Improving antibiotic prescribing for children in the resource-poor setting

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Antibiotics are a critically important part of paediatric medical care in low- and middle-income countries (LMICs), where infectious diseases are the leading cause of child mortality. The World Health Organization estimates that >50% of all medicines are prescribed, dispensed or sold inappropriately and that half of all patients do not take their medicines correctly. Given the rising prevalence of antimicrobial resistance globally, inappropriate antibiotic use is of international concern, and countries struggle to implement basic policies promoting rational antibiotic use. Many barriers to rational paediatric prescribing in LMICs persist. The World Health Organization initiatives, such as 'Make medicines child size', the Model List of Essential Medicines for Children and the Model Formulary for Children, have been significant steps forward. Continued strategies to improve access to appropriate drugs and formulations, in conjunction with improved evidence-based clinical guidelines and dosing recommendations, are essential to the success of such initiatives on both a national and an international level. This paper provides an overview of these issues and considers future developments that may improve LMIC antibiotic prescribing.

Introduction

In low- and middle-income countries (LMICs), the diagnosis of serious bacterial infections usually relies on clinical judgement without the benefit of diagnostic tests available elsewhere. Rapid access to effective antibiotics plays a critical role in improving outcomes in this setting. There is a well-established association at the population level between antibiotic consumption and antimicrobial resistance (AMR) [1]. Rational antibiotic prescribing is a central component of strategies to limit the spread of AMR globally [2]. While prescribing practices have generally been well documented in high-income countries, there are limited data for LMICs. The World Health Organization (WHO) estimates that >50% of all medicines are prescribed, dispensed or sold inappropriately and that half of all patients fail to take medicines correctly [3]. Many countries do not implement basic policies to promote rational antibiotic use [4], and <40% of patients with infections are treated according to clinical guidelines [5].

Historically, simple access to effective medicines for children in LMICs has also been challenging. However, following almost universal adoption of the World Health Assembly resolution WHA 60.20 'Better Medicines for Children' and the subsequent launch of the WHO initiative 'Make medicines child size' in 2007 [6], there have been some landmark developments; these include the WHO Model List of Essential Medicines for Children (EMLc) [7] and the WHO Model Formulary (WHO MF) for Children [8].

Meanwhile, despite the consensus that AMR continues to pose a global threat, national and global responses remain inadequate. From the child health perspective, there is a lack of national and international neonatal- and paediatric-specific AMR surveillance data, which limits the development of evidence-based guidelines and the implementation of effective prevention measures. As there are very few new antibiotics in the late stages of the drug-development pipeline, it is critical to make best use of existing antibiotics to preserve their efficacy for as long as possible [2, 9]. In 2011, the WHO published a policy

Box 1

The World Health Organization's policy package to combat antimicrobial resistance (adapted from Leung *et al*. [2])

Commit to a comprehensive, financed national plan with accountability and civil society engagement
Strengthen surveillance and laboratory capacity
Ensure uninterrupted access to essential medicines of assured quality
Regulate and promote rational use of medicines, including use in animal husbandry, and ensure proper patient care
Enhance infection prevention and control
Foster innovations and research and development for new tools

package identifying key strategies required to combat AMR (summarized in Box 1).

This review summarizes the current issues relating to rational antibiotic prescribing for children in LMICs. We focus particularly on the challenges of improving antibiotic prescribing, as these remain the drugs most widely prescribed for children in this setting.

Antibiotic consumption and antimicrobial resistance

Understanding the extent of antibiotic consumption is an essential starting point for strategies aimed at improving rational antibiotic use, but quantifying antibiotic consumption in LMICs is itself challenging, particularly so in children [10]. Methods used for the study of antimicrobial consumption in adults, such as the ATC/DDD (Anatomical Therapeutic Classification/Defined Daily Dose) methodology [11], fail to reflect variation in paediatric dosing with bodyweight and surface area. The existing studies of LMIC paediatric antibiotic consumption indicate the scale of the problem. Methodological differences make comparisons difficult [10]. The Antimicrobial Resistance and Prescribing in European Children (ARPEC) study recently published initial results of a large international point prevalence survey using a standardized methodology [12]. Of the institutions from LMICs included (almost all of them teaching hospitals), the proportion of children prescribed antibiotics ranged from ~40 to 60%. The establishment of this methodology facilitates meaningful comparisons between similar institutions and geographical regions, as well as the examination of prescribing trends.

An estimated 80% of all antibiotic prescribing occurs in the community [13]. Systematic data on community antibiotic prescribing in relation to children in LMICs is very

sparse. A large WHO study of community prescribing highlighted significant variation in prescribing by type of healthcare facility and by geographical location. The study encountered significant methodological and logistical challenges in collecting data, and there were no data specifically relating to children [14]. Furthermore, it is also recognized that there is often a wide difference in the prescribing practice between individual countries/regions defined as LMICs. Exploration of these regional variations is beyond the scope of this review, because the available data are very limited to date.

World Health Organization model list of essential medicines for children

Given that the availability of medicines is known to influence rational drug consumption, an important step forward has been the development of an essential medicines list (EML). The EMLs are designed to be country specific and based on local knowledge of disease prevalence and resistance factors. However, since its development in 1975, the distinct needs of children had been largely ignored, until the EMLc was established in 2007.

The EML aims to identify the core medicines required to cover the most common clinical needs. There is a strong emphasis on the requirement for national policy decisions, with local ownership and implementation. In addition, a number of guiding principles for essential drug programmes have emerged. An explicit formulary should ensure that therapeutic choices are consistent and cost effective and should help to ensure adequate supply. This will also enable national pricing negotiations to ensure that generic medicines are supplied at market rates.

There are several issues with EMLs; for example, current evidence suggests that although 70% of WHO member nations adopt the EML concept, only 30% employ EMLs to influence reimbursements and procurements [15]. Although evidence suggests that the use of positive formulary lists reduces prescription rates in the short term, there is a lack of data regarding their long-term effects [16]. Strategies such as limiting branded products to one or two per therapeutic class have yet to be rolled out internationally. Denmark follows this policy, managing 4900 branded drugs compared with 10 000 in the UK and 23 000 in Germany [16].

Cost, accessibility and availability

Medicine budgets pose a high economic burden on households and health systems, accounting for 60–90% of household expenditure and 25–65% of public and private expenditure in LMICs [17]. Correct access to essential medicines would potentially save up to 10.5 million lives

per year [18]. The World Trade Organization Declaration on the Trade Related Aspects of International Property Rights (TRIPS) agreement (the Doha agreement, 2001) made it possible for countries to maintain medicines at affordable levels and thus protect public health. However, implementing these rights is problematic due to complex tariffs and health service priorities.

Up to 90% of the population in LMICs purchase medicines through out-of-pocket payments, making medicines the largest family expenditure item after food. As a result, medicines are unaffordable for large sections of the global population [19]. Financial pressures often mean that patients may purchase medicines on a daily basis, so courses of treatment are frequently not completed or not even started at all. Additionally, patients may store antibiotics from uncompleted courses, well beyond the expiry date, and later take them for self-diagnosed conditions or give them to family members and friends [20, 21]. In one study, 60% of Chinese parents had administered unprescribed antibiotics to their children [22]. This has important implications for antimicrobial resistance and needs to be considered by all practitioners. The overuse of cheap, broad-spectrum antibiotics in addition to poverty and overcrowding will continue to foster antimicrobial resistance in this setting.

In 2001, a resolution endorsed by WHO Member States called for the development of a standardized method for measuring medicine prices, which resulted in the launch of the WHO/Health Action International (HAI) Project on Medicine Prices and Availability [23]. The project aims to contribute to target 17 of the Millennium Development Goals: 'in cooperation with pharmaceutical companies, [to] provide access to affordable, essential drugs in developing countries'. The WHO/HAI methodology aimed to sample a list of 30 medicines deemed essential to treat a range of common conditions (acute and chronic) that cause substantial mortality and morbidity. Of the antibiotics included in this survey, ciprofloxacin was identified in 96% of surveyed countries and amoxicillin, ceftriaxone and cotrimoxazole in 89%. The availability of these antibiotics varied by drug and by region. Generic brands were poorly available in the public *vs.* private sector in low-income countries (36.1% in low-income *vs.* 44.3% in low-middle-income countries and 76.3% in the private sector). At the same time, the median price range for generics in the public sector was 1.1 times the international reference pricing, with African prices averaging 34–44% more than international reference prices [23].

A study on key medicines for children included in national EMLs and treatment guidelines, which also assessed the availability of these medicines in 14 countries in central Africa, found availability to be poor [24]. Only three countries had >50% of key paediatric medicines available from central medical stores at the time of the survey. Private pharmacies tended to have more medicines in stock than primary healthcare clinics. Additionally, pae-diatric formulations are usually more expensive than the adult equivalents, which leads to inappropriate or unsafe use of adult dosage forms [25]. This would appear to suggest that enforcing low pricing would have a beneficial effect on availability and accessibility. However, caution is essential as, paradoxically, reducing the price may provide a disincentive to stock low-priced generics at the point of purchase in favour of higher-priced branded products [23].

For those fortunate enough financially to access antibiotics, there are further obstacles. Two-thirds of antibiotics are sold over the counter, without written prescriptions [26]. Consumers can therefore purchase antibiotics for self-diagnosed problems without any medical consultation. In many settings, oversupply in an alternative marketplace further complicates the supply chain. Easily available medicines can artificially inflate consumer demand and, consequently, drug availability and pricing. These factors affect the ability of healthcare facilities to maintain stocks of essential medicines and of governments to plan healthcare expenditure. Where antibiotics are freely available, alternative (nonmedical) sellers are often the first point of call [27]. The inadequate regulation of antimicrobial supplies has important consequences for AMR, especially in LMICs where antibiotic choices are often limited. Selective pressure control strategies, such as antimicrobial cycling or the banning of monotherapy of partner drugs when used in combination therapy, depend on compliance with drug-use regulations. Overuse of antibiotics needs to be tackled through a combination of increased public awareness, training of pharmacists, legislation and adequate enforcement and monitoring of antimicrobial use and resistance.

Counterfeit medicines

Control of the quality of antimicrobial agents is vital for the delivery of effective therapy. Lower-than-stated doses in antibiotics can result in selection of drug-resistant strains as well as therapeutic failure. Counterfeit drugs have been estimated to account for 6–20% of all drug sales and are most commonly antibiotics [28]. In a systematic review of the availability of counterfeit and substandard antibiotics in LMICs, the median prevalence was 28.5%, with inadequate amounts of active ingredients found in 93% of studies [29]. Counterfeit medications (which also include expired drugs accessible to patients) represent only one class of substandard medications. Other products are inadvertently manufactured at substandard quality or rendered partly or totally inactive due to improper storage. Many antibiotics are heat and moisture labile and therefore liable to deteriorate in ambient tropical conditions [30]. Appropriate storage is expensive and requires training; in some cases, reformulating preparations specifically for tropical countries is theoretically desirable [31]. To our

knowledge, studies assessing the link between antibiotic quality and AMR have not been documented, and this issue deserves further investigation.

Evidence-based prescribing guidelines – choice of drug

The choice of an appropriate antibacterial agent, dose and optimal duration of therapy depends on a number of variables, including the site of infection, host factors, bioavailability and palatability of the medication, local resistance patterns and, importantly, knowledge of the infectious agent. In paediatric practice, especially in LMICs, diagnoses of infectious syndromes are often based solely upon symptoms and signs. Clinical specimens to identify causative agents are not, or cannot, be practicably obtained for many infections. Clinicians diagnose and treat syndromes often without knowledge of whether the causative organism is bacterial. This makes the decision of whether to treat and with which antibiotic challenging, and probably contributes to the heterogeneity of results from clinical trials and guidelines.

Standard treatment protocols have been developed to aid clinical decision making and have been shown to improve rational prescribing [32]. The WHO Drug Action Programme 'Guide to Good Prescribing' aims to enhance clinician education by providing a framework that promotes an evidence-based approach to prescribing [33]. The goal is to use antibiotics with proven efficacy and safety data, with consideration of the rationale behind the choice of drug, its cost and its pharmacokinetic properties. In order to study, monitor and assess prescribing practices uniformly, the WHO has created a protocol based on recommendations by Laing et al. [4]. In a study of Gambian prescribing practices using this protocol and a global review of the literature, Risk et al. [34] highlighted extensive variations in antibiotic prescribing, with substantial overprescription of antibiotics for common childhood illnesses. Their review highlighted the low number of drugs prescribed according to EML in Asia (38.9% in India and 56.5% in Nepal) compared with Tanzania (93.1%), Sudan (73.5%) and Gambia (95%); >50% of childhood fever encounters resulted in the prescription of antibiotics [34].

The WHO Pocket Book of Hospital Care for Children offers guidance on clinical diagnosis and management of suspected severe bacterial infections in children in resource-poor settings [35]. Whilst the second edition has the useful introduction of a blank front page for local antibiotic guidelines, the generic recommendations list only eight major antibiotics (Table 1) for the treatment of all severe bacterial infections in childhood. Therefore, to avoid selective pressure, these drugs must be used rationally in conjunction with appropriate guidelines. Such protocols should ideally be evaluated in clinical trials

to determine whether efficacy can be maintained while reducing the propensity for resistance.

Appropriate dosing

Paediatric formularies and dosing recommendations

When prescribing medicines for children, it is important to consider not only what the most appropriate drug is, but also what are the right dose and duration of therapy [36]. In addition to accessing the medicines themselves, access to accurate, up-to-date dosing information can be difficult in LMICs. However, the advent of the WHO Model Formulary for Children mentioned above has brought significant advantages [8]. This formulary is freely accessible online and also available in paper copies. The medicines listed match up with the second EMLc [37] and provide dosing guidance as recommended by the WHO Expert Committee on the Selection and Use of Essential Medicines [8]. Other paediatric and neonatal formularies are available [38–40], some of which have specific schemes to enable access from LMICs, such as the British National Formulary for Children (BNFC), which is electronically accessible free of charge to developing nations included in the WHO's HINARI programme [38, 41].

Nevertheless, ensuring reliability of access to either online or paper versions of formularies can be challenging in LMICs. Another source of information is the dosing guidance provided within the summary of product characteristics that should be enclosed in the packaging of authentic medicinal products. Unfortunately, paediatric dosing information can be absent from the summary of product characteristics, or unclear, or lacking a high-quality evidence base [42]. This relates to the fact that unlicensed and off-label use of medicines is widespread in paediatric clinical practice throughout the world [43]. A variety of paediatric medicines initiatives have been developed to address these issues, but there is still much progress to be made [44].

Establishing the correct weight and the right dose

Assuming that access to a dosing guideline is achieved, then the recommended dose may relate to the age of the child (for age-band-based dosing), the bodyweight (weight-bands or milligram per kilogram dosing) or the body surface area. It is not always possible to know the age or bodyweight of a child in an LMIC setting, where calibrated scales are often unavailable, so pragmatic solutions are essential, particularly in emergencies. When age is known, then age-based formulae can be used for dosing, including the advanced paediatric life support (APLS) and Nelson's formulae [45]. In an emergency, alternative methods may be employed, such as the Broselow Tape, which can estimate bodyweight, tracheal tube size and

Table 1

Antibiotic generic recommendations from the World Health Organization pocket book of hospital care [35]

Condition	Drug	Dose
Dysentery	Ciprofloxacin oral	15 mg kg^{-1} BD for 3 days
	Second line: ceftriaxone IV	50–80 mg kg^{-1} daily for 3 days
Mastoiditis	Cloxacillin/flucloxacillin IV	50 mg kg^{-1} QDS for 10 days
	Second line: ceftriaxone IV	
Meningitis	**1** Ceftriaxone IV or	50 mg kg^{-1} BD for 7–10 days
	2 Cefotaxime IV or	50 mg kg^{-1} QDS for 7–10 days
	3 If no known resistance locally to chloramphenicol and β-lactams:	
	chloramphenicol IV plus	25 mg kg^{-1} QDS for 10 days
	ampicillin IV or	50 mg kg^{-1} QDS for 10 days
	chloramphenicol IV plus	
	benzylpenicillin IV	60 mg kg^{-1} (100 000 U kg^{-1}) QDS for 10 days
Osteomyelitis	Cloxacillin/flucloxacillin IV if >3 years old	50 mg kg^{-1} QDS (IV therapy for 10 days then switch to oral)
	Second line: ceftriaxone IV or clindamycin IV	
Otitis media, acute	Amoxicillin oral	40 mg kg^{-1} BD for 5 days
	Or where there is no known resistance to co-trimoxazole then give oral co-trimoxazole	4 mg kg^{-1} trimethoprim plus 20 mg kg^{-1} sulfamethoxazole BD for 5 days
Infant sepsis and meningitis	Ampicillin IV plus	50 mg kg^{-1} QDS for 7–10 days (3 weeks for meningitis)
	gentamicin IV or	5–7.5 mg kg^{-1} daily for 7–10 days (3 weeks for meningitis)
	ceftriaxone IV (also plus gentamicin, dose as on line above)	50 mg kg^{-1} daily for 7–10 days (3 weeks for meningitis)
	If staphylococcal infection is suspected, flucloxacillin IV	50 mg kg^{-1} QDS for 7–10 days (3 weeks for meningitis)
	plus gentamicin IV	5–7.5 mg kg^{-1} daily for 7–10 days (3 weeks for meningitis)
Older child sepsis	Ampicillin IV plus	50 mg kg^{-1} QDS for 7–10 days
	gentamicin IV or	7.5 mg kg^{-1} daily for 7–10 days
	ceftriaxone IV monotherapy	50 mg kg^{-1} daily for 7–10 days
	If staphylococcal infection is suspected, flucloxacillin IV	50 mg kg^{-1} QDS for 7–10 days
	plus gentamicin IV	7.5 mg kg^{-1} daily for 7–10 days
Typhoid	Ciprofloxacin oral	15 mg kg^{-1} BD for 7–10 days
	Second line: ceftriaxone IV or	80 mg kg^{-1} daily for 5–7 days
	azithromycin oral	20 mg kg^{-1} daily for 5–7 days
Urinary tract infection	Co-trimoxazole oral	10 mg kg^{-1} trimethoprim plus 40 mg kg^{-1} sulfamethoxazole BD for 5 days
	Second line: ampicillin IV plus gentamicin IV	As for sepsis
Pneumonia	Ampicillin IV plus	50 mg kg^{-1} QDS for at least 5 days
	gentamicin IV or	7.5 mg kg^{-1} daily for at least 5 days
	Second line: ceftriaxone IV	80 mg kg^{-1} daily for at least 5 days
	If staphylococcal infection is suspected, cloxacillin IV	50 mg kg^{-1} QDS for 7–10 days then switch to oral cloxacillin (3 weeks therapy in total)
	plus gentamicin IV	7.5 mg kg^{-1} daily for at least 5 days

BD, twice daily; IV, intravenous; TDS, three times daily; QDS, four times daily.

drug dosages based on body length [46]. However, the accuracy of this method in different geographical populations and different age groups has been shown to vary [47, 48]. A recent innovation is the 'Mercy TAPE', which allows improved accuracy and robustness of paediatric bodyweight estimation; the principle is based on the 'Mercy method' using surrogate anthropometric measures, namely mid-upper arm circumference for body habitus and humeral length for height [49]. In LMICs, broadening access to simple devices such as the Broselow or Mercy TAPE could facilitate significant improvements in the reliability of bodyweight-based dosing for children.

When no dosing information for children is to hand, clinicians in LMICs may want a quick calculation to convert the adult dose to an appropriate dose for children. Histori-cally, different calculations have been used for this purpose, based on age, bodyweight or body surface area; the majority of calculations are not used routinely and are summarized elsewhere [50]. Some have recommended using the 'Salisbury Rule' approach, as follows:

'Up to 30 kg, a child's drug dose may be (Wt × 2)% of adult dose, Over 30 kg, a child's drug dose may be (Wt + 30)% of adult dose',

as this can produce results that are similar to the British National Formulary/British National Formulary for Children guidelines [50].

However, the use of calculations and equations is known to increase the risk of medication errors [51]. There is also an ongoing debate regarding the best methodol-

ogy to derive paediatric dosing recommendations [52]. Nonetheless, once the dose for the child has been decided (whether using the formulary, summary of product characteristics or dose calculation), then administering this dose will depend on access to an appropriate formulation, which again is not always possible, as discussed further below.

Duration of therapy

Reducing the duration of antibiotic therapy has a number of advantages, namely increasing patient adherence, decreasing cost and minimizing antimicrobial resistance [53]. Several studies have highlighted that shorter duration of therapy may be feasible. Schrag *et al.* showed that by using a high-dose short course amoxicillin regimen, overall exposure of patients' flora to the antimicrobial agent was reduced [54]. Kerrison *et al.* demonstrated that carriage of penicillin- and co-trimoxazole-resistant pneumococci was lower in paediatric patients receiving 90 mg kg^{-1} day^{-1} of amoxicillin for 5 days than for those receiving 40 mg kg^{-1} day^{-1} for 10 days [53]. Following a multinational randomized controlled trial, Molyneux *et al.* concluded that 5 days of treatment may be sufficient for the treatment of bacterial meningitis in LMICs. However, critics have questioned whether these results are applicable globally and call for further research into therapy duration for severe bacterial infections, including meningitis [55].

Biomarkers

Novel diagnostics may aid in risk stratification of serious bacterial infections and in treatment duration decisions. In paediatrics, biomarkers such as C-reactive protein and procalcitonin are useful tools to guide commencement and cessation of antibiotic therapy [56, 57]. However, their usefulness outside of lower respiratory tract infections has yet to be evaluated fully. The development of near-patient testing technologies for distinguishing bacterial *vs.* nonbacterial infections, such as the successful use of rapid diagnostic tests (RDTs) for malaria in reducing inappropriate antimalarial use, are a potential step in the right direction [58]. However, although RDTs aim to improve care in malaria-endemic settings, a negative RDT increases antibiotic use as clinicians consider alternative causes of acute febrile illness [59]. The integration of new RDT technologies for bacterial infections should therefore be used in conjunction with rational decisions on the appropriateness of antibiotic therapy if a significant increase in antibiotic consumption is to be avoided.

Formulation issues

Access to age-appropriate formulations of medicines for children can be problematic in both developing and devel-

oped countries [60]. Indeed, one of many issues raised by EMLs is the fact that most do not contain paediatric formulations, thus hindering supply and availability [61]. Most medicines are initially developed for adults, and the majority are available only in solid-dosage forms [62]. Children at different stages of development may be unable to swallow solid-dosage forms, so liquid formulations are essential [63]. Although these issues are not restricted to antibiotics alone, the importance of formulations deserves specific consideration in this context because these are the most widely prescribed class of medicines in paediatrics. Antibiotic formulation palatability has also been identified as a major determinant of prescription decision and compliance in LMICs [64].

Age-appropriate formulations are frequently unavailable commercially, so are made locally as 'extemporaneous preparations' [65]. Duncan *et al.* recently evaluated the WHO MF for children to assess the following: (i) how many of the dosage forms listed were deemed suitable for children at the age and dose recommended; and (ii) whether the dosage forms listed were available in the UK. For this analysis, an 'age-appropriate' dosage form was defined as [abbreviated] 'a dosage form for which a child of a specified age would have the natural ability to use . . . without the product having to be altered from its original "intended" presentation, prior to administration' [66]. For neonates, infants and young children, ~30% of the preparations (dosage form and strength) in the MF were judged as age appropriate, in contrast to 80% for older children (aged 6–11 years). Surprisingly, 37% of the 340 assessed medicinal products were not commercially available in the UK, which suggests that access in LMICs may also be challenging [66].

To overcome formulation-related issues, many people (healthcare practitioners, parents or patients) have to resort to manipulating the dosage form provided by, for instance, tablet cutting/splitting/crushing/mixing/dissolving [67, 68]. However, any manipulations (even simply adding the drug to food) will usually have unknown or unpredictable effects on the pharmacokinetics and pharmacodynamics [69], with associated implications for therapeutic safety and efficacy [70]. Evidence is typically sparse in these situations, and there are few guidelines available [71, 72]. This is despite the fact that some extemporaneous formulations can potentially cause harm, including toxicity or therapeutic failure. Adverse events may result from inaccurate dose administration, occurring when, for example, the drug is unstable in liquid formulation (e.g. isoniazid [73]). However, developing age-specific formulations is expensive, so these problems persist [74]. It must also be remembered that access to multiple formulations of different strengths can potentially increase the risk of medication errors [75]. In the LMIC setting, the provision of open-access guidelines to help standardize the approach to intravenous medicines administration and extemporaneous prepara-

tions of commonly used medicines could help avoid some of these associated risks.

Conclusions

There is an urgent need to improve the quality of antibiotic prescribing throughout the world, particularly in resource-poor settings. In view of the growing threat posed by AMR, this has become a global health priority. The development of sound research methodology to capture antibiotic prescribing data from different countries has been a significant step forward, and there is now an opportunity to use global point prevalence surveys as a tool to monitor and improve prescribing internationally. Feeding back point prevalence survey results to individual institutions allows local teams to make meaningful comparisons of their prescribing practice with that of others and to identify markers of good-quality antimicrobial prescribing and strategies for improvement, including antimicrobial stewardship [76, 77]. Stewardship programmes in the paediatric context have been shown to reduce the length of hospital stay and also have pharmacoeconomic benefits [78], and implementation in LMICs is encouraged by the WHO [2]. To date, however, it has become clear that altering clinicians' prescribing habits takes time, and the importance of education and training is paramount. Rational prescribing, AMR and stewardship must be emphasized in both undergraduate and postgraduate teaching programmes, as well as in primary and secondary care. Studies in the resource-poor setting should focus on developing cheap and simple stewardship programmes. These initiatives are currently too costly, which makes any progress challenging in the current economic climate. With appropriate use of open-access resources and effective dissemination of this information, the resulting changes in antimicrobial prescribing policy and practice have the potential to bring great benefits to children around the world.

Competing Interests

All authors have completed the Unified Competing Interest form at http://www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

Appendix 1

World Health Organization Essential Medicines list of anti-infective agents 2011 [37]

Essential	Complimentary	Other agents
Amoxicillin, amoxicillin and clavulanic acid, benzathine benzylpenicillin, benzylpenicillin, cephalexin, cefazolin, ceftriaxone, cloxacillin, phenoxymethylpenicillin, azithromycin, chloramphenicol, ciprofloxacin, doxycycline, erythromycin, gentamicin, metronidazole, nitrofurantoin, co-trimoxazole, trimethoprim	Cefotaxime, ceftazidime, cilastatin, clindamycin, imipenem and vancomycin	Antituberculosis antibiotics: rifampicin, isoniazid, streptomycin, ethambutol, pyrazinamide

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