treatment course. Second, the appropriateness of the antibiotic provided during the illness is not known, since the underlying aetiologies of reported symptoms are not reported. Third, the outcome measure is based on maternal reports of symptoms and treatments given to the reportedly sick child, which might be affected by recall bias in either direction such that they may not correctly report or fully understand the types of medicines provided to the child with these symptoms. A recent validation study found that antibiotic provision for pneumonia was correctly recalled by 66% of 950 caregivers in Pakistan and Bangladesh using a similar interview format. This increased to 81% of 589 caregivers in Bangladesh, and 72% of 361 caregivers in Pakistan with the aid of drug charts.³² Additionally, to reduce such recall bias, Demographic and Health Survey and Multiple Indicator Cluster survey interview teams are trained to encourage caregivers to report trade names, or show the packets of the medicines provided to sick children, and each team includes a nurse or other medically trained professional to appropriately categorise the medications. Fourth, survey data were not available for all countries and years, and modelling of the outcome was required to fill data gaps for country-years with missing values. These modelled estimates are associated with wide UIs that complicate interpretation of results. This is particularly problematic for country groupings where there is a severe paucity of national survey data, such as upper-middle-income countries or European LMICs.

Based on 132 Demographic and Health Surveys and Multiple Indicator Cluster Surveys that took place in 73 LMICs between 2005–17, we found a limited but steady increase in reported antibiotic use among sick children under 5 years of age in LMICs. However, results should be interpreted with caution because of wide and overlapping UIs. Our modelled estimates further suggest that this increase across LMICs was mainly driven by low-income countries, where reported antibiotic use for sick children under 5 years of age increased 34% from 2005 to 2017. Nevertheless, low-income countries, particularly African and South-East Asia LMICs, continued to have the lowest antibiotic use for sick children under 5 years in every year between 2005 and 2017 compared with other income and regional groupings. Our investigation expands the evidence base on antibiotic use patterns from LMICs where surveillance of antibiotic consumption and resistance has been prioritised in recent years. Strengthened surveillance systems are crucial in settings that are at particular risk of high rates of antibiotic resistance development and spread.

Contributors

GA-B, LH-A, and EWJ designed and conceptualised the study. GA-B, LH-A, and EWJ compiled, prepared, and analysed data. GA-B, LH-A, FEK, SS, AM, and EWJ contributed to interpretation of findings. GA-B and EWJ wrote the first draft of the paper. GA-B, LH-A, FEK, SS, AM, and EWJ reviewed, revised, and contributed to writing the paper. All authors read and approved the final manuscript.

Declaration of interests

We declare no competing interests.

Data sharing

The data that support the findings of this study are publicly available from the Demographic and Health Surveys Program at <https://dhsprogram.com/>.

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