



# Addressing Resistance To Antibiotics In Pluralistic Health Systems

Gerald Bloom, Annie Wilkinson, Göran Tomson, Phyllis Awor, Xiulan Zhang, Syed Masud Ahmed Wasif Ali Khan, Victoria Blessing, Li Wang, Xiaoyun Liang, Stefan Peterson

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There is growing international concern about the threat to public health of the emergence and spread of bacteria resistant to existing antibiotics. An effective response must invest in both the development of new drugs and measures to slow the emergence of resistance. This paper addresses the former. It focuses on low and middle-income countries with pluralistic health systems, where people obtain much of their antibiotics in unorganised markets. There is evidence that these markets have enabled people to treat many infections and reduce mortality. However, they also encourage overuse of antibiotics and behaviour likely to encourage the emergence of resistance. The paper reviews a number of strategies for improving the use of antibiotics. It concludes that effective strategies need measures to ensure easy access to antibiotics, as well as those aimed at influencing providers and users of these drugs to use them appropriately.

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## Acronyms

ACT	Artemisinin-based Combination Therapy
ESBL-E	Enterobacteriaceae
HIV	Human Immunodeficiency Virus
ICCM	Integrated Community Case Management
NGO	Non-Governmental Organisation
UK	United Kingdom
UNICEF	United Nations Children's Fund
WHO	World Health Organization

## **Abstract**

There is growing international concern about the threat to public health of the emergence and spread of bacteria resistant to existing antibiotics. An effective response must invest in both the development of new drugs and measures to slow the emergence of resistance. This paper addresses the former. It focuses on low and middle-income countries with pluralistic health systems, where people obtain much of their antibiotics in unorganised markets. There is evidence that these markets have enabled people to treat many infections and reduce mortality. However, they also encourage overuse of antibiotics and behaviour likely to encourage the emergence of resistance. The paper reviews a number of strategies for improving the use of antibiotics. It concludes that effective strategies need measures to ensure easy access to antibiotics, as well as those aimed at influencing providers and users of these drugs to use them appropriately.

Key Words:

Antibiotics, anti-microbial resistance, pluralistic health systems, drug use, regulation, global public good

# 1. A Major Global Challenge

Over the past few years it has become apparent that a growing proportion of bacteria are resistant to the available drugs. If present trends continue we could return to the situation before the discovery of antibiotics, when infectious diseases were major killers in all parts of the world.

Recent statements by senior political leaders and the World Health Organization have recognised this serious threat to global public health. Such statements are important, but concerted and sustained action is now needed to make a substantial impact. The issue extends far beyond replenishing the pipeline of new drugs. Countries will need to act on multiple fronts to contain antibiotic resistance, and international coordination will be essential. To be truly effective these efforts have to be multi-sectoral and interdisciplinary. The One Health initiative - which asserts the interdependence of animal and human health - has been proposed as a guiding framework. There are, however, considerable differences in the risks and challenges faced by governments and populations across the world.

Most action on resistance to antibiotics has taken place in countries with well-organised health systems. These countries have collected a large proportion of the world's surveillance data and they have gained a lot of experience with treating infections with resistant organisms. Problems remain but rates of antibiotic use and resistance are typically lower in such settings. This report focuses on the situation in other countries.

In many low and middle-income countries, where the majority of the world's population live, there is much less information on the topic and often less pressure on governments to act. A number of studies suggest that a large proportion of their populations are colonised with multidrug resistant bacteria (Morgan *et al.* 2011). A recent study, for example, found that 42 per cent of villagers sampled in Shandong Province, China, were carrying beta-lactamase-producing Enterobacteriaceae (ESBL-E) which causes resistance to some third generation antibiotics (Sun *et al.* 2014). This compares to a reported prevalence of 3 per cent in Sweden (Strömdahl *et al.* 2011). Widespread resistance, in rural and urban populations, is due to several factors (Okeke 2010). Where many people live in poverty, they are exposed to pathogens through poor sanitation and crowded housing, especially in urban slums. A large proportion of them will have increased susceptibility to infection because of malnutrition, chronic illness and/or infection with Human immunodeficiency virus (HIV). In a number of countries there are major problems with the quality of drugs and with inappropriate use of antibiotics, thus increasing the likelihood that resistant organisms will emerge (Morgan *et al.* 2011). The consequences of antibiotic resistance are especially damaging for the poor, who often have to choose between going without treatment and spending a lot of money on expensive second or third line drugs. In these contexts, the spread of antibiotic resistance has the potential to reverse gains made in life expectancy over the last few decades.

One important element of a strategy for addressing the problem of antibiotic resistance is to invest in the development of new drugs. This needs to be complemented by measures to slow down the emergence of resistance to existing and newly developed products. In order to be effective, these measures must also address the problems that poor people face in coping with infectious diseases. The existence of large numbers of people harbouring resistant organisms is a major threat to global public health, since dense transport networks mean that resistant genes travel widely to create a global pool of bacteria. Also, given the capacity of many companies to copy new drugs, it will be very difficult to keep them from entering these markets and, thereby, stimulating new types of resistant organisms to emerge.

This report pulls together evidence from recent review articles and a search of the literature for evidence these reviews have missed. The scope of this paper is limited to human health systems and especially to outpatient use, since most antibiotics are obtained outside hospitals (European Centre for Disease Prevention and Control 2014). It does not look at veterinary use, which accounts for a substantial proportion of total antibiotic consumption. The term 'antibiotics' covers a wide range of drugs that target an enormous variety of organisms. We employ this generic term, although the design of interventions has to be much more specific.

The Chief Medical Officer of the United Kingdom (UK) has drawn an analogy between the challenges of antibiotic resistance and those of climate change, in terms of their impact on human well-being and the scale and complexity of the problem. An effective response will involve the co-evolution of new drugs, new practices and new forms of governance for sustainable health systems.

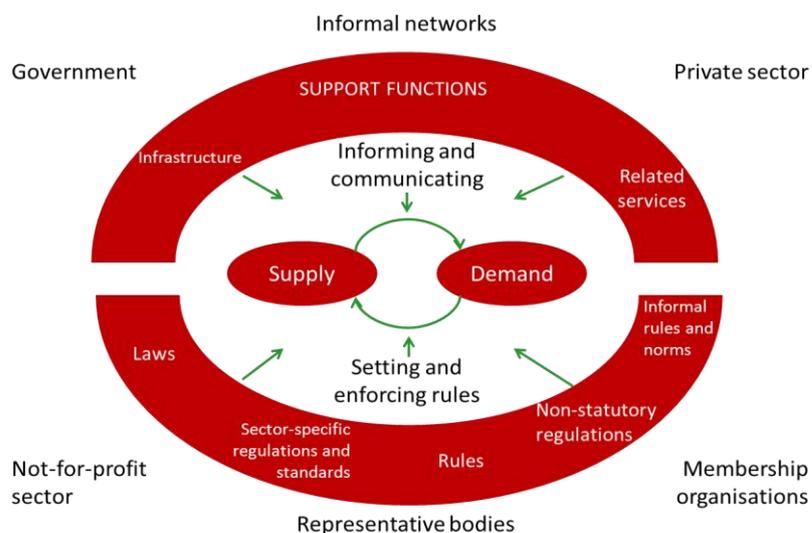
## 2. Use of Antibiotic Drugs in a Pluralistic Health System

In contrast with the situation several decades ago, it is possible to obtain antibiotic drugs almost everywhere. Some countries have achieved this by building a highly organised government health service with a network of outpatient clinics staffed by trained personnel, who work under effective supervision. In other countries a pluralistic health system has emerged, which combines government provision and health markets (Peters and Bloom 2012). In these systems government health facilities cannot meet the demand for health services and a wide variety of providers have emerged to fill the gap. These providers span a spectrum from medical specialists to informal providers, whose services often combine Western and local medical systems. The informal providers work largely outside the regulatory framework.

The evidence is patchy on how pluralistic health systems perform in ensuring appropriate use antibiotics (Heyman *et al.* 2014). In Bangladesh, for example, substantial falls in mortality from post-natal sepsis and childhood pneumonia over the past decade have been attributed to easy access to inexpensive antibiotics, often from so-called 'village doctors', based at market stalls (National Institute of Population Research and Training 2012). In the same country, a number of studies have revealed problems with sub-standard drugs, overuse of antibiotic drugs and inadequate doses of these products (Ali and Bhuiya 2012; Bhuiya 2009). These findings suggest that actions to limit access to antibiotics could have adverse consequences, and that measures are needed to improve the way these products are used and reduce unnecessary use, which can stimulate the emergence of resistance.

One option for addressing the challenge of antibiotic resistance would be to enact and enforce laws that reserve the right to prescribe antibiotics to licensed health workers. Although this could be made a long-term goal, it may not be realistic in many pluralistic health systems, where people seek treatment for common infections from drug shops and informal providers. In this circumstance, governments face a choice between denying many people access to life-saving drugs and turning a blind eye to nominally illegal practices. The alternative is to find ways to engage with these markets to improve antibiotic use. This requires new understandings of the factors that influence provider performance and of the role of government as regulator and steward of the health sector (Ahmed *et al.* 2013).

Figure 1: Conceptualising a Pluralistic Health System



Source: Adapted from Elliot *et al.* (2008)

Figure 1 presents a framework for analysing a pluralistic health system. At the centre are the users and providers of health advice, services and/or drugs. They are influenced by actors, who perform a number of functions. This influence is mediated through different types of formal and informal relationship. In this case they are also shaped by the attributes, perceived or otherwise, of antibiotics. An intervention aimed at changing antibiotic use needs to take these relationships, and the likely responses of different actors, into account. The discussion that follows elaborates on this 'user context', including the socio-technical qualities of antibiotics, the key actors who supply, prescribe or consume antibiotics, and the ways in which their practices are interdependent. Finally, the paper examines options to improve the use of antibiotics.

### **2.1. Socio-technical dimensions of antibiotics**

Antibiotics are a classic example of the successful diffusion of innovation. In terms of resistance, antibiotics are a victim of their own success; they are low cost, easy to distribute and consume, and they have demonstrated an ability to cure sickness. However their perceived value has diverged from their real value and their use is not always optimum. To understand this process, it is important to recognise the social-technical dimensions of antibiotics, particularly the way they are embedded in meanings, networks, markets and norms.

Some pervasive beliefs and meanings have been attached to antibiotics which influence how they are used (Whyte *et al.* 2002; Haak 2003). They are perceived as 'strong' medicines with a capacity to treat a range of ailments. This is not simply a result of their demonstrated disease-curing properties. It is also because they have been promoted consistently over decades of public health programming. Many of these programmes have focussed on access to drugs and even recommended mass or presumptive treatment. As such, they have cultivated practices, where antibiotics are used indiscriminately and/or pre-emptively, as opposed to in a disease-specific manner for confirmed cases. Messages from drug companies and advocacy groups have often reinforced these practices.

In some contexts, antibiotics are associated with Western medicine and modernity. As imported goods they can be regarded as high-tech and high-status. These associations can make them particularly desirable. Alternatively, antibiotics can be 'indigenised'. They have been re-interpreted into existing indigenous therapeutic systems where colours and notions of hot and cold are associated with effectiveness (Bledsoe and Goubaud 1988). Strength-building properties have been linked to their use. Their use as preventatives, which in some situations has biomedical validity, has also acquired erroneous associations; they have been used as a prophylaxis after having unprotected sex or eating contaminated food. Their protective qualities are believed to help people stay healthy and able to do arduous work.

### **2.2. Actors in pluralistic health systems**

One aspect of most pluralistic health systems is the variety of providers of health care and drugs in terms of their training, their skills and their relationship with the formal regulatory system. The private sector often includes specialised hospitals, private doctors, large and small health service non-governmental organisations (NGO) and many informal providers of health services and drugs. The latter function largely outside the health regulatory framework and account for more than half of outpatient visits in some countries (Sudhinaraset *et al.* 2013). The boundaries between public and private sectors are often porous, with government health workers accepting cash payments (official or informal), practising privately and establishing informal links with the private sector. Most antibiotics are purchased in these markets.

As well as health providers there are the producers of drugs and their representatives. Producers can be multi-national companies or local ones. Some countries, such as China and Bangladesh, have strong domestic drug industries, which include partners of large trans-national companies, local producers of

generic drugs and manufacturers of sub-standard products. These companies sell their products to the full range of health care providers, directly or through distributors. Drug regulation is often patchy.

A number of actors influence (or could influence) the use of antibiotics. They include government regulatory agencies, professional and business associations and citizens' groups at local and national levels. In many cases, their roles and responsibilities are not clearly defined. Indeed, there are an increasing number of intermediaries in health systems. The rapid spread of access to mobile phones and the internet is creating new channels for communicating directly with providers and users of antibiotics. A number of providers of information and producers of content for these expanding information channels also influence the use of antibiotic drugs. The former include government health information systems, the mass media (printed and electronic), mobile phone operators and a number of internet sites. Producers of content include NGOs, advocacy groups and commercial advertising agencies.

Finally, patients are key actors in the health system. This is especially important where antibiotics are readily available over the counter. Self-medication may be attractive because it saves time and money. The popularity of antibiotics may also be due to its 'liberating' effect in that a patient can avoid the moral judgements and instructions of therapeutic practitioners (Whyte 1988).

### **2.3. Factors influencing providers of antibiotics:**

A number of factors influence the performance of the suppliers of antibiotics. The availability of diagnostic tests is an influential conditioning factor. Knowledge of disease symptoms and appropriate treatment is also important. Some studies have documented low levels of knowledge of the appropriate use of antibiotics (Minzi and Manyilizu 2013; Kotwane *et al.* 2010), whilst others have found that many informal providers have basic knowledge about appropriate treatment of common health problems (Gautham *et al.* 2013). Over the past two decades there has been a substantial international effort to develop guidelines for treatment of sexually transmitted diseases, upper respiratory tract infections and other common health problems, when it is not possible to make a definitive diagnosis (syndromic treatment). The World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) recommend the use of integrated community case management of malaria, pneumonia and diarrhoea in children (see Box 2). These guidelines are widely available and are often included in training courses.

Knowledge, however, is not enough. Health workers often do not follow good practice guidelines. A recent study of informal providers and licensed doctors in India, for example, found similar levels of inappropriate drug use (Das *et al.* 2013). Other studies have found that training, on its own, does not bring about lasting differences in behaviour (Shah *et al.* 2011). Several factors influence this deviation from best practice.

First are payment mechanisms that link health worker income to the value of drugs they sell. Financial incentives are found at all levels. In China, for example, a large proportion of the revenue of health facilities comes from drug sales and rates of antibiotics use are extremely high (Li *et al.* 2012). Village doctors in Bangladesh do not charge consultation fees but instead make a profit on the drugs they sell (Bhuiya 2009). In such contexts, decisions about their purchase and consumption are frequently driven by financial concerns as opposed to rational therapeutic ones. Doctors and patients adjust use according to what can be afforded (Bartoloni *et al.* 1998; Dua *et al.* 1994). Poverty can drive practices which can add to antibiotic resistance. Poor patients may self-medicate in order to avoid the costs associated with a consultation with a medical professional. Some save money by not taking a full course or by using sub-standard products.

A second factor arises from the multiple, and often conflicting, sources of advice to health workers from wholesalers, advertisements and so forth. Materials that drug companies distribute often

emphasise all possible uses of the product but neglect cost-effectiveness and potential risks (Lexchin 2010). Prescribers of antibiotic drugs are linked to the producers and/or importers of these products through one or more distribution networks. The distributors of these drugs influence the people to whom they supply by providing information and advice – which cannot be considered impartial – and offering financial incentives to achieve a high volume of sales (Rahman and Agarwal 2013). In many countries, quality assurance systems are weak and a substantial proportion of antibiotic drugs are counterfeit, sub-standard or out of date (Peters and Bloom 2012).

A third factor arises from norms and engrained routines. Especially important are local experiences of disease burdens and of the most effective way to relieve symptoms rapidly. In Bangladesh and China, for example, health workers frequently treat a fever with more than one antibiotic along with steroids. In sub-Saharan Africa, a generation of doctors have been taught to presumptively treat fevers with antibiotics and anti-malarial drugs. As drug use patterns become standard practice, diverging from them carries risks for providers. There is both a reputational risk and a fear of bad clinical outcomes (Chandler *et al.* 2012). The risk of not treating and missing cases is perceived to be worse than using antibiotics which are perceived to be 'risk free'. At the community level popular choices are legitimised by doctors' previous prescribing. Studies have shown the replication of doctors' prescriptions within communities (Haak 1998) and certain drugs become well known so that users come to judge the quality of a provider by their willingness to provide these powerful drugs.

The overall picture is one of antibiotics as embedded in perceptions, complementary technologies, networks, markets, regulations, norms and infrastructures. This has important implications. For one, a systems perspective is needed. The factors outlined above are highly interdependent. Norms cross generations and formal and informal sectors and are driven by market dynamics. A recent paper by Tomson and Vlad (2014) argues that interventions to address the challenge of antibiotic resistance need to be informed by a systems perspective. This paper defines the relevant system as including suppliers and users of antibiotic drugs and the local, national and global actors, who influence them. These interdependencies are not well understood. Indeed there is evidence that they are sometimes mischaracterised. For example, qualified doctors often blame patients or the informal sector, when their practices are frequently no better. 'Patient demand' is often noted to be a major factor in influencing healthcare providers' inappropriate prescribing. However observations of clinical interactions have not always confirmed this (Paredes *et al.* 1996). Little is known about the relationships between drug companies and informal providers. The lack of clarity surrounding these interactions, including the interests and politics at work, hinders the development of strategies to contain antibiotic resistance.

For another, much of what some analysts label as irrational is actually driven by alternative rationalities, which make sense given histories and circumstances. Drug sellers act as rational economic actors, and can make relatively high profit margins on inexpensive antibiotics (Gumpert 2014). Moreover, in contexts with high disease burdens and where diagnostics are unavailable it may be rational to use antibiotics as a frontline treatment, especially when the risks of overuse are deferred or unknown. Labelling such practices as irrational can lead to blindness to the underlying conditions which influence drug use and which will influence the effectiveness of interventions.

### 3. Measures to Improve the Use of Antibiotic Drugs

In exploring strategies for improving the use of antibiotic drugs it is useful to analyse the health system as a knowledge economy, which makes the benefits of expert medical knowledge and specialised commodities, such as drugs, widely available (Bloom *et al.* 2008). An important characteristic of the health knowledge economy is the asymmetry in knowledge between experts and the people who rely on their advice. Mature health systems have created organisational arrangements that enable experts to provide advice and services while encouraging them to act in the interest of their clients. These arrangements include self-regulating professions, government involvement in financing and managing the provision of health services, the creation of specialised agencies to translate scientific knowledge into practice guidelines and a highly regulated pharmaceutical industry. In countries where these arrangements are not solidly in place, alternative strategies are needed to address the challenge of information asymmetries and ensure that people have access to reliable and trustworthy information and advice (Leonard *et al.* 2013).

*Box 1:* Components of a strategy for addressing antibiotic resistance

- Measures to enhance the capacity to make specific diagnoses through developing new low cost technologies and making them widely available
- Development of guidelines for syndromic treatment that take into account changing patterns of resistance
- Measures to ensure the quality of available drugs
- Improved access to reliable and trustworthy information by providers and users of health services
- Measures to influence the provision of antibiotic drugs by the public and private sectors through changes in incentives and regulation
- Measures to reduce the burden of infectious disease
- Research and development of new drugs and alternative therapies

Sources: Bennish and Ali Khan (2010); Laxminarayan *et al.* (2013)

Recent reports on the subject of antibiotic resistance by the Lancet Commission (Laxminarayan *et al.* 2013) and the World Health Organization (WHO 2014) have highlighted the limited amount of data on surveillance. Effective strategies for improving the use of antibiotics will include several elements. Many of those listed in Box 1 have been tested at relatively small scale, but they have not yet produced sustained and wide-ranging improvements to antibiotic use. The recognition that health systems are complex and adaptive (Paina and Peters 2012) leads to the recommendation that interventions must be systemic, with action at multiple levels (Tomson and Vlad 2014). In May 2014 the WHO released a draft global action plan on antibiotic resistance, but it remains to be seen whether effective global governance institutions can be created. National level political commitments, frameworks and institutions are also important (Stalsby and Tamhankar 2014). For example, the creation of a high-level task force to oversee national efforts contributed to Sweden's success in limiting antibiotic use (Molstad *et al.* 2008). Another level concerns health facilities and communities. Box 2 provides details of a promising approach to ensure access but not excess at the community level.

Policies on antibiotics need to make them available, whilst preserving their efficacy for other people and future generations. Users can sometimes benefit from reductions in the use of antibiotic drugs, by saving money and reducing the risk of adverse side-effects. However, there is often a conflict between immediate individual benefits and global public good. The people who benefit from easy access to drugs in informal markets are largely poor, whilst the beneficiaries of measures to reduce the risk of

antibiotic resistance come from all social classes and all geographical regions. Measures to benefit the latter should not require sacrifices by the former. Antibiotics can be viewed as a non-renewable resource (Cars *et al.* 2008) requiring exploration from the point of view of the politics of rationing in a fair way.

*Box 2: Integrated Community Case Management*

Pneumonia, diarrhoea and malaria are still major childhood killers despite being treatable. Diagnosis and management of all three are poor in many parts of the world as health facilities are not always accessible and medicines are not always available or appropriately used. The Integrated Community Case Management (ICCM) strategy was developed by UNICEF and WHO to support the delivery of effective community based care. Community health workers are trained, supplied, and supervised to identify and treat malaria with Artemisinin-based Combination Therapies (ACTs), pneumonia with oral antibiotics, and diarrhoea with oral rehydration salts and zinc. Cases are diagnosed by taking disease histories, monitoring respiratory rates and using malaria rapid diagnostic tests.

By extending the rational use of drugs to the community level the strategy has the potential to improve both access to healthcare and reduce antibiotic resistance. However because the ICCM has been developed and rolled out for use within the public health system its impact is limited in pluralistic health contexts where many people seek care from the private sector. Recognising this the MINIMAX study adapted the ICCM so that it could be used in drug shops in Uganda, including the supply of respiratory timers and subsidised pre-packaged drugs. Improvements were seen in diagnostic and treatment practice. The challenge is to take this approach to scale.

Source: Awor *et al.* 2014

A number of studies have demonstrated the lack of appropriate and effective health regulatory systems in many low and middle-income countries (Alfifi *et al.* 2005; Ensor and Weinzierl 2006; Sheik *et al.* 2012; Bloom *et al.* 2014). A narrow view of regulation views it as a government function involving administrative and bureaucratic controls. This kind of regulation plays an important role in protecting the public against incompetent medical practices and dangerous medicines. However, it has limitations in countries with weak government management and governance structures. Another view is that regulation is the outcome of a series of relationships between states, enterprises and civil society organisations (Black 2002; Smith 2004; Bourgon 2011). This decentred understanding of regulation recognises that states, on their own, cannot ensure the effective functioning of complex markets. Box 3 outlines a multi-pronged approach to health market regulation, which takes into account the different types of relationship with a regulatory aspect. It includes actions at local, national and global levels (van Zwanenberg *et al.* 2013).

A second way of understanding relationships in pluralistic health systems is as partnerships. The governments of many low and middle-income countries have managed a variety of partnerships with non-state organisations for years. For a partnership to survive each partner must believe that the benefits it derives from the effort of creating and maintaining it outweigh the potential losses from the constraints to pursuing its narrow interests. The way a partnership balances the interests of the different members reflects the governance arrangements put in place and the relative power of the different partners (Buse and Harmer 2004).

Box 3: Strategies for influencing market actors

- **Administrative and bureaucratic controls** (malpractice law, licensing and accreditation of providers and facilities and registration of products). In countries with pluralistic health systems, the formal laws are often not enforced and it is important to define clearly when governments can and should act. The experience of Nigeria (Garuba *et al.* 2009), where a government regulatory agency has substantially reduced the volume of sub-standard drugs, illustrates that governments with major governance weaknesses can act effectively to address a widely perceived problem. It is unlikely that measures to restrict access to antibiotic products would command high levels of public support.
- **Market-supply oriented approaches** (self-regulation, contracting, social franchises, incentives and subsidies). There have been many small-scale experiments with alternative approaches for altering incentives to improve performance mostly involving NGOs or social entrepreneurs. A number have been successful, but to date very few have had impact at scale on a sustainable basis. A few interventions have focused specifically on improving the use of antibiotic drugs.
- **Consumer or citizen-oriented approaches** (consumer education, a right to information by citizens, consumer rights, patient redress, citizen empowerment and liability norms). These approaches are important in reducing knowledge asymmetries and in making service providers accountable for their performance.
- **Collaboration oriented approaches** including co-production of services and regulation across key stakeholders and partnerships for transparency and accountability. There are a number of examples of partnerships with big pharma to provide access to specific drugs at an affordable price. There are fewer examples of this kind of collaboration to strengthen regulation or address a specific problems such as antibiotic resistance.

Source: Bloom *et al.* 2014

One major challenge in countries with weak management and governance structures is to involve powerful organisations in partnership arrangements, while protecting the interests of the relatively poor and powerless. For example, pharmaceutical companies could make a substantial contribution towards improving antibiotic use but there is a tension between their search for short-term profits and the longer-term benefits of ensuring they are only used when needed. This raises questions about the degree to which large companies can be made accountable to local stakeholders and the potential role of global agreements on standards of behaviour. The increasing global presence of companies from rapidly growing middle-income countries and the consequent involvement of their governments in governance arrangements is creating another level of complexity, since these important global actors are concurrently building institutions to make their own pluralistic health systems more coherent.

Governments have a key leadership role in overseeing the creation and oversight of these institutions. This may work better if other strong actors, who can express the interests of the different stakeholders, are involved. These could be strong NGOs, citizen organisations, faith based organisations, professional associations and so forth. There is limited evidence about the approaches that work well in building institutions in low and middle-income countries (Fukiyama 2004; Chang 2007). It is increasingly

accepted that a learning-by-doing approach is needed for managing change (Bloom and Wolcott 2013; Peters *et al.* 2009).

## 4. Making Progress Towards the *Sustainable* and *Just* Use of Antibiotics

Access to antibiotic treatment is highly sought after by the rich and poor in most countries. Where governments have been unable to provide this access, markets have emerged to meet this demand. In the absence of supportive institutional arrangements, undesirable practices have emerged. Measures to slow the emergence of organisms resistant to antibiotics must include interventions to increase access to the benefits of effective and appropriate antibiotic treatment, if they are to secure wide support in low and middle-income countries. A proportion of the resources invested in the global response to antibiotic resistance should be allocated for this purpose to ensure they are managed justly, as well as sustainably.

Initiatives to improve antibiotic use in pluralistic health systems will entail changes in behaviour and in the ethical norms underpinning this behaviour at local, national and global levels. It will require active participation by a variety of actors in several inter-related interventions.

- Generation of reliable surveillance data and production of treatment guidelines. This will involve building social and technical capacity to undertake surveillance of local patterns of disease and the changing resistance to antibiotics. This information can be incorporated into revised treatment guidelines. Government agencies, specialised research institutes and pharmaceutical companies can contribute.
- Provision of reliable information and guidance to providers of antibiotics. The channels for reaching providers (all categories of health worker and drug sellers) include training courses, government guidelines, marketing material by drug distributors and the mass media. The rapid increase in use of mobile phones is creating an important opportunity for making guidelines widely available to providers, including community health workers, informal village doctors and drug shops. However, it raises important issues about the need for formal or informal regulation of the information and advice provided.
- Supply of good quality antibiotics at an affordable price. This will involve identifying and removing counterfeit products and assuring the quality of products in the market through some form of regulatory partnership between government, the pharmaceutical sector and citizen groups. It will also involve keeping prices low through bulk procurement (by government, NGOs, or other agencies) and, in some cases, public subsidies. Measures to reduce rationing by price will need to be complemented by those aimed at reducing inappropriate use. Innovations in packaging full courses of appropriate combinations of drugs could also simplify treatment decisions.
- Development of new diagnostic technologies. The development of low cost diagnostic technologies will reduce the need to treat people on the basis of symptoms alone. However, measures are needed to provide wide access to these technologies and ensure their quality and accuracy. The conditions under which adherence to test results will follow are insufficiently understood.
- Testing and taking appropriate models for treating common infections to scale. The major challenge is to establish mechanisms that encourage large numbers of providers of antibiotic treatment to change their behaviour. These measures will include accreditation of providers, modification of payment mechanisms and the involvement of intermediary organisations to give technical support and monitor performance. These organisations include NGOs, faith-based organisations, social entrepreneurs and companies that provide services or distribute drugs. These

organisations are unlikely to be able to finance their activities on a commercial basis and will need support from governments and other funders of social activities. In addition, measures are needed to ensure that drug producers and distributors provide accurate information and put a stop to incentives that encourage inappropriate use of antibiotics.

- Empowering communities to make informed decisions. A substantial effort will be needed to understand how people use antibiotics and develop strategies that enable them to cope with health problems more effectively. These should include reliable information about safe use of antibiotics and be attuned to local constraints and existing trust-based institutions.
- Advocacy, governance and coalition building. The implementation of a sustained effort to induce system-wide changes in the use of antibiotics will require informed and committed coalitions at national and global levels. It will need to build agreement on the importance of the issue and on the core elements of a strategy for addressing it. It will be important to ensure that the perspectives of poor and powerless people are taken into account so they are not required to bear unnecessary risks of treatment failure or high costs. One core aim of this kind of coalition would be to establish basic standards of conduct for health workers and for drug companies that emphasise the needs of patients and of the community. These coalitions will need to be able to monitor progress in ensuring access to treatment and reducing inappropriate use of antibiotics. The government will need to build its capacity to play an effective role in this process.
- Learning approach to change management. There are no blueprints for implementing multi-level changes at scale in complex and rapidly changing contexts. Each actor has only a partial understanding of the system and there is a big possibility that unintended outcomes will emerge. Also, actors have their own economic, social and political interests. There are a number of possible pathways of development with different implications for sustainability and justice (Leach *et al.* 2011). That is why it is important to employ a learning approach to the management of system change. Integrative social science, and its capacity to convene a conversation around understanding complex systems and the potential consequences of alternative interventions, can make an important contribution to this process. This could involve: (i) studies of the factors influencing the performance of specific aspects of the system; (ii) experimentation with promising interventions with the aim of applying lessons at scale; (iii) monitoring responses to policy initiatives to identify unexpected outcomes; and (iv) reflexive approaches to planning and stewardship that involve all actors in building common understandings of the challenge and of potential pathways of development.

The need to make the management of antibiotic use more sustainable and just is an example of the kind of challenges the world faces in a number of sectors. A successful effort to build coalitions that address this issue effectively would provide an important example of the approaches needed to ensure that powerful technologies are managed in a just and sustainable way.

## Bibliography

- Afifi, N. H., Busse, R. and Harding, A. (2005) 'Regulation of Health Services', in A. Harding and A. S. Preker (eds) *Private Participation in Health Services*, Washington: Human Development Network, Health, Nutrition and Population Series
- Ahmed, S. M., Evans, T., Standing, H., Mahmud, S. (2013) 'Harnessing Pluralism for Better Health in Bangladesh', *The Lancet* 382.9906: 1746–1755
- Ali, A. S. and Bhuiya, A. (2012) 'The Role of Drug Sellers in the Informal Medical Markets: An Exploratory Study for Effective Interventions', unpublished paper funded by Results for Development.
- Awor. P., Miller, J., Peterson, S. (2014) Systematic literature review of Integrated Community Case management and the private sector in Africa – relevant experiences and potential next steps. *J Global Health*.
- Bartoloni, A., Cutts, F., Leoni, S., Austin, C. C., Mantella, A., Guglielmetti, P., Roselli, M., Salazar, E. and Paradisi, F. (1998) 'Patterns of antimicrobial use and antimicrobial resistance among healthy children in Bolivia', *Tropical Medicine and International Health* 3: 116–123
- Bennish, M. and Ali Khan, W. (2010) 'What the Future Holds for Resistance in Developing Countries', in A. Sousa, D. Byarugaba, C. Amabile, P. Hsueh, S. Kariuki, I. Okeke (eds), *Antimicrobial Resistance in Developing Countries*, New York/Dordrecht/Heidelberg/London: Springer
- Bhuiya, A. (ed.) (2009) *Health for the Rural Masses: Insights from Chakaria, Dhaka, Bangladesh*: ICDDR, B
- Black J. (2002) 'Critical Reflections on Regulation', CARR Discussion Paper 4, Centre for Analysis of Risk and Regulation, London: London School of Economics and Political Science
- Bledsoe, C. H. and Goubaud, M. F. (1988) 'The reinterpretation and distribution of western pharmaceuticals: an example from the Mende of Sierra Leone' in S. van der Geest and S. Whyte (eds) *The Context of Medicines in Developing Countries*. Dordrecht: Kluwer Academic Publishers, 253–276
- Bloom, G., Henson, S. and Peters, D. (2014) 'Innovation in Regulation of Rapidly Changing Health Markets', *Globalization and Health* 10: 53
- Bloom, G., Standing, H. and Lloyd, R. (2008) 'Markets, Information Asymmetry and Health Care: Towards New Social Contracts', *Social Science and Medicine* 66.10: 2076–2087
- Bloom, G. and Wolcott, S. (2013) 'Building institutions for health and health systems in contexts of rapid change', *Social Science and Medicine* 96: 216–222
- Bourgon J. (2011) *A New Synthesis of Public Administration: Serving in the 21st Century*, Montreal: McGill University Press
- Buse, K. and Harmer, A. (2004) 'Power to the Partners? The Politics Of Public-Private Health Partnerships', *Development* 47.2: 49–56
- Cars, O., Hogberg, L., Murray, M., Nordberg, O., Sivaraman, S., Lundborg, C., So, A. and Tomson, G. (2008) 'Meeting the Challenge of Antibiotic Resistance', *British Medical Journal* 337: 11438

Chandler, C. I. R., Mangham, L., Njei, A. N., Achonduh, O., Mbacham, W. F. and Wiseman, V. (2012) "'As a clinician, you are not managing lab results, you are managing the patient": How the Enactment of Malaria at Health Facilities in Cameroon Compares with new WHO Guidelines for the Use of Malaria tests', *Social Science and Medicine* 74.10: 1528–1335

Chang, H. (2007) *Institutional Change and Economic Development*, London: Anthem Press

Das, J., Hoolla, A., Das, V., Mohana, M., Tabak, D. and Chang, B. (2012) 'In Urban and Rural India, a Standardized Patient Study Showed Low Levels of Provider Training and Huge Quality Gaps', *Health Affairs* 31.12: 2774–84

Dua, V., Kunin, C. M. and Vanarsdale White, L. (1994) 'The use of antimicrobial drugs in Nagpur, India. A window on medical care in a developing country', *Social Science and Medicine* 38: 717–724

Elliot D., Gibson, A. and Hitchens, R. (2008) 'Making markets work for the poor: rationale and practice', *Enterprise Development and Microfinance* 19.2: 101–119

Ensor, T. and Weinzierl, S. (2006) *A Review of Regulation in the Health Sector in Low and Middle Income Countries*, Working Paper, Oxford: Oxford Policy Management

European Centre for Disease Prevention and Control (2014) *Surveillance of antimicrobial consumption in Europe 2012*, Stockholm: European Centre for Disease Prevention and Control

Fukiyama, F. (2004) *State Building: Governance and World Order in the Twenty-First Century*, Cornell: Cornell University Press

Garuba, H., Kohler, J. and Huisman, A. (2009) 'Transparency in Nigeria's public pharmaceutical sector: perceptions from policy-makers', *Globalization and Health* 5: 14

Gautham, M., Shyamprasad, K. M., Singh, R., Zacharia, A., Singh, R. and Bloom, G. (2013) 'Informal Rural Health Care Providers in North and South India', *Health Policy and Planning*, 29.1: i20–i29, [http://heapol.oxfordjournals.org/content/29/suppl\\_1/i20](http://heapol.oxfordjournals.org/content/29/suppl_1/i20)

Gumpert, A. (2014) 'Profits and Public Health: How private market incentives affect the availability and distribution of ORS and zinc in drug shops in Bushenyi, Uganda', unpublished masters thesis, Stockholm: Karolinska Institutet

Haak, H. (2003) 'Improving antibiotic use in low-income countries: an overview of evidence on determinants', *Social Science and Medicine*, 57: 733–744

Haak, H. (1988) 'Pharmaceuticals in two Brazilian villages: lay practices and perceptions', *Social Science and Medicine* 27: 1415–1427

Heyman, G., Cars, O., Bejarano, M-T. and Peterson, S. (2014) 'Access, excess, and ethics-towards a sustainable distribution model for antibiotics', *Upsala Journal of Medical Sciences* 119: 134–141

Kotwani, A., Wattal, C., Katewa, S., Joshi, P. C. and Holloway, K. (2010) 'Antibiotic use in the community: what factors influence primary care physicians to prescribe antibiotics in Delhi, India?', *Family Practice* 10: 1–7

Laxminarayan, R., Duse, A., Wattal, C., Zaidi, A. K. M., Wertheim, H. F. L., Sumpradit, N., Vlieghe, E., Hara, G. L., Gould, I. M., Goossens, H., Greko, C., So, A. D., Bigdeli, M., Tomson, G., Woodhouse, W., Ombaka, E., Peralta, A. Q., Qamar, F. N., Mir, F., Kariuki, S., Bhutta, Z. A., Coates, A., Bergstrom, R.,

Leach, M., Scoones, I. and Stirling, A. (2011) *Dynamic Sustainabilities: Technology, Environment, Social Justice*. London: Routledge (Earthscan)

Leonard, D., Bloom, G., Hanson, K., O'Farrell, J. and Spicer, N. (2013) 'Institutional Solutions to the Asymmetric Information Problem in Health and Development Services for the Poor', *World Development* 48: 71–87

Lexchin J. (2010) 'Statistics in drug advertising: what they reveal is suggestive what they hide is vital', *International Journal of Clinical Practice* 64: 1015–1018

Li, Y., Xu, J., Wang, F., Wang, B., Liu, L., Hou, W., Fan, H., Tong, Y., Zhang, J. and Lu, Z. (2012) 'Overprescribing in China, driven by financial incentives, results in very high use of antibiotics, injections, and corticosteroids', *Health Affairs* 31.5: 1075–82

Minzi, O. and Manyilizu, V. (2013) 'Application of basic pharmacology and dispensing practice of antibiotics in accredited drug-dispensing outlets in Tanzania', *Drug Healthcare and Patient Safety* 5: 5–11

Molstad, S., Erntell, M., Hanberger, H., Melander, E., Norman, C., Skoog, G., Lundbog, C. S., Söderström, A., Torell, E. and Cars, O. (2008) 'Sustained reduction of antibiotic use and low bacterial resistance: 10-year follow-up of the Swedish Strama programme', *The Lancet Infectious Diseases* 8: 125–32

Morgan, D. J., Okeke, I. N., Laxminarayan, R., Perencevich, E. N. and Weisenberg S. (2011) 'Non-prescription antimicrobial use worldwide: a systematic review', *The Lancet Infectious Diseases* 11: 692–701

National Institute of Population Research and Training (NIPORT) (2012) *Bangladesh Maternal Mortality and Health Care Survey 2010*, Dhaka: NIPORT, Measure Evaluation and ICDDR, B

Okeke, I. N. (2010) 'Poverty and root causes of resistance in developing countries' in A. D. J. Sosa, D. K. Byarugabal, C. F. Amabile-Cuevas, P-R. Hsueh, S. Kariuki and I. N. Okeke(eds.) *Antimicrobial resistance in developing countries*, New York/ Dordrecht/Heidelberg/London: Springer

Paina, L. and Peters, D. H. (2012) 'Understanding pathways for scaling up health services through the lens of complex adaptive systems', *Health Policy and Planning* 27: 365–373

Peters, D. H. and Bloom, G. (2012) 'Developing world: bring order to unregulated health markets', *Nature* 487: 163–165

Peters, D., El-Saharty, S., Siadat, B., Janovsky, K. and Vujicic, M. (2009) *Improving Health Service Delivery in Developing Countries: From Evidence to Action*, Washington: World Bank

Paredes, P., De La Peña, M., Flores-Guerra, E., Diaz, J. and Trostle, J. (1996) 'Factors influencing physicians' prescribing behaviour in the treatment of childhood diarrhoea: knowledge may not be the clue', *Social Science and Medicine* 42: 1141–1153

Radyowijati, A. and Haak, H. (2003) 'Improving antibiotic use in low-income countries: an overview of evidence on determinants', *Social Science and Medicine* 57: 733–744

Rahman, H. and Agarwal, S. (2013) 'Drug detailers and the pharmaceutical market in Bangladesh' in G., Bloom, B. Kanjilal, H. Lucas, and D. Peters (eds) *Transforming Health Markets in Asia and Africa: Improving quality and access for the poor*, Oxford: Routledge

- Shah, N. M., Brieger, W. R. and Peters, D. H. (2011) 'Can Interventions Improve Health Services from Informal Private Providers in Low and Middle-Income Countries? A Comprehensive Review of the Literature', *Health Policy and Planning* 26.4: 275–87
- Sheik, K., Saligram, P. and Prasad, L. (2012) *Mapping the Regulatory Architecture For Health Care Delivery In LMIC Mixed Health Systems: A Research Tool And Pilot Studies In Two Indian States*, New Delhi: Public Health Foundation of India
- Smith, D.K. (2004) 'Beyond the Rule Of Law? Decentered Regulation In Online Investing', *Law and Policy* 26: 439–76
- Stålsby Lundborg, C. and Tamhankar, A. J. (2014) 'Understanding and changing human behaviour - antibiotic mainstreaming as an approach to facilitate modification of provider and consumer behaviour', *Uppsala Journal of Medical Sciences* 119: 125–133
- Strömdahl, H., Tham, J., Melander, E., Walder, M., Edquist, P. J., Odenholt, I. (2011) 'Prevalence of faecal ESBL carriage in the community and in a hospital setting in a county of Southern Sweden', *European Journal of Clinical Microbiological Infectious Diseases* 30: 1159–1162
- Sudhinaraset, M., Ingram, M., Lofthouse, H. K. and Montagu, D. (2013) 'What is the Role of Informal Healthcare Providers in Developing Countries? A Systematic Review', *PloS ONE* 8.2: e54978
- Sun, Q., Tärnberg, M., Zhao, L., Stålsby Lundborg, C., Song, Y., Grape, M., Nilsson, M., Tomson, G. and Nilsson, L. E. (2014) 'Varying high levels of faecal carriage of extended-spectrum beta-lactamase producing Enterobacteriaceae in rural villages in Shandong, China: implications for global health', *PLoS ONE* 9.11: e113121
- Tomson, G. and Vlad, I. (2014) 'The need to look at antibiotic resistance from a health systems perspective', *Uppsala Journal of Medical Sciences*, 119: 117–124
- WHO (2014) *Antimicrobial Resistance: Global Report on Surveillance*, Geneva: World Health Organization
- Whyte, S. R. (1988) 'The power of medicines in East Africa' in S. van der Geest and S. R. Whyte (eds) *The context of medicines in developing countries: Studies in pharmaceutical anthropology*, Dordrecht: Kluwer, 217–234
- Whyte, S. R., van der Geest, S. and Hardon, A. (2002) *Social Lives of Medicines*, Cambridge: Cambridge University Press
- Wright, G. D., Brown, E. D. and Cars, O. (2013) 'Antibiotic resistance - the need for global solutions', *The Lancet Infectious Diseases*, 13: 1057–1098
- Van Zwanenberg, P., Ely, A. and Smith, A. (2013) *Regulating Technology: International Harmonization and Local Realities*, Abingdon: Earthscan