

Antimicrobial resistance and universal health coverage

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ABSTRACT

The WHO launched a Global Action Plan on antimicrobial resistance (AMR) in 2015. World leaders in the G7, G20 and the UN General Assembly have declared AMR to be a global crisis. World leaders have also adopted universal health coverage (UHC) as a key target under the sustainable development goals. This paper argues that neither initiative is likely to succeed in isolation from the other and that the policy goals should be to both provide access to appropriate antimicrobial treatment and reduce the risk of the emergence and spread of resistance by taking a systems approach. It focuses on outpatient treatment of human infections and identifies a number of interventions that would be needed to achieve these policy goals. It then shows how a strategy for achieving key attributes of a health system for UHC can take into account the need to address AMR as part of a UHC strategy in any country. It concludes with a list of recommended priority actions for integrating initiatives on AMR and UHC.

INTRODUCTION

In 2015, the WHO launched a Global Action Plan on antimicrobial resistance (AMR) to address a challenge, which its director general characterised as: *'threatening the very core of modern medicine and the sustainability of an effective global public health response to the enduring threat of infectious diseases'*.¹ The emergence and spread of pathogens resistant to antimicrobials poses a big challenge to policy makers, who need to oversee the transformation of health systems that evolved to provide easy access to these drugs into ones that provide *access to appropriate antimicrobial treatment while reducing the risk of the emergence and spread of resistance*. They also need to persuade health workers, producers and distributors of antimicrobials and the general public that the right of access to the benefits of antimicrobials needs to be complemented by responsibility for preserving their efficacy.

There is a broad scientific consensus on the magnitude of the challenge to the efficacy of existing antimicrobial drugs.²⁻³ A

Key questions

What is already known about this topic?

- ▶ The WHO and world leaders are giving high priority to initiatives to make progress towards universal health coverage (UHC) and to address the challenge of AMR.
- ▶ In many health systems, widespread inappropriate use of antimicrobials is combined with inadequate access to them, especially for the poor.
- ▶ Health system strengthening efforts have tended to neglect measures to ensure access to appropriate antibiotic treatment of infections.

What are the new findings?

- ▶ An effective strategy for addressing antimicrobial resistance (AMR) needs to both ensure access to effective therapy for common infections and reduce the risk of emergence of resistance.
- ▶ A systems framework for UHC is necessary to work across the continuum from prevention to care and to address the many factors that lead to AMR.

Recommendations for policy

- ▶ It is important to understand the linkage between the two priorities and ensure that the use of antimicrobials is both just and sustainable.
- ▶ Action is needed at national and global levels to ensure there is an integrated approach for making progress towards UHC and for addressing AMR.

number of pathogenic organisms have been found to be resistant to a variety of antimicrobial agents in a number of countries around the world.⁴ Several authors have explored the likely impact on avoidable sickness and death, increased cost of treatment of infections and lost income and wealth.^{3 5 6} A recent World Bank estimate suggests that global domestic product per annum will be decreased by between 1.1% and 3.8% by 2050, if AMR remains unchecked and that an investment of US\$9 billion per year will be needed to avoid this outcome.⁷ In this paper, we argue that some of this investment should be spent on building the capacity of



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health systems to provide access to effective treatment of common infections while reducing the risk of AMR.

UNIVERSAL HEALTH COVERAGE (UHC) AND AMR

The WHO is leading two health initiatives with big implications for the use of antimicrobials. First, Sustainable Development Goal 3 includes a commitment to achieve UHC by the year 2030. This implies significant increases in access to healthcare, including treatment of infections. Second, the Global Action Plan on AMR aims at 'ensuring, for as long as possible, continuity of successful treatment and prevention of infectious diseases with effective and safe medicines that are quality assured, used in a responsible way and accessible to all who need them'.¹ Neither initiative is likely to succeed in isolation from the other. Action to address AMR should go hand in hand with measures to strengthen attributes of health systems that contribute to progress towards UHC such as: equity, quality, efficiency, accountability, sustainability and resilience. This paper explores the ways that efforts to both make progress towards UHC and delay the emergence and spread of AMR are interconnected. It focuses on the use of antimicrobials for outpatient treatment.

A number of global statements have recognised the need to address the many routes of contact between micro-organisms and antibiotics including through ingestion by humans and animals and leakage into the environment.^{8–11} A recent WHO publication incorporates this understanding into a regional action plan for the Western Pacific Region.¹² Figure 1 focuses only on the drivers of human antibiotic use. It takes into account the widespread existence of pluralistic health systems, which include a mix of providers of healthcare and drugs in terms of their ownership and their

relationship to the regulatory system.¹³ Access to and use of antibiotics in such a system involves interactions between technical dimensions, such as availability of treatment guidelines, low cost diagnostic technologies and good quality drugs, behavioural dimensions, such as knowledge, incentives and cultural beliefs, and the influence of a wide range of actors including healthcare practitioners, drug companies, medical schools and regulatory agencies.

National governments and key stakeholders can undertake a number of actions to integrate AMR and UHC. Some priority actions for low-income and middle-income countries with relatively weak drug management and regulatory arrangements could include the following:

Prevention

- Improvements in basic public health and disease prevention.

Access and responsible use

- Improved access to appropriate and affordable treatment of infections, especially for the poor through enactment and enforcement of regulations, dissemination of treatment guidelines based on AMR surveillance data, along with awareness raising on the responsible use of antimicrobials and the challenge of AMR.

Financial incentives

- Realignment of incentives within drug value chains and delinking health worker income from the volume of antimicrobial drugs supplied.
- Measures to reduce financial barriers to access to antimicrobial treatment of infections, linked with measures to encourage judicious use of these drugs.

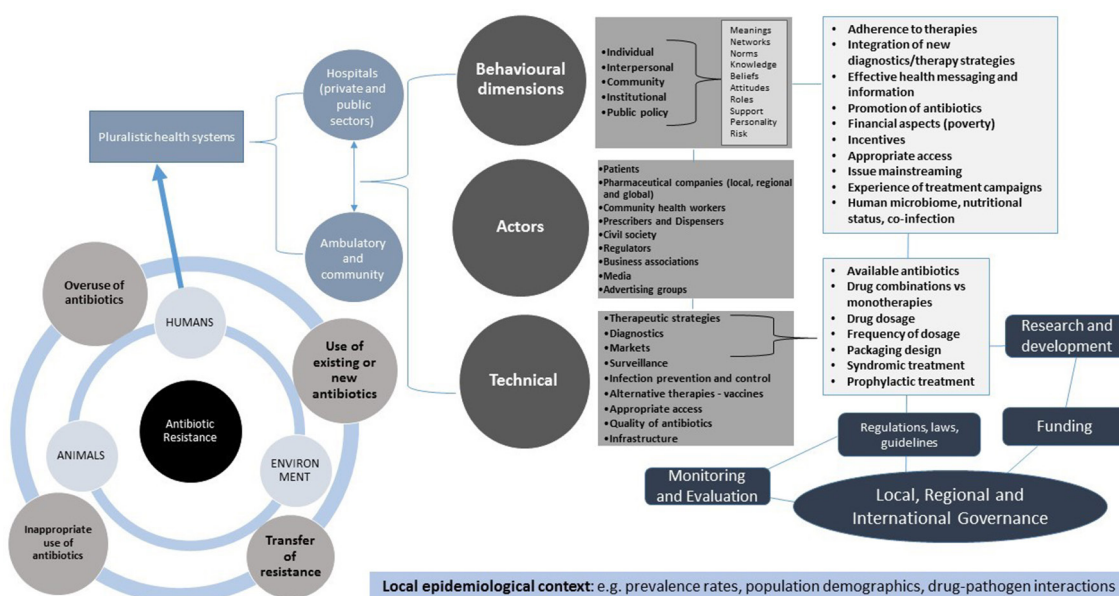


Figure 1 A complex system: human drivers of antibiotic resistance in pluralistic health system. Source: Antimicrobial resistance in the Asia Pacific region: a development agenda. Geneva: World Health Organization, 2017.

Institutional arrangements and partnerships

- ▶ Strengthening the capacity of governments to play a role as regulator and steward of the health system, incorporating oversight of the private and informal sector.
- ▶ Creation of partnerships, across the plurality of providers of drugs and information, that foster shared visions, interests and commitments.

These actions are described in more detail below.

Prevention and population level action to decrease the burden of infections

The risk of emergence and subsequent transmission of AMR genes can be reduced by immunising the population against common infectious diseases and measures to reduce exposure to infections through contaminated water and food and reduce the susceptibility of people to infections by improving nutrition and treating conditions such as HIV infection. It is important that UHC strategies take this into account.

Ensuring access to effective and appropriate treatment of infections

In countries with a pluralistic health system, it is typical for people to seek treatment for a large proportion of common infections in weakly regulated markets.¹³ These arrangements have enabled people to obtain treatment for many infections and reduce mortality. However, there are problems with the use of substandard drugs, taking partial courses of treatment and overuse of antimicrobials. The simultaneous existence of insufficient access to safe, effective and affordable treatment of common infections and high levels of inappropriate use of antibiotics creates special challenges for government action.¹⁴

Enacting and enforcing laws that reserve the right to prescribe antibiotics to licenced healthcare workers may not be realistic in many pluralistic health systems, where governments face a choice between denying many people access to life-saving drugs and turning a blind eye to nominally illegal practices. An alternative is for governments to strengthen their role as regulator and steward of the health sector and act to improve the performance of informal health workers and drug sellers in providing antibiotic treatment of common infections. This will require a combination of measures to ensure drug quality, encourage the use of treatment guidelines and alter incentives that encourage excessive use of antimicrobials.

Ensuring access to reliable information and advice

Health workers, drug sellers and the general public make decisions about when and how to use antimicrobials in a complex health knowledge economy.¹⁵ The boundaries between information consumed by providers and the public are blurred: healthcare worker training institutes teach about the use of these drugs; government health services issue public health messages and organise special programmes, which sometimes recommend treatment

without a specific diagnosis; companies that produce or distribute drugs provide information and advice to healthcare workers and drug sellers; advertising companies seek to influence the general public through the mass media; and the internet and mobile phones have become important sources of health information and advice for patients and providers. Government regulators, organised professions and industry associations issue guidelines and standards.

Until recently, all these sources have emphasised the efficacy of antimicrobials in treating sickness and saving lives. The emphasis of policy debates has been on the right of access to these drugs. Antibiotics have developed a reputation for being 'strong' medicines with the capacity to cure a range of ailments.¹⁶ Patients expect to have access to these drugs. Health workers use antibiotics for any possible indication of infection and risk being accused of missing an infection if they deviate from this practice. Efforts to limit the use of antibiotics have to contend with these ingrained beliefs, norms and entitlements.

A number of measures will be needed to align the knowledge economy with current and emerging scientific knowledge. Strategies are needed to educate and support healthcare providers in responsible prescribing. For example, guidelines could be developed for treating common infections, taking prevalent patterns of AMR into account. These guidelines could be incorporated into training courses and supplied to formal and informal providers of health advice and drugs. Strategies to raise awareness and reduce consumer demand for antimicrobials is also needed. The general public should be given basic information on when to use antimicrobials. Two important sources of information on antimicrobials are the publications that pharmaceutical companies produce and advertising on the mass media and social media. Voluntary standards and/or government regulations will be needed to provide impartial advice on the use of antimicrobials.

Management of supply chains for antimicrobials

The organisation of the production, distribution and supply of antimicrobials to patients strongly influences the way people use these products. In many countries, there are serious problems with counterfeit and substandard products. The packaging of antimicrobials influences the way they are taken. For example, it would be possible to produce combination therapy products and package them in full courses of treatment.

Drug wholesalers influence the people to whom they supply by providing information and advice and offering financial incentives to encourage a high volume of sales.¹⁷ The influence of pharmaceutical marketing is considerable. Strategies to reduce the provision of misleading information and perverse incentives throughout the supply chain are needed. They need to involve government and private companies.¹⁸ Governments need to set basic quality standards for drugs. They may also set

standards concerning treatment guidelines and the contents of promotional and advertising material. Effective interventions need the involvement of the pharmaceutical sector and leaders of the medical profession to encourage adherence to agreed regulations and professional and industry quality standards.

Guidelines to promote responsible use

The international community has supported a number of initiatives to promote treatment of infections where people do not have easy access to a medical doctor. They have typically employed a syndromic approach, in which people with symptoms of an infection are treated with an antibiotic without a definitive diagnosis. Some initiatives have advocated prophylactic use of antibiotics by high-risk groups, such as sex workers. These initiatives have contributed to the now widespread public perception of the efficacy and strength of antimicrobials and to the high level of demand for them. The problem of AMR raises questions about these strategies.

The alternative is to develop practical approaches for diagnosing and offering specific treatment for infections. New low-cost diagnostic tests are needed that can identify a specific pathogen or, at a minimum, distinguish between bacterial and viral infections. This could be linked to the development of appropriate ways of organising their use in countries without high levels of access to the formal healthcare system.¹⁹ There are significant challenges to the development, regulatory approval and clinical integration of diagnostic tests that use new technologies. It will probably involve collaboration between private, non-profit and academic institutions.

Research is needed to establish appropriate treatment guidelines for common infections in a context of changing patterns of AMR. These guidelines need to be updated based on the dynamics of antibiotic usage and evidence of emerging resistance.²⁰ Promotion of sequential use, cycling strategies or mixing strategies of different antibiotics have all demonstrated positive effects on the reduction of AMR.²¹ There is also a need to look more thoroughly at the scientific and societal perspectives of drug combination therapy as a means of combating drug resistance. As a first step, the scientific community will need to strengthen its assessment of appropriate usage, defining parameters for deciding which antimicrobials are effective in which areas of the world and useful at various levels of the healthcare system. The WHO Global Development and Stewardship Framework to Combat AMR can facilitate progress in this area together with a broader public-private engagement.

Finance

Strategies for making progress towards UHC emphasise measures to reduce the financial burden of healthcare on poor families. Out-of-pocket payments by individuals account for a substantial share of total health expenditure in a number of countries. They account for 70% of total health expenditure in India, and 70% of those

payments are for drugs. This section focuses on ways that strategies for health finance can influence the use of antimicrobials.

Many countries are increasing the contribution of government and health insurance to total health expenditure. If a scheme covers outpatient treatment of infections, it can substantially reduce the financial barriers to access to antimicrobial treatment. This is likely to lead to increases in the use of these drugs. This can save lives, but it can also lead to unnecessary use. This is a particularly high risk if the payment of health workers and the facility is linked to the volume of drugs they supply. Measures to reduce the cost of antimicrobials to patients need to be complemented by actions to ensure that these drugs are used appropriately by providing treatment guidelines, monitoring the quality of treatment, altering the pattern of incentives and supporting surveillance for AMR.

In countries where the poor rely heavily on informal providers of healthcare and drugs, it may take a long time to provide universal health insurance. Other measures will be needed to increase access to effective treatment. One option is for government, donor agencies and philanthropic organisations to reduce the cost of antimicrobials through more effective procurement and/or by supplying drugs at a subsidised price. This might involve programmes to address common infections such as childhood and postnatal infections. The provision of subsidised antimicrobials would need to be linked to measures to ensure they are used appropriately.

The Global Action Plan on AMR calls for substantial investments to combat AMR. A large proportion of these funds is likely to be allocated to the development of new antimicrobials, on the understanding that the use of any new drugs would be severely limited. This is unlikely to command support unless there is also investment in measures to increase access to effective treatment of common infections. A combined investment strategy would address the factors that contribute to the emergence of resistance and acknowledge the need to ensure universal access to antimicrobials. That would increase the likelihood of winning wide political support. The effective implementation of this kind of strategy would depend on effective partnerships, as highlighted below. Without high levels of support, it may be difficult to prevent the production and commercial use of new antimicrobials that are developed.

Partnerships

The achievement of progress towards UHC, while containing AMR, hinges on partnerships and coalition building. The activities of many stakeholders need to be aligned to the cause of providing *access to appropriate antimicrobial treatment while reducing the risk of resistance*. 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.²² Powerful actors such as pharmaceutical companies, especially the generic manufacturers who supply cheap medicines to private providers, have not been sufficiently persuaded that entering into partnerships aiming to limit sales of antibiotics is in their economic interest.

A sustained effort to induce system-wide changes in the use of antibiotics will require informed and committed coalitions at national, regional and global levels. Partnerships between the public and private sector, and the formal and informal sector, are especially important. Collaboration is also needed between those responsible for health prevention and health provision. This will require a one-health approach that extends beyond the boundaries of the government health system. 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 and so that no one is left behind. One aim of this kind of coalition would be to establish basic standards of conduct for healthcare workers and for drug companies that emphasise the needs of patients and of the community. This may require new business and financial models to address perverse incentives. 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.

CONCLUSIONS: A SYSTEMS APPROACH TO ADDRESSING AMR

Table 1 illustrates how the actions described above can be integrated into the routine functioning of a health system, through linking them to core health system attributes and dimensions of health system strengthening towards UHC.

Simple interventions can have unintended consequences. For example, measures to restrict access to antibiotics to a doctor's prescription may reduce equity by decreasing access to treatment by the poor. Also, strategies that focus disproportionately on one aspect of the system, such as ensuring access to treatment of infections, will have limited impact if basic public health and disease prevention are neglected. The different health system attributes are highly interdependent and stewardship requires a multilevel systems perspective.²³

Actions that are not based on an understanding of the interdependencies relevant to antibiotic supply and use may have relatively little impact. For example, qualified doctors often blame patients or the informal sector for inappropriate antibiotic use, when their own practices are frequently no better. 'Patient demand' is often noted to be a major factor in influencing inappropriate prescribing by healthcare workers. However, observations of clinical interactions have not always

Table 1 Health system attributes and universal health coverage actions for addressing AMR

| Health system attributes | Actions for addressing AMR |
|-------------------------------|--|
| Equity | Reduce the burden of infectious disease among the poor by strengthening basic public health and prevention Ensure access to appropriate antibiotics at an affordable cost, including by the poor Ensure that measures aimed at reducing inappropriate use of antimicrobials do not interfere with access to them by the poor |
| Quality | Regulate the quality of antimicrobials Include AMR in medical curriculum and training programmes Ensure that guidelines for treatment of infections take into account surveillance findings Ensure that advice on antimicrobial use provided to healthcare workers and through advertisements reflects best-practice guidelines and acknowledges the threat of AMR Increase access to low-cost diagnostic technologies for more accurate diagnosis |
| Efficiency | Alter financial incentives that encourage overuse of antimicrobials Reduce need for expensive treatment of infections with resistant organisms |
| Accountability | Provide information on surveillance findings Provide information on appropriate treatment for different infections |
| Sustainability and resilience | Strengthen public health services and immunisation to reduce exposure to infections Establish partnerships for management of antimicrobials Carry out awareness and educational campaigns to change understanding of healthcare workers and the population on appropriate use of antimicrobials Invest in research and development (R&D) of new drugs and in new approaches for providing effective treatment of common infections |

Source: WHO. Antimicrobial Resistance in the Asia Pacific region: a development Agenda. 2017. WHO, Geneva. AMR, antimicrobial resistance.

confirmed this.²⁴ Also this demand has been stimulated by the many public campaigns to convince people of the value of antibiotics. Other factors that influence the decisions to use antibiotics need to be considered, such as perverse financial incentives and inadequate understanding of appropriate treatment guidelines.

There are no blueprints for implementing multi-level changes at scale in complex and rapidly changing contexts. These changes include measures to address immediate problems, such as inadequate access to treatment and problems with drug quality, and the longer term need to change attitudes and create more effective mechanisms to govern and manage antimicrobial use. It is important to employ a learning approach to the management of this kind of system change.

National action plans need to take into account regional and global interdependencies. Dense transportation links, the movement of large quantities of goods and people, the behaviour of international pharmaceutical companies and international media influence national systems. Countries with larger national incomes and higher levels of economic and social organisation have a stake in the success of measures by relatively low-income countries to reduce their burden of infectious diseases and increase access to effective treatment. Measures to address AMR will need to be built on the foundation of strong regional and global agreements on actions that address the concerns of all countries and all social groups through a whole-of-society approach.

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