Improving antibiotic use in low-income countries: An overview of evidence on determinants

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Abstract

Inappropriate use of antibiotics has often been identified as a problem in effective health care delivery. High levels of antibiotics use, often clinically unnecessary, have led to a steady increase in drug resistance. Low-income countries, are thought to have an important role in this phenomena. Effective intervention in these practices is often difficult because of the paucity of information on determinants of antibiotic use. This review provides information from studies on the factors that influence the use of antibiotics by health providers, dispensers and community members in low-income countries. A proper understanding of these factors is a precondition to develop more effective policies and programmes to address inappropriate antibiotic use.

The review encompasses physicians’ practices, the role of drug dispensers, and the drug use practices by community members. Although useful data was identified, one of the most important findings of the review was the scarcity of research data.

If interventions into antibiotic use are to be effective, future research must focus on the socio-cultural ‘rationality’ of antibiotic usage, preferably combining quantitative and qualitative methods. Research programmes alone are unlikely to improve antibiotic use, and findings should guide the development of priority programme activities, which include a carefully designed mix of activities by governments, health delivery systems, health training institutions, professional societies, pharmaceutical companies, consumer organisations, and international organisations. Strategies that lean too heavily on professional education are unlikely to result in large-scale or long-lasting improvement.
Background

Diseases of bacterial origin are a major cause of morbidity and mortality in low-income countries. Many of these conditions can be prevented with improved personal hygiene, immunisation, and environmental sanitation, but antibacterial drugs are still the main therapy for many of them. This key role of antibiotics has led to high levels of consumption and spending for this category of drugs. Antibiotics are available to the public from a variety of sources in developing countries, including hospitals, pharmacies, licensed medicine stalls and drug-stores, roadside stalls and hawkers. They can be purchased without a prescription in most developing countries, even when this practice is illegal. This widespread availability has lead to inappropriate use by patients and health care providers, and a steady increase in drug resistance. Drug use is influenced by cultural preferences and beliefs. People draw these originally ‘foreign’ objects into their own world by clothing them with explanations and meanings from their own culture. However, despite some ethnographic accounts of antibiotic use, the factors that determine their poor usage remain badly understood. Most research documents go little further than the mere quantitative aspects of antibiotic use (for example, rates, percentages and costs). Quantitative studies rarely answer the question ‘why do people take antibiotics’. Similarly, recommendations for improvement go little beyond calling for a ‘change of attitude’, designing training activities, or implementing unspecific drug policies.

Developing countries, home to the majority of the world’s population, have an important role in the emergence of global resistance. The World Health Organization recently proposed a large number of measures to curb growing antibiotic resistance, including reducing the burden of disease and improving access to appropriate antimicrobials in the developing world.
Background (cont’d)

Antimicrobial use is determined by an interplay of knowledge, expectations and interactions of prescribers and their patients, dispensers, economic incentives, characteristics of health systems, and the regulatory environment’. Hence, reducing global antibiotic resistance is as much an issue of behavioural change, as changing health systems and developing new antibiotics.

This study has to be seen against a background of antibiotics often being perceived as ‘strong’ medicine: capable of curing almost any kind of disease. Perceived effectiveness of antibiotics can even reach magic proportions. A respondent in a Brazilian study once remarked on the popular antibiotic Ambra-Sinto® (tetracycline-HCl):

“If Ambra-Sinto® does not help, nothing will!”

This background has made it so difficult to achieve lasting change in antibiotic consumption patterns. Poor use of antibiotics not only creates resistance, but also leads to poor quality of health care.

Objectives

This study set out to review available reports in the world literature on factors that influence the use of antibiotics by prescribers, dispensers and community members in low-income countries. It analyses available information and recommends changes in health policies of a number of stakeholders. Detailed findings of the study have been described elsewhere\(^2,3\).

Methods

Reports on determinant studies of antibiotic prescribing, dispensing and use in developing countries were identified in a number of ways:

- Searches of Medline, Popline, AIDSline, and the Social Science Citation Index;
- Searches of databases of WHO (WHOLIS), WHO/PAHO (Lilacs), WHO EMRO, Scielo (Brazil), the INRUD drug use bibliography, and website of ICIUM);
- Requests in drugs-related electronic discussion forums, such as E-drug, Indices, Ip-health, and Pharmweb;
- Requests to organisations such as Health Action International, INRUD, and the Alliance for the Prudent Use of Antibiotics.
- Contacts with individuals and organisations from personal databases;
- Identification of ‘grey literature’ from lists of references.

Only original empirical research, focusing on social science research, having a minimum level of scientific adequacy, and employing some analysis of data were included.

Included were:
- Studies on metronidazole

Excluded were:
- Studies on antimalarial drugs;
- Quantitative research reports that only presented rates, percentages or indicator values, if in addition no determinants were analysed.
On the studies that were identified:

Relatively few studies were available; from some regions none at all:

<table>
<thead>
<tr>
<th>Region</th>
<th>Community</th>
<th>Prescribers</th>
<th>Dispensers</th>
<th>&gt; 1 Target</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia</td>
<td>4</td>
<td>8</td>
<td>3</td>
<td>6</td>
<td>21</td>
</tr>
<tr>
<td>Africa (Anglo)</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Africa (Franco)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Latin America</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Middle East</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>NIS</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>9</strong></td>
<td><strong>13</strong></td>
<td><strong>7</strong></td>
<td><strong>8</strong></td>
<td><strong>37</strong></td>
</tr>
</tbody>
</table>

Methods used to examine use, prescription and dispensing of antibiotics:

<table>
<thead>
<tr>
<th>More quantitative</th>
<th>More qualitative</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Structured questionnaire</td>
<td>• Semi-structured q’naire</td>
</tr>
<tr>
<td>• Patient record review</td>
<td>• Focus groups</td>
</tr>
<tr>
<td>• Case simulation</td>
<td>• Clinic observation</td>
</tr>
<tr>
<td>• Review prescribing data</td>
<td>• Pharmacy observation</td>
</tr>
<tr>
<td>• Assess drug availability</td>
<td>• Informal interviews</td>
</tr>
<tr>
<td>• Calendar recording</td>
<td>• In-depth interviews</td>
</tr>
<tr>
<td>• Self-administered q’naire</td>
<td></td>
</tr>
<tr>
<td>• Review secondary data</td>
<td></td>
</tr>
<tr>
<td>• Review sales data</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Focus of prescriber determinant studies

- Lack of correct knowledge
- Mistrust or delay in lab results
- Peer norms, modelling
- Inadequate drug supply
- Economic incentives
- Fear of clinical failure
- Meeting patient demand
- Cultural beliefs and traditions
- Marketing influences

Not addressed in any of the studies:
Prescriber’s communication skills; poor infection control practices; poor supervision practices; diagnostic uncertainty. Others?

Fear of clinical failure, expressed by a Filipino pediatrician:

“Some doctors are scared that something might happen to their patients, so they start with a very strong antibiotic, for instance a first generation of cephalosporin, while all you need is to give penicillin or co-trimoxazole (...) Many doctors do not only treat the patients but also themselves. It is in fact to treat my anxiety - if anything goes wrong, I know the patient is on antibiotics“.


Large variations in antibiotic prescribing in health centres in Ghana. Why?

<table>
<thead>
<tr>
<th>Variations in prescribing</th>
<th>Health Centre 1</th>
<th>Health Centre 2</th>
<th>Health Centre 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Number of drugs per prescription</td>
<td>3.1</td>
<td>5.1</td>
<td>9.1</td>
</tr>
<tr>
<td>Average % of patients receiving at least 1 antibiotic</td>
<td>42%</td>
<td>79%</td>
<td>98%</td>
</tr>
<tr>
<td>Average Number of antibiotics per patient</td>
<td>1.1</td>
<td>1.4</td>
<td>2.0</td>
</tr>
</tbody>
</table>

Focus of dispenser determinant studies

- Meeting customer demand
- Economic incentives
- Lack of regulation, enforcement
- Marketing influences
- Lack of correct knowledge
- Unclear role of health providers
- Modeling local physicians

Not addressed in any of the studies:
- Folk beliefs and traditions; (lack of) regulation; knowledge levels; marketing influences, dispenser’s communication skills; poor supervision practices; fear of clinical failure. Others?

Improving knowledge may not always be the solution. In the words of a Sri Lankan drug seller:

“The patient knows what he wants and we know the price!”


Applying knowledge or meeting customer demand? Dispenser in Bangladesh.

<table>
<thead>
<tr>
<th>Health complaint</th>
<th>% of pharmacies requiring a prescription</th>
<th>% of pharmacies dispensing antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute diarrhoea (adult)</td>
<td>0%</td>
<td>92%</td>
</tr>
<tr>
<td>Fever &amp; dysuria (young woman)</td>
<td>0%</td>
<td>58%</td>
</tr>
<tr>
<td>Urethral discharge (adult male)</td>
<td>33%</td>
<td>67%</td>
</tr>
</tbody>
</table>

Antibiotics dispensed
- Tetracycline, Sulphathiazol, Neomycin, Streptomycin, Furazolidon
- Pipemidic acid, Sulphathiazol, Nitrofurathion, Norfloxacin, Nalidixic acid
- Ciprofloxacin, Co-trimoxazol, Benz.Penicillin, Dicloxacillin, Spectinomycin

Large variations in antibiotic dispensing in Bolivian pharmacies (simulated clients). Why?

**Not addressed in any of the studies:**

- Lack of access to health care; marketing influences. Others?

- Added value of a medical doctor is not always clear to community members. Stated by an Indian patient:
  
  "...whenever I get these symptoms and go to a doctor, he gives me the same medicine and charges me 10 rupees. So why not just buy the medicines?"


**Focus of community determinant studies**

- Untrained sources of advice
- Folk beliefs and traditions
- Economic considerations
- Gender preferences
- Lack of appropriate knowledge

**Antibiotics were used for short periods of time in a Mexican community. Is cost the only reason?**

- Average number of days of antibiotic use:
  - 1: 50%
  - 2: 45%
  - 3: 40%
  - 4: 35%
  - 5: 30%
  - 6-10: 25%
  - >10: 20%


**Market sales of drugs in Benin.**

Photograph: Sjaak Van der Geest
Some findings

Antibiotic prescribing
Research on antibiotic prescribing often focussed on showing poor pharmaco-
therapeutic knowledge. Other potential determinants attracted much less attention.
Some of the findings on selected determinants are shown below.

• **Lack of knowledge**
  Doctors tend to use newer, more expensive agents, as opposed to cost effective,
  proven, and well-established antimicrobial agents. Studies tried to show that
  differences in prescribing rates relate to different levels of knowledge and training,
  but evidence is very limited. For example, prescribing rates for Metronidazole in
  Bangladesh were the same for ‘doctors' and ‘medical assistants'. Public and private
  sector physicians in Indonesia explained in similar rates that diarrhoea is mostly
  caused by viruses, but both groups prescribed them in over half of the cases.

• **Perceived patient demand**
  Patient demand is often believed to influence doctors' prescribing decisions. Various
  studies document physicians’ opinions that they fear losing patients if they do not
  provide what patients desire. However, one Peruvian patient simulation study
  showed that while physicians believed that mothers expect a prescription for their
  children, mothers' behaviour (passive or demanding), did not change whether
  antibiotics were prescribed, which ones, and how many.

• **Economic incentives**
  Prescribers may obtain financial incentives from the patient and the industry by
  selling a drug. Higher profit margins of expensive drugs may induce inappropriate
  practices. From rural China, it was reported that physicians prescribed more
  expensive antibiotics for insured patients, because of higher profits.

• **Fear of bad clinical outcomes**
  Potential bad clinical outcomes may lead physicians to take the "safe" route and
  prescribe one or more antibiotic. Peruvian physicians explained that mothers of
  children with diarrhoea come only once, and that antibiotics are therefore often
  prescribed at the first visit. Moreover, antibiotics are often seen as risk-free, and side
  effects thought to be minimal as long as the ‘right' antibiotic is selected.

• **Timely laboratory results**
  Access to quality laboratory services is often seen as pivotal to the correct use of
  antimicrobials. Lack of laboratory facilities (or patients’ inability to pay for lab
  services), have been blamed for over prescribing of antimicrobials. Interestingly,
  some studies show that when laboratory facilities are available, their use is not
  necessarily higher.
Some findings (cont’d)

Antibiotic dispensing
Dispenser studies often focussed on the desire to meet customer demand and economic incentives. Key in antibiotic dispensing is that community members often place more value on drugs than on a medical consultation when looking for a cure. Available studies give a picture of severely inappropriate dispensing practices. There is often little differentiation between a pharmacist, pharmacy attendants, or even street vendors of drugs. All are regarded as knowledgeable. However, a variety of people (trained and untrained, and even family members or children) may attend customers.

• Lack of knowledge
Surprisingly, levels of knowledge on correct antibiotic dispensing have been little researched. Dispensers in Nigeria argued that as most clients were living in unsanitary personal and environmental situations, antibiotics were indicated in almost all cases of disease. As dispensers are part of the communities they serve, and often have limited additional training, cultural perceptions of antibiotic use may play an important role in their practices.

• Perceived client demand
Dispensers easily defer to clients' ideas on necessary medicines. Chemists in Kenya, were willing to sell smaller doses of antibiotics when requested. Pharmacy staff in Nigeria stated that they would not refuse to meet patients' demands for antibiotics, as they feared that patients would go to another pharmacy. Few studies have sought to investigate this particular feature.

• Economic incentives
Economic incentives play an important role in dispensing drugs, including antibiotics. Quantities of antibiotics dispensed in Bolivian pharmacies varied according to clients' ability to pay. In India, pharmacies changed antibiotic prescriptions to suit the financial means of customers.

• Pressure of pharmaceutical promotion
Despite a variety of opinions on the pharmaceutical industry’s influence on drug dispensing, very little research has been carried out. Only fragmentary information is available.

• Lack of regulation and enforcement
Drugs are routinely dispensed without prescriptions. Dispensers in India stated that they simply ignored legislation on dispensing antibiotics, as they knew that enforcement was impossible. In Kenya, chemists were reported as selling antibiotics under the name ‘Septrin®’, although another antibiotic was actually provided.
Some findings (cont’d)

Community use of antibiotics
Community determinant studies tended to focus on the sources from which community members acquire antibiotics or information on them. Folk beliefs on indications and effectiveness of antibiotics were also popular research topics. Knowledge on antibiotic use, economic considerations, marketing influences, were hardly researched.

Drug store customers in the Philippines, India, Mexico and Brazil based their decisions to buy antibiotics on advice that was given by friends or relatives. Physicians’ prescribing practices appear to affect community antibiotic use. Doctors seem to ‘legitimise’ popular pharmaceuticals. Lay people’s advice is often strongly influenced by earlier medical prescriptions. A study in Brazil illustrated this as follows:

“A family from one of the villages proudly showed me their own domestic pharmacy, containing among other items, tetracycline-, chloramphenicol-, and steroid- preparations. All of the drugs had been prescribed by a physician, the mother declared with satisfaction. However, she used them completely according to her own ideas”.


People may establish their own criteria for antibiotic use, and many examples of biomedically incorrect antibiotic use have been provided in the literature. Methods used in traditional medicine may be imitated. For example, antibiotic powder may be poured into a wound, or mixed with pork fat and rubbed on lacerations.

In some local settings, a particular antibiotic may be very popular. In Brazil, Terramycin® (oxytetracycline) is widely used to treat all kinds of intestinal disturbances, and regarded as a practical intestinal stabiliser. Another tetracycline, Ambra–Sinto® (tetracycline-HCl), is regarded as the best treatment for small children who are teething.

Antibiotics are often believed to have the ability to prevent disease. For example, in the Philippines, antibiotics are commonly taken to prevent diarrhoea especially after eating foods of doubtful hygienic status. Studies in Zimbabwe and in the Philippines found that STDs are believed to be preventable by taking an antibiotic immediately after visiting a prostitute.
Implications

The few studies that could be identified often employed the more traditional quantitative data collection methods, such as structured questionnaires and reviews of patient records. More innovative social science methods, such as focus group discussions, in-depth interviews, and observation of practice were few times applied. The more powerful qualitative methods, such as community recording calendars and informal interview techniques were hardly applied. Hence, the depth of our understanding of antibiotic usage behaviours is limited. A number of cross-cutting observations can be made from the available literature:

• **Popular appropriation - antibiotics widely available to, and used by the community.** A variety of folk beliefs and traditions, and a rich process of knowledge exchange has come into use in communities in the developing world. Moreover, antibiotics are often taken to be a solution to poor life conditions. Poor access to quality care, economic considerations, and a desire for self-efficacy are driving forces.

• **Powerful image - antibiotics as the ultimate disease treatment** Antibiotics are often perceived as ‘strong’, almost magical, medicines, capable of curing or preventing many kinds of illnesses.

• **Risk perceptions** Antibiotic use is often perceived as having little risk - the “risk” of not giving an antibiotic is often felt to be much higher! Antibiotics may even be used on a “trial and error” basis for diagnosis, or given in small doses to test for “risky” side-effects.

• **Modelling antibiotic use - who models who?** Senior professionals may model juniors; doctors may model dispensers; and doctors and dispensers may model community antibiotic use. This chain seems very important, but is little explored. Influence of industry promotion on antibiotic use is poorly studied.

• **Who actually demands antibiotics?** Blame for incorrect drug use, including antibiotic use, is often laid with the patient. However, patient simulation research indicated a limited influence of “demand”, and more from physicians’ or dispensers’ fixed decision. Placebo effect may play a role in felt efficacy of antibiotic treatment!

• **The knowledge-practice gap** Current interventions focus on education and training. However, the assumption that improved knowledge will lead to improved practice remains to be proven. Physicians with adequate knowledge may nonetheless practice ‘incorrectly’.

The line between antibiotic usage by prescribers, dispensers, and their patients may be thin in developing countries. The three categories often belong to similar ethnic or geographical group(s), and they may share perceptions of health, illness, and antibiotic use. They may even copy and influence each other’s practices in using of antibiotics.
Conclusions

This review concludes that few studies examined determinants of antibiotic use in developing countries. From large areas in the world, no suitable studies of determinant were available at all. In addition, only few of them satisfied a minimum level of methodological quality. Systematically expanding our knowledge of factors that determine antibiotic use, their responsiveness to change, and cost-effective strategies, is indispensable to address poor use of antibiotics. Combining quantitative and qualitative methods, and using multiple methods to ‘triangulate’ findings, with each method looking into different aspects of a problem, is likely to yield the best information. Quantitative research can best be used to test the relative importance of various determinants, while qualitative research may be used to explore why antibiotics are used the way they are.

- **What types of research are not a current priority?**
  Quantitative or “indicator-based” studies may be of use, as they can define problems, but they do not answer the question “Why?”. Pure ethnographic studies do not lead to action, and studies must connect to intervention design.

- **What types of research can lead to better intervention programmes?**
  More focussed research on determinants preferably combining findings from the 3 target groups. Better use of qualitative methods (case simulations, FGDs, in-depth interviews), preferably using multiple methods and triangulation of data. Research in geographic areas with large research gaps (NIS, China, francophone Africa, Middle East, and Pacific region) is desirable.

- **Priority research on prescribers** would include the knowledge/practice gap; modelling practices of peers and seniors; quality of communication with patients; role of diagnostic services; and the role of supervision.

- **Priority research on dispensers** would include the correctness of knowledge; modelling roles of physicians and the pharmaceutical industry; impact of cultural notions about antibiotic use; role of customer demand; and quality of communication.

- **Priority research topics on community antibiotic use** would include the cultural notions about antibiotics and their use; knowledge exchange within community networks; and the relation between lack of access to health care and inappropriate use.

The rapid growth in antimicrobial resistance demands concerted action. Governments, public and private institutions, and medical leaders need to implement policies and programmes that encourage changes in the way antibiotics are used. Industrialised and low-income countries may have both common ground and differences with respect to determinants of antibiotic use. However, directly applying evidence of effectiveness from industrialised countries, is unlikely to be successful, as other factors may interfere.