Consumption of oral antibiotic formulations for young children according to the WHO Access, Watch, Reserve (AWaRe) antibiotic groups: an analysis of sales data from 70 middle-income and high-income countries

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Summary

Background The 2017 WHO Model List of Essential Medicines for Children (EMLc) groups antibiotics as Access, Watch, or Reserve, based on recommendations of their use as first-choice and second-choice empirical treatment for the most common infections. This grouping provides an opportunity to review country-level antibiotic consumption and a potential for stewardship. Therefore, we aimed to review 2015 levels of oral antibiotic consumption by young children globally.

Methods We analysed wholesale antibiotic sales in 70 middle-income and high-income countries in 2015. We identified oral antibiotic formulations appropriate for use in young children (defined as child-appropriate formulations [CAFs]) using wholesale data from the IQVIA-Multinational Integrated Data Analysis System database, and we estimated 2015 antibiotic consumption in reference to the 2017 WHO EMLc Access, Watch, Reserve (AWaRe) antibiotic groups. We used three metrics for assessment of intra-country patterns: access percentage, defined as the number of CAF standard units of Access antibiotics divided by the total number of CAF standard units; amoxicillin index, defined as the number of amoxicillin CAF standard units divided by the total number of CAF standard units; and access-to-watch index, defined as the ratio of Access-to-Watch CAF standard units.

Findings The overall median volume of CAF antibiotic standard units sold in 2015 per country was 74·5 million (IQR 12·4–210·7 million). The median access percentage among the 70 countries was 76·3% (IQR 62·6–84·2). The amoxicillin index was low (median 30·7%, IQR 14·3–47·3). The median access-to-watch index was 6·0 (IQR 3·1–9·8). CAF antibiotic consumption patterns were highly variable between the 70 countries, without a clear difference between high-income and middle-income countries.

Interpretation Antibiotics in the Access group have a key role in treating young children globally. A simple combination of metrics based on the AWaRe groups can be informative on individual countries' patterns of antibiotic consumption and stewardship opportunities. These metrics could support countries in the development of programmes to improve access to core Access antibiotics, particularly amoxicillin.

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Introduction

Increasing rates of antimicrobial resistance are a threat to global child health. The Sustainable Development Goals for child mortality due to pneumonia and sepsis are currently not predicted to be achieved.[1,2] Ensuring appropriate access to antibiotics while avoiding excess use, especially of unnecessarily broad-spectrum agents, is a major challenge in all settings, but particularly so in lower-income and middle-income countries.[3,4] About 90% of all antibiotics are used in the community, and this setting is potentially where the largest effect for antibiotic access and stewardship could be achieved.[5] However, the optimal approach to monitoring antibiotic use in the community remains unclear, especially when detailed data for indication are absent.[6]

Child-appropriate formulations (CAFs) can be defined as oral liquid formulations and oral solid formulations that are primarily dispersed or become liquid upon swallowing.[7] In antibiotic sales or high-level aggregate dispensing data, the volume of CAFs is likely to be directly linked to antibiotic drug use among young children, mostly those younger than 5 years, who find swallowing solid formulations challenging.[8,9] Manipulation, such as crushing, of formulations suitable for adults is not recommended because of increased dosing variability and issues around stability.[10] Children in hospital treated with antibiotics receive parenteral treatment in 79% of cases and neonates treated with antibiotics receive parenteral treatment in 98% of cases.[11] Given that hospital consumption of antibiotics accounts for 10% or less of the

Research in context

Evidence before this study

Reported data for patterns of community antibiotic use among children are scarce, and much of it is focused on specific databases in high-income countries. We therefore searched MEDLINE using the following search strategy: "("antibacterial" OR "antibiotic") AND ("drug utilization" OR "practice patterns") AND (date limit 2010 to current)" without any language restrictions to identify reports of antibiotic prescribing patterns in paediatric ambulatory care. The search was last done on Feb 4, 2018. Studies of antibiotic prescribing only in specific indications, such as community-acquired pneumonia, were excluded. Relevant publications from several high-income countries (Canada, Denmark, France, Germany, Greece, Ireland, Italy, Latvia, Netherlands, Norway, Serbia, Spain, South Korea, UK, and USA) were identified; however, only a few from low-income or middle-income countries (Bangladesh, Brazil, Indonesia, Madagascar, Nigeria, Senegal, and pooled data from The Gambia, Ghana, Kenya, Nigeria, and Uganda) were available. No unifying approach in presenting prescribing patterns could be identified across these studies, making studies difficult to compare. Published data confirm, however, that antibiotic use is highest, and generally at least double that of older children, in children 5 years or younger. When reported, respiratory tract infections, including otitis media and pharyngitis, accounted for more than 60% of antibiotic prescriptions for young children. In line with this finding, some studies identified very high percentages of amoxicillin use of 50% or more in children aged 5 years or younger.

Added value of this study

We first defined child-appropriate oral formulations (CAFs) and then analysed wholesale pharmacy data from a global database to describe global patterns of antibiotic use among young children at the country level. We described the relative use of CAF antibiotics by Access, Watch, Reserve (AWaRe) grouping, including the ratio of Access-to-Watch group use (access-to-watch index) and the percentage of total prescribing accounted for by amoxicillin (amoxicillin index). Joint interpretation of these three metrics will help to identify broad areas for national antibiotic stewardship and guideline development, even when information about indication is not available. All three metrics should be interpreted together to obtain a rounded picture of national patterns of antibiotic use. A first analysis of global patterns of CAF antibiotic use shows that very high access percentages are noted in some high-income and middle-income countries; the percentage of use of antibiotics unclassified under the grouping can be considerable and might be a challenge for interpreting patterns; and the percentage of use accounted for by amoxicillin is highly variable even in countries with high access percentages.

Implications of all the available evidence

High access percentages are achieved across countries with highly variable health-care systems and income classification. Reviewing national access percentages and aiming to promote Access antibiotic use could be the first step for states wanting to engage in national antibiotic stewardship. Use of unclassified antibiotics should be reviewed and reduced, or reclassification into the AWaRe groups considered at national level. The access-to-watch index can be used to ensure that the use of Watch relative to Access antibiotics is minimised, and is especially useful when there is residual use of unclassified antibiotics. For children, countries should strongly promote the use of amoxicillin for most common antibiotic treatment indications encountered in community practice.

total use of antibiotics, and in light of low use of oral medications among inpatients, use of CAFs can be assumed to be broadly representative of community antibiotic use in this age group.

The 2017 revision of the WHO Model List of Essential Medicines for Children (EMLc) attempts to mirror the pressure on health-care systems and clinicians to conserve antibiotics by classifying antibiotics into three groups: Access, Watch, or Reserve.[12] Access antibiotics are to be used as first-line or second-line treatments for key infections, and high-quality formulations of these antibiotics should be widely available at low cost. Watch antibiotics are considered to have a higher potential for selecting antibiotic resistance. Reserve antibiotics should be considered antibiotics of last resort, to be used under specialist guidance and with specific monitoring. The explicit recommendation by WHO is that this new categorisation should also be used to inform antibiotic stewardship at a national and global level.[13]

A comprehensive list of common infection syndromes was generated and included in the 2017 EMLc. For each of these syndromes, recommended first-line and second-line antibiotics were defined and included in the Access list. The EMLc includes 17 core Access antibiotics (ie, those that are always defined as Access rather than Access-Watch) and nine Watch antibiotics that are classified as Access only for defined indications (ie, Access-Watch antibiotics).[13,14] In a stewardship context, countries might be able to enhance the use of Access antibiotics without affecting overall access to adequate antibiotic treatment. Children are most frequently treated with antibiotics for respiratory tract infections,[15–20] with amoxicillin as the recommended first-line treatment. Therefore, we expect that amoxicillin would dominate Access antibiotic prescribing and overall antibiotic use in children. We aimed to review the current levels of use of CAFs for antibiotics globally to assess patterns of use of Access, Watch, and Reserve antibiotics.

Methods

Study design data sources

We did an analysis of 2015 wholesale antibiotic sales data from 70 middle-income and high-income countries. We used data from the IQVIA-Multinational Integrated Data Analysis System (IQVIA-MIDAS) database to describe global patterns of antibiotic use in young children. The IQVIA-MIDAS is a commercial database, which contains annual pharmacy retail sales data collected throughout the supply chain. These data include information about the overall volume of antibiotics sold to retail and hospital pharmacies by wholesalers. Sales of generics and branded products alike are included. No information on individual prescriptions—eg, indication or age of the patient—is available.[21]

Because not all wholesalers contribute in the represented countries, adjustments are made to estimate the probable total sales volume based on knowledge of the market share of participating wholesalers.[21] The exact data collection mechanism and method of adjustment for variable country-level coverage are not publicly available, which limits an assessment of data representativeness. Consequently, between-country comparisons should be made with caution.[4] However, IQVIA-MIDAS and its predecessors have been used for evaluations of global antibiotic consumption patterns.[4,22] Previous analyses were able to document high coverage of at least 80% in most countries, with particularly strong representation of the retail sector.[22] Information about current coverage was not available.

Data for antibiotic sales (defined as products with an associated Anatomic Therapeutic Chemical code J01) from 70 countries for 2015 were considered. Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica, and Panama are reported collectively as Central America in the IQVIA-MIDAS database. The same is true for Benin, Burkina Faso, Cameroon, Côte d'Ivoire, Democratic Republic of the Congo, Gabon, Guinea, Mali, Senegal, and Togo as French west Africa. These regions were not included in our analyses. No country-level data for low-income countries are included in IQVIA-MIDAS. Therefore, only data from high-income and middle-income countries as defined by the World Bank are shown.

Antibiotic consumption was estimated on the basis of sales volume reported in standard units. Each standard unit is defined by IQVIA-MIDAS as a single tablet, capsule, ampoule, vial, or a 5 mL liquid preparation for oral consumption.[23] To identify antibiotics likely to have been prescribed and dispensed to young children, we classified all recorded oral antibiotic formulations as either child-appropriate and specifically designed for easy use in children or not. CAFs were identified by two senior paediatric specialist pharmacists and independently by YH and JAB (appendix). Parenteral antibiotic formulations were not considered because it is generally not possible to identify vials or ampoules for use in children.

Data analysis

Patterns of antibiotic consumption were described in reference to the 2017 WHO EMLc Access, Watch, Reserve (AWaRe) grouping. Because the EMLc AWaRe grouping of antibiotics excludes some antibiotics, we also included an unclassified group in addition to the Access, Watch, and Reserve groups. The unclassified group comprised antibiotics belonging to a class represented in the EMLc by only one or two specific agents (eg, narrow-spectrum penicillins of which phenoxymethylpenicillin is the only member of this group on the EMLc), antibiotic classes not represented in the EMLc (eg, second-generation cephalosporins), and fixed combinations of antibiotics excluding β-lactam plus β-lactam inhibitor combinations and co-trimoxazole (regardless of whether any or all components are included in the EMLc).

Only the core Access antibiotics were considered part of the Access group.[14] We included Access-Watch antibiotics in the Watch group, because most oral Access-Watch antibiotics are to be used as first choice treatment for a small number of indications (azithromycin for cholera; ciprofloxacin for dysentery, low-risk febrile neutropenia, or pyelonephritis).

We considered three metrics to assess intra-country patterns and to help identify broad areas of antibiotic use that would most likely benefit from stewardship efforts. We first determined the percentage of use of Access, Watch, Reserve, and unclassified antibiotics for each of the represented countries, which allowed us to evaluate the AWaRe distribution, focusing on the access percentage. These percentages were calculated for each country as the number of CAF standard units of antibiotics in each group divided by the total number of CAF standard units. We then determined the amoxicillin index. This index was calculated as previously described as the number of amoxicillin CAF standard units divided by the total number of CAF standard units.[6] Finally, we calculated the relative use of Access-to-Watch antibiotics expressed as the ratio of Access-to-Watch CAF standard units (ie, access-to-watch index).

The access percentage and access-to-watch index patterns were described relative to the rounded median of the 70 countries for which data were available. On the basis of published data suggesting that a high percentage of total antibiotic prescribing in young children is accounted for by amoxicillin, the amoxicillin index was described relative to the rounded upper quartile. We analysed all data using Stata (version 13.1).

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. 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

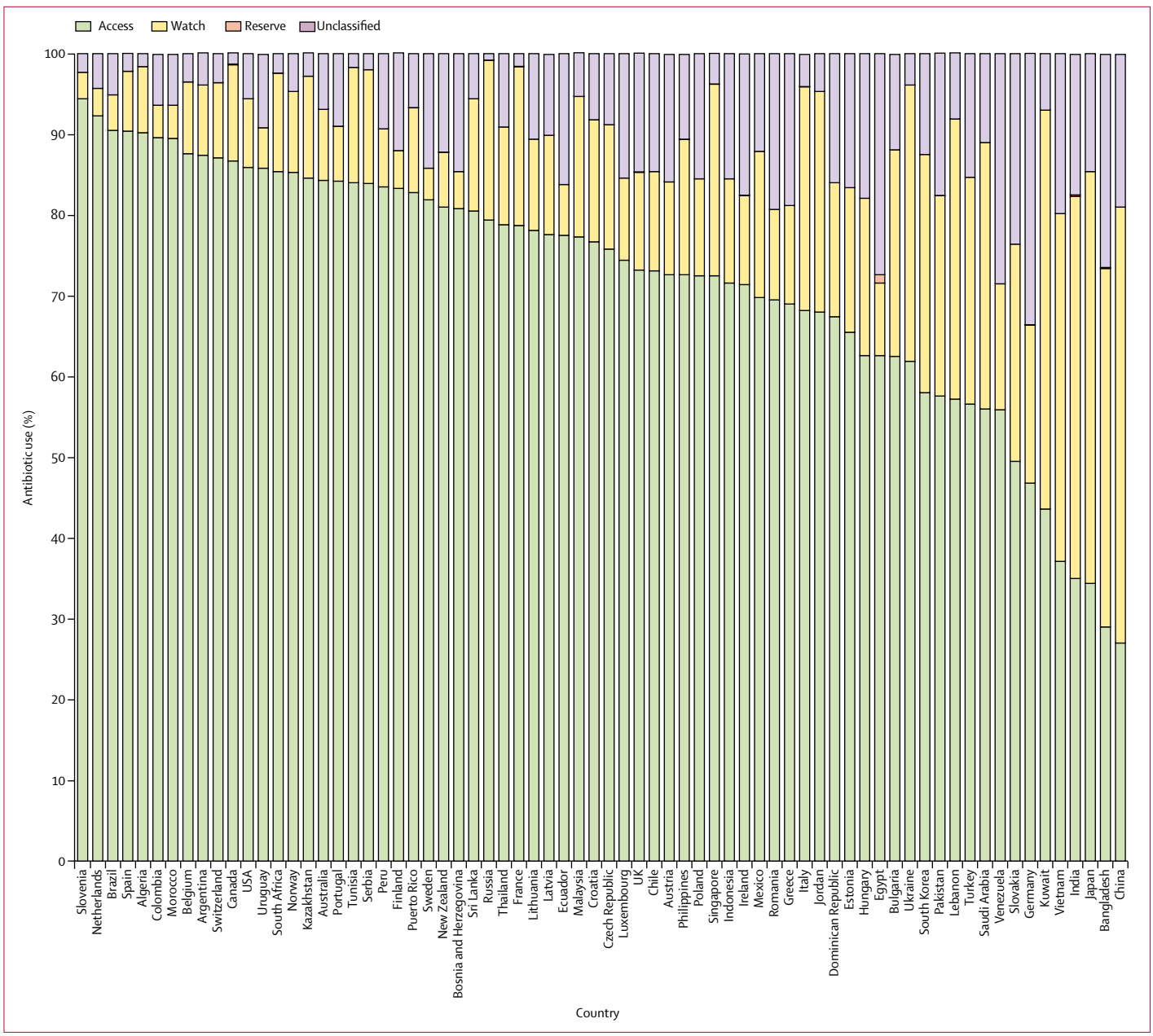

Figure 1: **Percentage antibiotic use of child-appropriate oral formulations according to WHO AWaRe grouping**
Only core Access antibiotics have been included in the Access group. AWaRe=Access, Watch, Reserve.

Results

Overall, the median volume of CAF antibiotic standard units sold in 2015 per country was 74·5 million (IQR 12·4–210·7 million). The country with the lowest volume of CAF standard units was Luxembourg (1·7 million) and the countries with the highest volume were India (4175·4 million), China (2406·7 million), and Pakistan (1472·6 million).

Much of the variation between the 70 countries in the percentage of CAF antibiotic use was accounted for by the Access and Watch groups (figure 1; appendix pp 1–2). The median Access group use was 76·3% (IQR 62·6–84·2), ranging from 94·4% (5·8 of 6·1 million standard units) of total use in Slovenia to 27·0% (649·8 of 2406·6 million standard units) in China. The median percentage of Watch antibiotic use was 12·3% (IQR 8·8–19·8). Percentage use was highest in China with 54·0% (1299·6 of 2406·6 million standard units) and lowest in Slovenia with 3·3% (0·2 of 6·1 million standard units). Reserve group use of 1% or more was only observed in

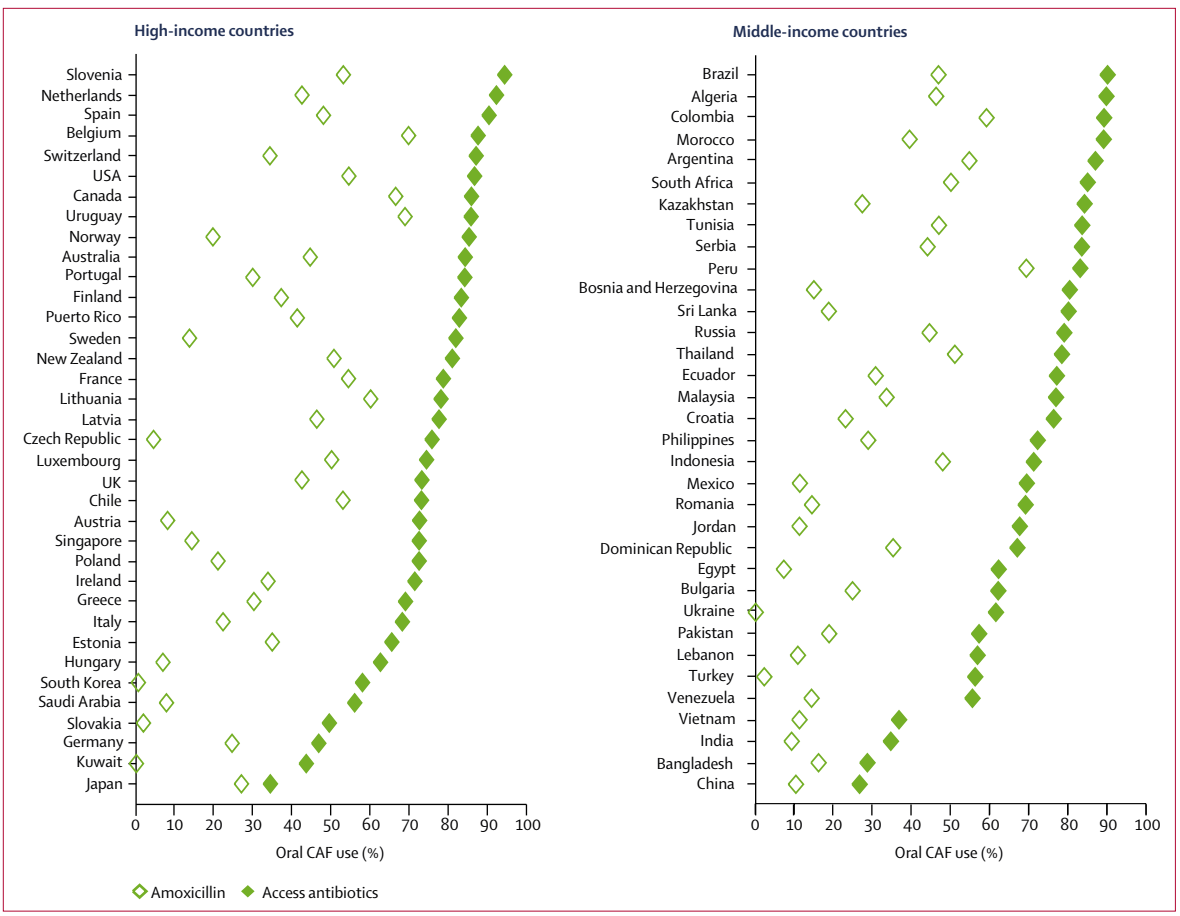

Figure 2: **Country-level amoxicillin and access percentages grouped by high-income and middle-income countries**
The amoxicillin percentage (percentage of CAF standard units of antibiotic used accounted for by amoxicillin) corresponds to the amoxicillin index. CAF=child-appropriate formulation.

Egypt with 1% (6·5 of 648·6 million standard units). In some countries, a considerable percentage of CAF antibiotics were unclassified (median 9·7%, IQR 4·7–15·5), ranging from 0·8% (2·4 of 297·6 million standard units) in Russia to 33·6% (41·0 of 121·9 million standard units) in Germany (appendix pp 1–2).

Amoxicillin use as a percentage of all CAFs was highly variable, with a median amoxicillin index of 30·7% (IQR 14·3–47·3). Amoxicillin use was highest in Belgium with an amoxicillin index of 69·8% (32·7 of 46·8 million standard units) and lowest in Kuwait with 0·1% (0·01 of 6·4 million standard units; figure 2; appendix pp 1–2). There were 11 countries with an amoxicillin index of less than 10% (Austria, Czech Republic, Egypt, Hungary, India, Kuwait, Saudi Arabia, Slovakia, South Korea, Turkey, and Ukraine), indicating that less than 10% of CAF antibiotic use was for amoxicillin in these countries.

The median access-to-watch index was 6·0 (IQR 3·1–9·8), interpretable as six standard units of CAF Access antibiotics being consumed for each unit of Watch antibiotics. The lowest access-to-watch index was in Bangladesh (0·5) and the highest in Slovenia (28·6). In general, the highest access-to-watch index was in countries with the highest proportional use of Access antibiotics; however, some countries with a high percentage of unclassified use had a high access-to-watch index despite comparatively low access percentages (eg, Luxembourg had an access-to-watch index of 7·3, access percentage of 74·4% [1·2 of 1·6 million standard units], and unclassified percentage of 15·4% [0·3 of 1·6 million standard units]; and Egypt had an access-to-watch index of 7·0, access percentage of 62·6% [406·1 of 648·6 million standard units], and unclassified percentage of 27·4% [177·7 of 648·6 million standard units; figure 3). There were six countries with an access-to-watch index of less than one (Bangladesh, China, India, Japan, Kuwait, and Vietnam), suggesting that fewer than one standard unit of Access antibiotics was consumed for each standard unit of Watch antibiotics in these countries.

28 countries had both an access percentage and access-to-watch index above the respective medians (appendix p 3). The remaining 42 countries either had an access percentage below the rounded median (≤75%) or an access-to-watch index below the rounded median (≤6).

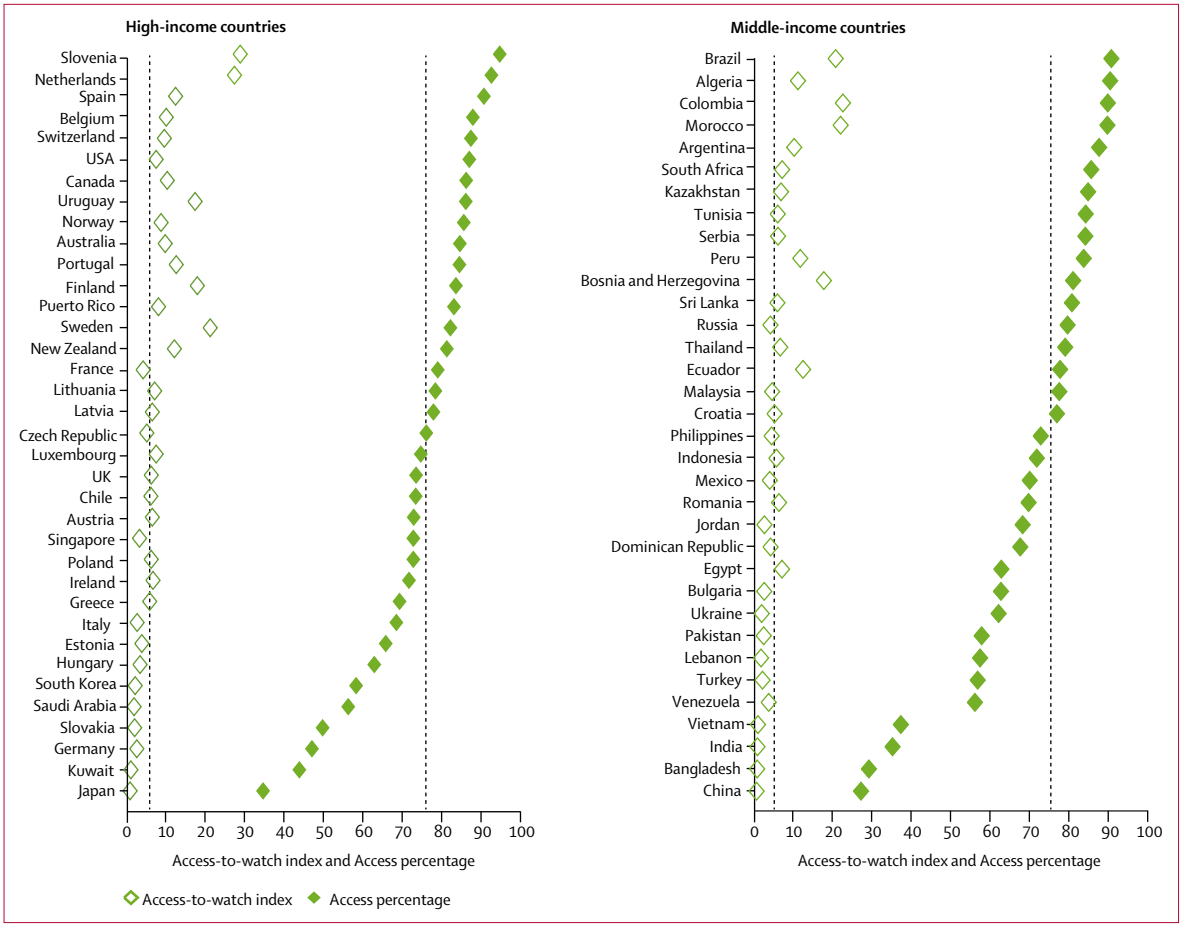

Figure 3: **Country-level access-to-watch index and access percentage (percentage of CAF standard units of antibiotic used accounted for by Access antibiotics) grouped by high-income and middle-income countries**
The two vertical lines indicate the rounded access-to-watch index median (6) and the rounded median access percentage (75%). CAF=child-appropriate formulation.

Eight countries (Croatia, Czech Republic, France, Malaysia, Russia, Serbia, Sri Lanka, and Tunisia) had an access percentage of more than 75% but an access-to-watch index of 6 or less. In these countries most of the non-Access group CAF antibiotics used were from the Watch group. Only seven countries (Austria, Egypt, Ireland, Luxembourg, Poland, Romania, and the UK) had an access percentage of 75% or less but an access-to-watch index of more than 6. In these countries, unclassified use was at least 15%.

There were only 13 countries with an access percentage of more than 75% plus an amoxicillin index of more than 50% (Argentina, Belgium, Canada, Colombia, France, Lithuania, New Zealand, Peru, Slovenia, South Africa, Thailand, USA, and Uruguay; appendix pp 1–2, 4). Two of these countries had an access-to-watch index of less than 6 (France 4·0, Thailand 5·8). In total, 29 countries had an access percentage above the median and an amoxicillin index in the upper quartile. Most of these countries (23 [79%] of 29) also had an access-to-watch index of more than 6.

The total sales volume of CAF standard units, percentage use of AWaRe and EMLc unclassified antibiotic CAFs, the amoxicillin index, and access-to-watch index for all countries are listed in the appendix.

Discussion

Our analysis confirms the key role of Access antibiotics for young children worldwide. Median percentage of Access antibiotic use was more than 76%, and the first quartile was 63% or more. Therefore, only 17 (24%) of 70 evaluated countries used less than 63% of Access antibiotics. Furthermore, we were able to verify that Access antibiotics are widely used not only in middle-income countries but also in high-income countries. Concerningly, the median percentage of Watch antibiotic use was 12% or more. The third quartile was nearly 20%, suggesting that in 17 (24%) of 70 countries Watch antibiotic use exceeded 20%. A high level of Watch group use was generally reflected in a low ratio of Access-to-Watch use—ie, the access-to-watch index. Amoxicillin use, as measured by the amoxicillin index, was variable

with amoxicillin generally accounting for a small fraction of overall prescribing.

As expected, patterns of CAF antibiotic use were highly variable across 70 countries. In line with data from hospital antibiotic use,[24,25] China and India, the two most populous countries, were among the countries with the lowest access percentage (27·0% for China and 35·0% for India), the highest watch percentage (54·0% for China and 47·3% for India), and considerable use of unclassified antibiotics (18·9% for China and 17·4% for India).

AWaRe unclassified antibiotics, including most fixed combinations of antibiotics, have been identified as being of particular interest for informing stewardship efforts.[26] The unclassified group might reflect either narrower-spectrum (β-lactamase-resistant penicillins) or broader-spectrum (second-generation cephalosporins) antibiotic use. The direction of the trend—ie, either towards narrower-spectrum or broader-spectrum antibiotic use—will be determined by country-specific patterns of unclassified group antibiotic consumption. The limitations of the AWaRe classification in this respect have been noted previously,[14] and further guidance is needed on how unclassified antibiotics can be incorporated into the classification to facilitate stewardship efforts. Our results showing that use of AWaRe unclassified antibiotics was as high as 33·6%, and that 25 countries exceeded the use of Watch antibiotics, support previous findings in India.[26] In these countries, relative use of CAF antibiotic groups can be difficult to interpret because reclassification of antibiotics under the AWaRe approach could result in shifts in access or watch percentages and the access-to-watch index.

Three aspects of community antibiotic use in young children are striking. First, young children have been identified as the highest users of antibiotics, and the use of antibiotics has been repeatedly shown to be much higher among younger children than among older children.[15,27–30] These findings provide some justification for focusing on CAFs given that establishing patterns of antibiotic use for the youngest age group would have the largest impact for antibiotic stewardship and antibiotic access.[2] Second, at least two-thirds and up to 90% of outpatient antibiotic prescriptions in young children are for respiratory tract infections.[15–20] These infections include upper respiratory tract infections, mainly otitis media and pharyngitis, in which antibiotic treatment might not be required in many cases. When antibiotics are prescribed, international guidance suggests that narrow-spectrum options, such as amoxicillin or phenoxymethylpenicillin, should be used.[13,31] Of note, data from the ambulatory sector in some lower-income and middle-income countries suggest that respiratory tract infections are a less dominant indication for antibiotic use than in most high-income countries, with undifferentiated fever being a more frequent reason for an antibiotic prescription.[17,32–34] The high use of antibiotics for patients with febrile illness in regions with endemic malaria even when rapid malaria diagnostics are available has been noted.[35] Third, and directly related to the importance of respiratory tract infections as an indication for community antibiotic prescribing in young children, a small number of specific antibiotics, all of them Access antibiotics, dominate use patterns in children. Amoxicillin alone accounts for up to 70% of overall community antibiotic use among young children in the Netherlands.[6,20] Very high amoxicillin use (making up 50% or more of all prescriptions) has also been described in Canada, France, Madagascar, Nigeria, Norway, Senegal, the USA, and the UK among children aged 5 years or younger.[6,15,17,19,27,36,37] In the USA in 2010, amoxicillin was the drug most frequently prescribed to children in the outpatient setting and accounted for more than 18 million prescriptions.[29] In Germany and the UK, narrow-spectrum oral penicillins, such as phenoxymethylpenicillin, comprise more than 10% of community antibiotic prescribing, and in Denmark these account for more than a third of all prescriptions in this age group.[6,18,28] By contrast, low amoxicillin use, often less than 10%, has been observed in Greece, Italy, and South Korea.[16,27] In these countries, other Access antibiotics—eg, amoxicillin-clavulanic acid—might be preferred.

Our analysis has several caveats. IQVIA-MIDAS provides estimates based on proprietary algorithms. For this reason, IQVIA-MIDAS data could potentially result in underestimation or overestimation of antibiotic sales, and this effect could differ by country. Furthermore, extrapolation from antibiotic sales to antibiotic consumption might lead to overestimation of antibiotic consumption if not all standard units sold are taken by the child.

Basing our analysis on standard units is unusual. The adoption of antibiotic dose units as a measure of antibiotic use might be simple to implement and generate easily interpretable data, especially in paediatrics, in which defined daily doses are not easily applicable.[38] An advantage of reporting antibiotic use in this way would be that a conversion into defined daily doses would be possible from the combined information about dispensed packs, pack-sizes, and standard units. However, reporting in standard units can be problematic when dosing regimens and treatment durations are highly variable between countries and between indications. Analyses would be biased towards higher Access group use, for example, if Access antibiotics are consistently administered for longer periods or dosed more frequently than Watch antibiotics. Moderate acuity infections treated with oral antibiotics are unlikely to require prolonged treatment or high-frequency dosing regimens.

We attempted to limit our analysis to formulations that would be suitable for administration to young children. The classification of CAFs was on the basis of expert opinion and might need further evaluation. Furthermore, non-CAFs can be used for the treatment of older children or when CAFs are not available, and CAFs might on

occasion be used in other patient groups, such as older patients or those with a neurological disability. Many liquid formulations and dispersible tablets have a strength that renders them unsuitable for adult dosing, therefore reducing the likelihood of these formulations being used in other patient groups.

Although the access percentage and access-to-watch index might be transferable to analyses considering non-CAFs, whether the amoxicillin index is likely to be as relevant to assessing antibiotic consumption patterns in adults as it is in young children is unclear. Some data for antibiotic use in children and adults, however, suggest that antibiotic prescriptions for respiratory tract infections are as common among adult patients in the community as for children.[30,39]

Because of the difficulties in determining which children might be using CAFs in each country and because of the probable influence of antibiotic dosing regimens and durations, we did not standardise antibiotic use according to population as has previously been done in international comparisons.[22] Because the focus of our analysis was the identification of broad areas for stewardship intervention at the national level, we primarily evaluated the relative use of different antibiotics under the AWaRe grouping.

Although the proportional use of antibiotics according to AWaRe, the access-to-watch index, and the amoxicillin index have the benefits of being informative, intuitive, and simple to calculate, they too have specific limitations. Countries with a high percentage of use of unclassified antibiotics might consider reclassification of these drugs into the AWaRe groups, for example, on the basis of relatedness to currently listed antibiotics. However, they can already use the access-to-watch index to evaluate the general tendency towards greater use of broader-spectrum drugs. The amoxicillin index begins to address the challenge that the AWaRe grouping does not directly provide information about the spectrum of antibiotics.[14] For example, amoxicillin-clavulanic acid is classified as an Access antibiotic but has been considered broad-spectrum in a quality indicator developed for assessment of community antibiotic use in Europe.[40] However, the amoxicillin index fails to reflect high frequencies of use of even more narrow-spectrum agents (eg, phenoxymethylpenicillin), such as in some Scandinavian countries.[28]

This study is, to our knowledge, the first attempt to develop simple metrics of global child community antibiotic use based on the WHO AWaRe classification. We showed considerable global variation in the use of CAF Access and Watch antibiotics. Interpreting access percentage, access-to-watch index, and amoxicillin index together can help to identify targets for national antibiotic stewardship efforts, particularly when the percentage of AWaRe unclassified antibiotics is low. In the first instance, countries with low access percentages could identify opportunities for greater use of these antibiotics for community-based treatment of young children. Countries with moderate or high access percentages but low amoxicillin index might prefer to focus on promoting the use of amoxicillin, especially for respiratory tract infections, as recommended in the AWaRe guidance. A low access-to-watch index might indicate unnecessary use of Watch antibiotics, which could again be specifically targeted. Challenges remain in settings with high percentages of unclassified antibiotic use, which might need to be reduced or integrated into the AWaRe classification, depending on exact patterns.

Contributors

YH, MS, and JAB designed the study. ICKW extracted the data. YH and CJ cleaned the data. YH, CJ, ICKW, and JAB analysed the data and generated the figures. All authors contributed to the interpretation of the results. YH and JAB did the literature search and drafted the first version of the manuscript, which was revised by all authors. All authors contributed to the final version of the manuscript.

Declaration of interests

JAB's husband is a senior corporate counsel at Novartis International AG (Basel, Switzerland) and holds Novartis stock and stock options. All other authors declare no competing interests.

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