



Cultural Contexts of Health and Well-being

Policy brief, No. 2

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Felicity Thomas, Göran Tomson

Antibiotic resistance: using a cultural contexts of health approach to address a global health challenge



**World Health
Organization**

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ABSTRACT

This policy brief has been developed in response to the contemporary challenge of antibiotic resistance (ABR). ABR poses a formidable threat to global health and sustainable development. It is now increasingly recognized that the systematic neglect of cultural factors is one of the biggest obstacles to achieving better health outcomes and better standards of living worldwide. Using a cultural contexts of health approach, the policy brief explores the centrality of culture to the challenge of ABR. The brief examines how the prescription and use of antibacterial medicines, the transmission of resistance, and the regulation and funding of research are influenced by cultural, social and commercial, as well as biological and technological factors. The brief moves beyond the ready equation of culture with individual behaviours and demonstrates how culture serve as an enabler of health and provide new possibilities for change.

KEYWORDS

ANTIMICROBIAL STEWARDSHIP
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BACKGROUND

This policy brief was developed through the WHO Regional Office for Europe. The evidence for health and well-being team of the Division of Information, Evidence, Research and Innovation, including Claudia Stein (Director), Nils Fietje (Research Officer) and Andrea Scheel (Consultant), was responsible for and coordinated its development.

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Summary

The resistance of microbes to antibiotics and other medicines poses a formidable threat to global health and sustainable development. It is estimated that, without an effective response, resistance to antimicrobial medicines might cause common infections to once again become fatal and, by 2050, lead to approximately 10 million deaths annually worldwide. Concerns about antimicrobial resistance (AMR) and, more specifically, antibiotic resistance (ABR) have grown in recent years and have been at the forefront of international focus and media attention as prominently exemplified by superbugs in hospitals (particularly *methicillin-resistant Staphylococcus aureus* (MRSA)) and the emergence of resistance genes to critically important antibiotics following their overuse in the livestock sector. These and other high-profile cases have prompted widespread calls, as part of the 2030 Agenda for Sustainable Development, for urgent cross-sectoral action to improve awareness, promote research, optimize the current use of and access to antimicrobial medicines, reduce other drivers of AMR risk, and invest more effectively and sustainably in new technological and health systems interventions.

Prevailing approaches to tackling ABR have tended to focus on top-down or expert-led approaches to scientific innovation, surveillance and antibiotic stewardship – assembling the evidence for action and calling on governments and other relevant actors to develop effective plans. While these approaches are essential, key challenges to the development and implementation of effective policy remain.

1. A wide range of social, commercial and cultural drivers of medicine prescription and use (cultural contexts) can confound one-size-fits-all policies.
2. A range of possible drivers of antibiotic resistance (cultural and ecological contexts of resistance) should be considered alongside efforts to manage antibiotic uses.

3. Any attempt to reduce inappropriate uses of antibiotics and reduce the risks of resistance requires systematic understanding of the histories and cultures of medicine uses, structural issues surrounding health and health care, and an appreciation of cultures of risk. Understanding existing and local conditions of health care access and fostering ownership of the ABR problem are required to achieve sustainable outcomes. As is the case for many health-related challenges, culture is not simply a barrier to implementation of policy, but a resource or opportunity through which lasting and co-constructed changes can be developed.

Adopting the cultural contexts of health approach set out in this policy brief allows one to recognize and address key challenges to the development and implementation of effective policies.

1. Antibiotic uses and related drivers of resistance do not occur in isolation. They relate to a wide range of social and cultural matters, including food security, poverty, health care provision and access, health care practices, norms concerning illness and recovery and even social representations and meanings of microorganisms (1). Appreciation of these conditions is crucial to any policy design or successful programme of action. Understanding these and other cultural contexts of antibiotic use and ABR should inform appropriate national action plan formulation (2).
2. Translation of high-income country (HIC) policies to low- and middle-income countries (LMICs) will not be effective if the contexts of medicine use and the specificities of settings are not taken into account.
3. Addressing the ABR challenge requires engagement and ownership by those implicated in the problem (3). It requires evidence generated in particular contexts or localities and a situated approach to drivers of inappropriate medicine uses, of infection and transmission of disease and resistance (4).

Executive summary

Background

Advances in biomedicine have led to significant improvements in human health prospects in many parts of the world. However, numerous complex health-related challenges have persisted or emerged in recent years. These challenges are difficult to address through science and technology alone. Attention must be paid to the social and cultural dynamics that shape patterns and experiences of health and illness. The needs of ageing populations, inequalities in health, and the damaging health effects of poverty, isolation, loneliness and mental illness are all shaped by complex and interrelated cultural, social and environmental conditions. In the present context, as subsequent sections of this ABR policy brief demonstrate, the prescription and use of antibacterial medicines, the transmission of resistance, and the regulation and funding of research are influenced by cultural and social, as well as biological and technological, factors.

Interest in how global health can be promoted through awareness of cultural differences and the development of culturally-sensitive health care services has increased in recent years (5, 6). In 2014, the *Lancet* Commission on Culture and Health emphasized the need to understand the cultural factors that affect health behaviours and clinical practice (7). In a number of reports, the WHO Regional Office for Europe has acknowledged the importance of culture to health and health policies (8, 9, 10). Health 2020, which has been adopted by all 53 Member States in the WHO European Region, prioritizes investing in a life-course approach, tackling major noncommunicable and communicable diseases, strengthening people-centred health systems, increasing public health capacity, and creating resilient communities and supportive environments (11). In particular, WHO's Global action plan on antimicrobial resistance emphasizes the need for a "whole-of-society" and One Health approach in tackling AMR, and further highlights that "all sectors and disciplines" should be engaged in the process of implementing the action plan (2). Focusing on the cultural contexts of health and generating novel research partnerships and new forms of evidence are critical to implementing the policy framework and achieving health and well-being for all (12, 13). Similarly, by emphasizing that health is seldom achieved alone, the

One Health and “planetary health” movements and the Sustainable Development Goals established by 2030 Agenda have highlighted the need to pay attention to social and ecological relationships. At a recent meeting of the Joint Programming Initiative on Antimicrobial Resistance, a global collaborative platform of 27 nations working to curb antibiotic resistance with a One Health approach, it was emphasized that “emotions, not just facts, drive decision-making” and that creative approaches that include an awareness of cultural contexts are essential for effective decision-making (14).

WHO has largely adopted a definition of culture that was initially proposed by the United Nations Educational, Scientific and Cultural Organization (UNESCO) and reaffirmed in 2002:

culture should be regarded as the set of distinctive spiritual, material, intellectual and emotional features of society or a social group, and... encompasses, in addition to art and literature, lifestyles, ways of living together, value systems, traditions and beliefs (15).

This definition of culture, as well as UNESCO’s emphasis on cultural diversity, helps to stress the importance of social relations, intangible cultural heritage and symbolic systems in shaping both clinical practice and patterns of health and disease. Additionally, it recognizes the ways in which “organizations, educational institutions and professions also develop cultures ... of thought and practice” (10). More recent work has developed this definition to capture the evolving and dynamic quality of culture (16) as the “overt beliefs and practices as well as the subtle and taken-for-granted conventions that frame our sense of reality, define what is normal and abnormal, and give our lives a sense of direction and purpose” (7, 10). Nevertheless, the UNESCO definition can result in interpreting culture solely as a barrier to the application of scientific or biomedical knowledge, or as a set of static, rather than dynamic and emergent, beliefs and practices (17). There is also a tendency to ignore the role of power relations and powerful actors in either resisting or fomenting cultural change. For example, the role of mass media may be a significant driver of cultural and social change in relation to health and medicine. As the case studies presented in this policy brief demonstrate, cultures are not only diverse and ever-evolving (18), but they can also serve as powerful enablers of health and well-being.

A cultural contexts of health approach to ABR

This policy brief contributes to a growing body of research aimed at understanding more clearly how cultural factors shape antibiotic use, the emergence and transmission of resistance, and the protocols that define how ABR is researched and regulated. It draws together research across the humanities, social sciences and biomedical sciences to present a series of case studies from across the European region and beyond to highlight how cultural contexts shape ABR. Based on an extensive review of relevant literature and databases (see Annex 1 for further details), the cultural contexts approach presented here reveals the numerous factors and agents that determine the pathways and outcomes of a complex health challenge. Focusing on ABR as a global health problem that is increasingly the focus of national and international health agencies (2), this policy brief highlights the individuals, resources, organizations and sectors that must work together to tackle the risks to health and well-being, as well as the social values and cultural norms that can be harnessed to address ABR. In addition to highlighting the multidimensional and multifactorial nature of ABR, the research outlined here also emphasizes the dynamic relations and circuits of knowledge that can be utilized to interrupt inappropriate uses of medicines and act to limit the transmission of resistance across health care and other settings (19, 20).

Developed through the WHO Regional Office for Europe, along with its expert group on the cultural contexts of health and the WHO Collaborating Centre on Culture and Health at the University of Exeter, this ABR policy brief highlights the advantages of adopting an approach to complex health challenges that recognizes how cultural contexts can impact the generation of scientific knowledge, development and delivery of health care practices, and personal and collective experiences of illness, health and well-being. It also reveals how culture can be a positive and affirmative resource that opens up new insights and helps to create novel strategies for change. The brief is intended to encourage researchers, practitioners and policy-makers to take cultural contexts into account when addressing complex health challenges such as ABR.

The following sections of this policy brief use case studies from the European region wherever possible – but also from outside Europe where necessary – to illustrate how cultural contexts can shape the prescription and use of antibacterial medicines in a variety of settings, accelerate or disrupt the transmission of resistance, and impact ABR policy and research priorities. Insights from the humanities and social sciences (outlined in Annex 2) and studies employing quantitative as well as qualitative methods together demonstrate how understanding the cultural contexts of health is a prerequisite for providing novel and inclusive ways of tackling ABR. This suggests that complex health challenges such as ABR can only be effectively addressed by:

1. harnessing, and, where necessary, challenging and transforming, cultural norms, relationships and practices;
2. recognizing how culture can act as an enabler of health and well-being;
3. facilitating change across diverse sites, sectors and organizations;
4. involving the people facing the problem and/or directly involved in its development in the process of solving it;
5. encouraging careful translation of research and practice to new settings and different cultural contexts.

Section I. The challenges of ABR

Antimicrobial is a term that refers to all chemicals and medicines that can kill microorganisms (viruses, bacteria, fungi and parasites). Antibiotic is a more specific term that refers to the medicines that kill or inhibit bacteria. Derived initially from soil microorganisms, antibiotics were first discovered in 1929 and were used to replace older chemical therapeutics, sulphonamides, during and after the Second World War. Mass production launched the so-called "antibiotic era", wherein these medicines became widely available in developed, or higher-income, settings from the 1950s onwards (21). The ability of microbes to undergo genetic changes that protected them from antibiotics and antimicrobials is referred to as AMR and ABR, and was recognized from the early days of laboratory experimentation and medicine development.¹

The social desirability of antibiotics, their charm and quasi-magical curative powers, were all testament to the success of medical science and treatment practices. However, the spectre of widespread and clinically relevant resistance was also well-known from the outset. Mary Barber, the British bacteriologist who pioneered early resistance studies, noted in 1948 (22):

The drug [penicillin] received such acclaim in the early forties that it came to be regarded by many in the nature of a charm, the mere sight of which was sufficient to make all bacteria tremble. Nothing, of course, could be further from the truth and the present widespread and often indiscriminate use of penicillin, particularly as a preventive measure is seriously menacing its future reputation.

While the threat of resistance has been a recurring theme in medical and policy circles over the last seven decades, ABR has become a critical global health challenge in the last decade. In 2015, when the Global action plan on antimicrobial resistance was adopted, the then-WHO Director-General, Dr Margaret Chan, emphasized the urgency of tackling the crisis, arguing that "we cannot allow hard-won gains for health to be eroded by the failure of our mainstay medicines" (2). In the following year, the draft political declaration of the High-Level Meeting of the General Assembly on Antimicrobial Resistance, which stressed the importance of adopting cross-sectoral action that recognized interconnections between human, animal

¹ AMR refers to the ability of microbes – including bacteria, viruses, parasites and fungi – to resist the effects of antimicrobial chemicals (including heavy metals and medicines). ABR is a more specific term that refers to the ability of bacteria to resist the effects of naturally occurring and synthetic antibiotic medicines.

and environmental health, referred to resistance to antibiotics in particular as “the greatest and most urgent global risk” (23).

It is predicted that, by 2025, many first-line antibacterial agents will be ineffective, heralding what some have referred to as a “post-antibiotic era” (24). Accelerating rates of ABR and the spread of multidrug-resistant bacteria indicate that it will become increasingly difficult to treat common infections or carry out basic surgical procedures safely (25, 26). It has been estimated that, by 2050, medicine-resistant infections – including bacterial, viral, fungal and parasitic infections – may contribute to as many as 10 million deaths per year (27). The rise in resistance as a key concern for human and animal health has largely been driven by global growth in production and uses of antibiotic medicines. It is also a function of the ability of microbes to freely transmit resistance (for example, from food production sectors to human bodies). Finally, the post-1970s slowdown in research and development of new or replacement antimicrobial medicines has heightened concerns and brought the imminent emergency into focus. This policy brief is structured in line with these three key challenges: antibiotic uses, transmission, and research and development.

Worries about resistance to antibacterial agents and policies aimed at tackling ABR are not new. In the early 1950s, shortly after the first antibiotics became commercially available in high-income countries, pharmacologists raised concerns about the ability of pharmaceutical companies to make efficacy claims and mis-sell medicines on the basis of verbal testimony alone. These concerns led to calls to rationalize and regulate antibiotic trials and sales, an approach referred to as rational therapeutics (28). This development limited the marketing power of pharmaceutical corporations, but it also prompted a backlash against perceived government encroachment on the prescribing autonomy of physicians and pushed antibiotic reform off the agenda for many years (21). Nevertheless, the notion of rational use persisted, with a tendency to label any clinically unnecessary use of antibiotics as irrational or misconceived. This label tends to overlook the often-rational desires for treatment in what may be challenging circumstances. For example, in low-income settings, it may be rational to rely on antibiotic medicines as a form of insurance against disease complications. Likewise, in hard-pressed and time-constrained health care settings, doctors may prescribe antibiotics in order to manage patient load and expectations of treatment. In this and other senses, the term “rational use” may lack sensitivity to the specific contexts

of medicine uses. A key lesson from a cultural contexts of health approach is that all health-related behaviours, including prescriptions and use of medicines, can be considered part of so-called situated rationalities (29) – that is, a socially and culturally coherent set of practices that need to be understood in the round rather than judged as either rational or irrational.

More recently, commentators have tended to distinguish between responsible use and inappropriate use of antibiotics. The latter circumvents the distinction between experts and lay publics, or between more rational and less rational theories of action. Here, the focus is less on individuals as consumers and more on the contexts and drivers of medicine uses. The conditions that shape medical practices, that affect doctor–patient relationships, that colour people’s belief in medicines or their charm or power, and that affect uptake of alternative approaches to infection (like vaccines), all become part of this broader analysis.

As the case studies in Section II demonstrate, even antibiotic use is itself driven by multiple factors, including financial incentives to prescribe (30); the pressures to sustain hierarchical professional cultures (31); a desire to protect the physician–patient relationship in an era of medical consumerism (32); and the need to maximize livestock production in increasingly challenging economic circumstances (33). Far from being irrational, the impact of these cultural, social and commercial as well as other economic factors is often indeed rational in the contexts in which they operate (34–36).

One consequence of the focus on rational use has been a tendency to view raising awareness of the impact of resistance (or the simple diffusion of information) as the main and sometimes the only function of policy. Once resistance was understood, then people would voluntarily reduce their use of medicines. The underlying diffusion model of policy – sometimes referred to as the Awareness, Behaviours and Choices (ABC) model (37) – can fail to appreciate the cultural contexts of medicine use and of resistance risks. The continuing prescription and sale of antibiotics in situations where levels of awareness are high, for example, indicates the limits of the diffusion model (38). More recently, this approach to policy is being replaced by evidence-informed policy-making (39–41). The WHO Evidence-Informed Policy Network (EVIPNet) aims to build capacity in terms of operationalizing more sophisticated models of knowledge,

policy-making and knowledge translation. In the case of AMR, EVIPNet Europe has been training seven EVIPNet member countries in putting together evidence briefs for policy (EBPs), which aim to increase country capacities to develop health policy (41). EBPs can assist in addressing complex health challenges such as ABR and AMR by pulling together the best available evidence and combining it with locally produced knowledge that considers culturally-specific contexts when presenting evidence-informed policy options (42). This need to stress regional and local evidence-based approaches was highlighted in a recent Wellcome Trust evidence call (4), and was emphasized by WHO in 2005 as one of the core strategies to contain AMR (3).

Focusing on inappropriate antibiotic use as a key driver of ABR is an important, though not the only, component of measures to reduce the burden of resistance. ABR is also associated with clinical, health care, agricultural and domestic practices that shape infection environments and, by extension, the transmission of resistance. Without effective sanitation and hygiene practices, infection control is likely to be over-reliant on antibiotic use. Poor sanitation can also provide the conditions for the emergence, persistence and spread of resistant bacteria. Even where sanitation is largely satisfactory, contemporary health care settings, for example, in care facilities for a growing elderly population, can pose significant infection and resistance risk challenges. Similarly, uptake of immunization, condom use, cross-infection controls, and disease control programmes are all key to preventing the causes of antibiotic use and resistance transmission.

Finally, ABR is also tied to innovation and research environments, and a key issue for the resistance threat has been the decline in investment in new antibiotics or their replacement with other therapies since the 1980s. A cultural contexts approach can offer insight into the drivers of product development (for example, new medicines or their alternatives), their uptake and relative successes or failures.

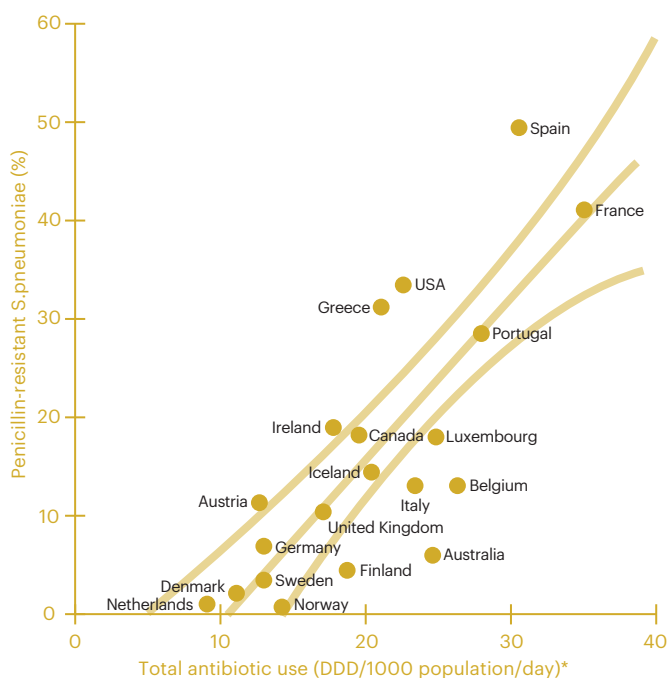
The use of antibacterial agents, the transmission of ABR, and the cultures of research and innovation are all addressed in the following sections.

Section II. Antibiotic sales, prescription and use

Introduction: the European context

Antibiotic use is a key factor contributing to growing rates of ABR (43, 44), and there is a correlation between antibiotic use and rates of ABR across countries (Fig. 1). However, the fact that similar levels of total antibiotic use amongst humans in Italy and Greece – or in Australia and the United States of America – produce very different resistance profiles for some bacteria, suggests that environment, community structure and other social and cultural factors, including where, how and which antibiotics are used, are also important. For example, in Norway in the 1970s, older and cheaper penicillins remained popular with health authorities, and health officials resisted introduction of newer and more expensive medicines. As it turned out, these older penicillins were less likely to produce resistance (45).

Fig 1. Correlation between antibiotic use and ABR
(taken from WHO, 2005 (3)).



* Defined daily dose (DDD) is the assumed average maintenance dose per day for a drug used for its main indication in adults.

Antibiotics are sold, prescribed and used in a diverse array of settings ranging from primary care clinics to dental surgeries, hospitals, veterinary facilities, and farms. Even within these broad categories, there are differences within countries, across regions and even within individual health care facilities composed of different organizational divisions and specific workplace cultures (46–48).

In some national settings, prescription from a qualified clinician or veterinarian is required before antibiotics are made available. In others, it is possible to buy antibiotics informally without a prescription (over-the-counter or OTC sales). OTC sales are common in Serbia and Spain (Fig. 1), and both countries record high levels of antibiotic use. OTC sales may be associated with a greater risk of non-regulated, counterfeit, and substandard medicines being marketed and consumed. They may also correlate with higher levels of consumer storage of antibiotics. Informal and OTC sales and storage of antibiotics tend to signify a lack of medical oversight in terms of matching medicines to symptoms, monitoring resistance risks, and medicine uses (49–50). The relationships between OTC sales, poor-quality medicines, and the charm-like qualities of those products are a key issue. In many parts of the world, antibiotics can be bought and sold as cure-alls, as signifiers of modern medicine, as substitutes for other, more onerous or expensive health care practices. As part of a cultural contexts of health approach, it is crucial to understand the drivers of those uses, appreciate the structural, historical, and other conditions that may make top-down policies ineffective, and devise culturally-informed approaches to reducing demand for non-sustainable or inappropriate uses. In the case of Spain, for instance, a better understanding of the historical contexts can provide important insights into the reasons for the country's high rates of OTC sales (Box 1). At the same time, it may be important not to generate undue fear of medicines. In many settings, antibiotics remain vital for health care treatment and it is important not to generate an anti-treatment culture. As anti-vaccination cases make clear, there are dangers in generating panic concerning valuable and effective medication.

Prescription rates, the type of medicines prescribed, and the consumption of those medicines can vary greatly. It should be noted that both sales and the number of prescriptions may be inaccurate indicators of consumption, which is why national sales data by volume may merely serve as a rough guide to use.

In addition, variations in completion rates for a course of antibiotics, the practice of sharing or selling unused medicines, and internet sales may all affect the likelihood of developing and spreading resistance.

There is a fourfold difference in total antibiotic use and consumption across the WHO European Region (51). Antibiotic use is lowest in the northern Scandinavian countries and highest in the southern Mediterranean countries (52). Significant variation in use is also evident across Europe in terms of the types and quantities of antibiotics used in veterinary medicine (53).

Box 1. Penicillin in Spain

Historically, Spain has recorded one of the highest rates of antibiotic consumption in the European Region. The reasons are manifold, but relate to the country's history, culture and politics. After the civil war ended in 1939, and in the aftermath of the Second World War, a legacy of a broken health system, widespread poverty, high infection rates and social taboos around sexually transmitted diseases combined with the sporadic appearance of a new wonder drug penicillin to usher in a period of high levels of antibiotic production and consumption.

General Francisco Franco identified penicillin as a miracle cure, as one pillar of his post-war promises. Its manufacture in Spain was part of his despotic industrial policy and the building of a self-sufficient modern state. Penicillin became a "state-controlled symbol of recovery" that helped to create an era of consumption. The repressive dictatorship viewed infections as matters of civilian and political order. Mass production and sales (most of which were over-the-counter without prescription), the normalization of antibiotic treatment, and the linking of national recovery to medicine availability combined to produce high levels of use and resistance (see Fig. 1).

This variation cannot be explained by epidemiological factors alone. Diverse sociocultural factors, including uncertainty tolerance, economic conditions, and shifting business and market models, influence and drive regional disparities. Understanding how antibiotics have become so popular within modern approaches to health and illness, sometimes referred to as the “charm” of antibiotic medicines (54,55), can also help to develop ABR policy interventions that take into account cultural beliefs and practices and work more effectively on the ground.

Stewardship of medicines

Antibiotic Stewardship (ABS) schemes aim to monitor and manage antibiotic use, often through a combination of technical interventions such as regimen cycling, restrictive measures, improved diagnostics, informational campaigns, and audit and feedback techniques (58). Here we focus on the success of these interventions, but it should also be noted that in some settings stewardship might be resisted for distributional equity reasons. Stewardship is a means of preserving antimicrobial medicines by taking measures to promote control, appropriate distribution and appropriate use (57). As such, one of its main aims is to conserve medicines, and medicine more generally, for future generations. It can therefore be interpreted as a benefit to medicine and medical effectiveness rather than immediate patient/doctor or clinical settings per se. In this sense, there are cultural issues of the uneven distribution of costs and benefits, which may be particularly challenging in LMIC settings asked to conserve antibiotic resources following their overuse in higher-income settings. Similarly, there are questions of collective versus individual benefit, as well as intergenerational issues of access to medical resources.

In some cases in the European Region, both ABS and surveillance schemes, as well as global networks and training programmes (54), have contributed to reducing antibiotic use. Following the spread of penicillin-resistant pneumococci among children in Sweden in the early 1990s, the Swedish Strategic Programme for the Rational Use of Antimicrobial Agents and Surveillance of Resistance (Strama) was established.

The scheme involves working at local and national levels, monitoring antibiotic use, introducing a national target for prescriptions, surveillance of resistance trends, infection control, and implementation of educational and communication strategies to raise awareness for behavioural change. Subsequent reviews of the programme indicate that, since its conception, Strama has resulted in a sustained reduction of antibiotic use and lower levels of resistance for most – but not all – bacterial species (59, 60). There are also regional surveillance initiatives, such as the Central Asian and Eastern European Surveillance of Antimicrobial Resistance (CAESAR) network established by the WHO Regional Office for Europe, which monitors resistance and publishes aggregated data on resistance annually for countries able to submit data (61).

These schemes are vital in terms of determining use rates and monitoring interventions. However, their translation beyond HICs may be limited – especially where prescriptions are not mandatory, where users and uses within human and animal health are largely unregulated, where access to health care services is limited, and where food security concerns and poverty hinder the ability to meet national or externally set targets (62).

ABS schemes have been implemented in primary and secondary care and in agricultural settings. In each case, there is a growing consensus of the requirement to supplement technical knowledge and skill acquisition (such as educational campaigns or instructions on how to use electronic prescription tools) with direct engagement and appreciation of the cultural contexts that underpin specific working environments and practices. The latter can help to foster “ownership” and creative innovations in relation to the AMR problem (63).

Antibiotic prescription and use in primary care

Primary care facilities, including general practitioner (GP) surgeries, dental practices, community pharmacies, and care homes, account for 80-90% of all antibiotic prescriptions in human health care (64, 65). Most of these prescriptions are provided in the absence of formal diagnostic tests. Many are thought to be administered in GP surgeries for conditions, including viral infections, that are unresponsive to antibiotics (66). This is not a failure of expertise or knowledge but rather patient pressure, the desire to bolster rates of patient satisfaction, the desire to insure patients against secondary infections and reduce return visits, and so-called action bias – that is, the desire to do something for the patient, as well as overreliance on crude tests rather than consultations for patients in care homes – are the key sociocultural factors contributing to suboptimal practices of antibiotic prescribing in GP or local practitioner surgeries (as well as hospitals) across the world (Box 2).

Box 2. Non-pharmacological drivers of antibiotic prescription in primary care

Primary care physicians are under increasing pressure to improve patient satisfaction and protect performance ratings (67). This reflects a shift in contemporary health care systems towards consumerist models. In Japan, the United Kingdom and the United States, physicians report prescribing antibiotics to protect against the perceived risk of reputational damage and legal reprisal (68). In some cases, physicians feel pressured into prescribing antibiotics by their patients (69).

In low-income countries, sociocultural factors shaping antibiotic prescription include high patient–doctor ratios which prohibit thorough discussion of patient symptoms (70). It has also been reported that lack of privacy in clinical settings may encourage doctors to prescribe antibiotics for some suspected conditions, such as gonorrhoea, without medical examination (71).

Cultural norms and expectations also affect the implementation of interventions designed to reduce antibiotic use. In the United Kingdom, GPs are turning towards C-Reactive Protein diagnostic tests as a defensive practice to convince patients that they do not need an antibiotic prescription (72). However, the same research found that patients would have been happy with a no-antibiotic decision if they had been given a full explanation. What they required was an engagement with their doctor that did not need to involve a medical procedure or prescription. Related research has cautioned against the use of diagnostic tests due to potential false results and their impact on limited health care resources (73).

Attempts to reduce antibiotic use are unlikely to be effective without an appreciation of the cultural norms of doctor–patient relationships and the effects of health care practices. Technical tools such as rapid bedside diagnostics may offer more precision, but in some contexts, they may accentuate the medicalization of certain health care and health system challenges.

Antibiotic prescription and use in secondary care

Hospitals, like primary care clinics, are critical sites of antibiotic prescription and use. Medical practitioners working in hospital environments are often faced with particular challenges, including immunocompromised patients and high rates of diagnostic uncertainty (74). Research conducted in Australia and the United Kingdom, but relevant to hospital prescribing practices elsewhere including the European region, indicates that in spite of the implementation of stewardship schemes, social norms and hierarchies in the hospital can lead to inefficient or inappropriate use of antibiotics (74, 75) (Box 3). In addition, informal practices may subvert any stated stewardship objectives. Research has found that nurses can play an informal role in obtaining antibiotics from different hospital divisions where restrictions are not in place (76), indicating that even though doctors hold official responsibility for prescribing practices, in some settings prescription and usage is driven, or at least mediated, by several actors (77, 78).

The value of antibiotics in hospital settings resides in their perceived ability to limit immediate patient risk (83) and protect the professional reputation of junior doctors. Suboptimal antibiotic practices – often expressed in terms of “irrational use” – in the hospital are reinforced by structural and organizational factors. For example, a qualitative study of practice in one United Kingdom hospital has indicated that up to two thirds of patients for whom oral antibiotics could be prescribed remain on intravenous (IV) antibiotics, which can increase the likelihood of infection and prolong the time spent in hospital (84). Junior doctors, the study suggested, were less likely to switch from IV to oral antibiotics, fearing something going wrong on their watch.

Although senior doctors were more comfortable switching a patient from IV to oral antibiotics, they did not always participate in daily ward rounds in the hospital (84), as a result of which the decision to switch to oral antibiotics was often deferred (84). It should be noted, however, that these decisions will be determined by specific institutional cultures and working contexts (85).

ABS schemes have so far produced mixed results (86–89). In a hospital in the United States with an ABS scheme in place, for example, physicians were found to wait until after the approval system was lifted at 10 pm to access restricted antibacterial agents, which resulted in delayed treatment, which could in turn pose resistance risks. Motivations for avoiding the ABS scheme included fear of refusal and a desire to avoid stressful telephone interactions with infectious disease (ID)-trained pharmacists or ID fellows (90). Similar findings and unanticipated consequences have been reported elsewhere (91, 92).

Box 3. Social hierarchies in the hospital

Hospital cultures have been found to valorize autonomous decision-making and independent work, and to accentuate social hierarchies between junior doctors and senior consultants (74). As a result, junior doctors will often overprescribe broad-spectrum antibiotics rather than consult with their seniors on what type of antibiotic to prescribe or whether to prescribe at all (79). Social hierarchy in the hospital has also been found to contribute to the existence of local “bubbles” of culture (80), with junior doctors adopting the off-textbook prescribing practices and preferences of their senior consultants (55), as a form of social etiquette and fraternal obligation (81).

Senior doctors prioritize clinical knowledge and experience and often consider themselves exempt from the constraints of top–down policy (81). Consultants have been found to resist the implementation of ABS guidelines developed without input from specialist clinicians (55). Hospital ABS initiatives have more recently sought to enrol pharmacists into the governance process (31, 82), partly in recognition of their detailed pharmacological knowledge. However, pharmacists report feeling disempowered and unable to intervene effectively in what have traditionally been deemed “medical” decisions (31).

Research in Singapore found that doctors were more receptive to the advice of a computerized antimicrobial stewardship support tool when it was requested rather than delivered automatically (93). Reducing prophylactic use of antibiotics in surgery can also be difficult to implement, as surgeons are particularly reluctant to compromise patient safety. Decision-making in surgery tends to be diffuse and uncoordinated, and communication between operatives is disjointed (94).

Antibiotic use in agriculture

Antibiotics are used in both animal and crop agriculture to support animal and plant health, to reduce the likelihood of infections, and in some cases, at subtherapeutic levels to promote growth. Agriculture-related use of antibiotics accounts for between one third and two thirds of total antibiotic sales, and includes use of critically important antibiotics (CIAs; antibiotics deemed vital to maintain human health). Antibiotic use in agriculture and livestock is potentially a major driver of ABR, in the environment, animals and people. The links between use in livestock animals and human health are sometimes contested but evidence suggests that pathways include: consumption of food produce with antibiotic-resistant bacteria, the transfer of antibiotic residues in meat products to people, exposure to environmental discharges from farms, and direct exchange of antibiotic-resistant bacteria through physical contact with animals. Globally, livestock consume around 60 000–70 000 tonnes of antibiotics every year, though this may be a considerable underestimate of total use. This figure likely exceeds direct human consumption, and is projected to increase significantly over the next few decades as demand for animal protein expands and livestock rearing practices intensify, particularly in Asia and Latin America (95). Although use of antibiotics has been restricted for non-therapeutic, growth-promotion purposes in the European Union (EU) since 2006, use of antibiotics to encourage growth is common elsewhere. Even within the EU, antibiotics continue to be used for prophylactic and metaphylactic purposes in some settings (96). Indeed, there is a grey area in which antibiotics can be prescribed for livestock animals if there is sufficient risk of infection. Attempts to reduce the overall volume of antibiotics used in a sector can sometimes lead to the use of more powerful antibacterial medicines, or replacement of antibiotics with other antimicrobial agents. For example, the pig sector has successfully reduced antibiotic

use in northern Europe, but this has led to increased use of zinc oxide to control post-weaning diarrhoea in piglets. The latter may modulate the molecular processes that facilitate ABR, and will itself be banned in the EU in 2022 (97). Some recent successes in reducing antibiotic uses in European livestock, as well as concerns over unintended consequences of replacement, highlight a number of cultural processes and factors that can drive antibiotic uses and ABR risks.

1. The power of supply chain actors in driving on-farm practices is clear. In integrated and contracted sectors and parts of the region, retailers, processors and restaurant chains can be particularly effective in specifying the methods of disease management and other relevant practices on farms. In LMICs and those parts of the region where farming is less organized in terms of contracted production, or where smaller farmers tend to pool produce, the effects of other value chain actors in shaping farm practice may be minimal. Similarly, in lower-income settings, the effectiveness of commercial or state regulation may be significantly attenuated by a lack of veterinary resources for surveillance and monitoring.
2. The drive to reduce costs and increase margins in the food and farming sector may be manifested through increased throughput (and pressure on animal bodies), increased stocking density, and higher likelihood of disease and/or reliance on antibiotics. Some of these aspects of intensified production are offset by advanced, non-antibiotic methods of disease prevention, but the economics of food production and global competition have made antibiotics a common feature of food production.
3. In lower-income settings, or sectors with lower sanitation standards or characterized by socioeconomic instability, scarcity of veterinary expertise and/or disease management options (such as vaccines and biosecurity), there may be few alternatives. Antibiotics may be the cheapest and only available means to control disease, a quick fix for poor hygiene and a guarantor of economic productivity. Without antibiotics or resourced interventions, there may be severe effects in terms of food security or the alleviation of rural poverty.

4. Consumers and consumer awareness may be key drivers of reducing antibiotic uses. Companies can compete for market share by advertising their policies of sourcing non-routine use of antibiotics in produce. Consumer preference can be fostered and encouraged by market actors, but it may also yield little more than niche markets that make little overall difference to mass consumption and supply chain activities.
5. Unintended consequences of reduction. Animal welfare and husbandry can reduce the need for antibiotics through better disease management. At the same time, there is a risk that animal welfare can suffer if all treatments are withdrawn from prescription. The price of produce, animal welfare standards, and food standards (for example, in relation to ABR risks) may be a difficult balancing act in highly competitive markets.
6. Business models and medicine sales. In human health, profits from medical sales are largely decoupled from treatment practices, whereas veterinary surgeries often rely on medicine sales for their business profits. This reliance on sales may reduce the willingness of key actors to limit prescriptions or sales.
7. As for human primary health care, a key relationship is between the clinician and the patient, or in this case between a veterinarian and livestock keeper. Issues of trust and familiarity may be key and will depend on shared understanding of farming issues, experience of disease and disease management in the past, and costs (98).

Business and market models influence the choice of antibiotic prescribed on the farm (98). In some cases, farmers and their veterinarians prefer powerful and fast-acting antibiotics – those that are also deemed critical for human health – both to improve animal welfare and to get an animal or flock to market.

The preference for antibiotics with short residence times in food animals (and, consequently, reduced risks of antibiotic residues in foodstuffs) tends to be accompanied by low levels of metabolism and therefore high risks of downstream resistance (in animal wastes, and the wider environment). The expectations of farmers, other food chain actors and the changing roles of veterinarians (including the privatization of services, commercialization of practices and increased specialization) (99), the regulatory culture, markets, and available medicines can all interact to shape antibiotic use in agricultural environments, sometimes producing suboptimal situations.

Efforts to encourage farmers and veterinarians to implement change, including stewardship of medicines and use of available diagnostic procedures, require focus on the specific cultures, business norms and practices of food production. Translation of norms and values from medical settings to veterinary and farm settings is not always straightforward. For example, farmers and veterinarians may have limited option to wait for a diagnostic test, the results of which may not prove conclusive in terms of decisions to treat; a “treat and see” culture may exist as a response to production exigencies and pressures; veterinarians are distinct from medical doctors in that they are permitted to benefit from selling medicines, which leads to potential conflicts of interest; farmers may be more or less restricted by the supply chain, the processors or retailers with whom they are contracted; and a culture of suspicion exists between the industry and the regulators. In some sectors and countries, farmers may conversely have strong social networks and cultural or cooperative norms that encourage the dissemination of best practice. Likewise, various actors in the value chain can be major sources of innovation and change. In view of the above points, antibiotic use and resistance management programmes are more likely to succeed if, through participatory research methods (detailed in Annex 2), they incorporate the views and perspective of farmers, veterinarians and other food industry actors.

Policy options

Prescription and use of antibiotics are shaped by cultures, values, norms and practices in primary and secondary health care settings and in the agricultural sector. In order to effectively address antibiotic use and resistance risks, attention should be paid to the cultural contexts in which decisions to prescribe and use antibiotics are made and monitored.

Research findings suggest that:

- interventions and support tools that are not culturally informed are unlikely to improve rates of commitment and compliance or lead to better human and animal health outcomes.
- ABS schemes can be extended to engage with cultural factors by:
 - devising training schemes that raise awareness of ABR among all health care practitioners;
 - developing tools that encourage practitioners to reflect on the cultural norms that influence their prescribing decisions;
 - establishing protocols that enable health care practitioners to question the prescribing practices of their colleagues;
 - promoting action-based, participatory research that devises appropriate interventions and facilitates their translation into different settings.

Further studies are needed to understand:

- how cultural contexts influence diagnosis and treatment in different health care settings;
- the impact of cultural and social factors such as peer pressure, the persistence of beliefs in antimicrobial effectiveness or the so-called “charm”, the implications of individualized benefits versus collective costs of medicine use, and the conservation of efficacy.

Section III. Cultural contexts of ABR transmission

Introduction

Tackling ABR effectively requires addressing the spread and prevalence of antibiotic-resistant microbes and antibiotic resistance genes in clinical and community settings and in built and natural environments. Cultures of travel, trade and tourism all contribute to ABR risk. Addressing the dynamics and drivers of ABR transmission may be as important as, or integral to, tackling antibiotic medicine use (100). For example, the emergence of antibiotic-resistant forms of gonorrhoea is a public health threat that may have similar consequences for sexual practices and culture as AIDS did in the 1980s and 1990s. Disease prevention and condom use would provide the most effective means to reduce sexually transmitted diseases in high-risk settings.

ABR transmission can also occur in the wider environment. Research has found that decreasing antibiotic use does not always correlate with a reduction in ABR rates (101–104). Antibiotic-resistant bacteria and antibiotic-resistant genes can persist and move between species even under low selective pressures (101). This section of the report examines the cultural factors – including the expectations, practices and norms that govern infection control, animal interactions, and food production – that contribute to the spread of ABR in clinical and non-clinical environments and which can be harnessed to interrupt ABR transmission.

Food and agricultural practices and ABR transmission

Shifting cultural practices relating to the nature of human–animal relationships and agriculture shape the spread of ABR. In order to understand and interrupt ABR transmission pathways in agricultural settings, it is important to appreciate the dynamics of food and animal production. The risk of transmission or spillover of resistant bacteria between humans and animals (and vice versa) is more pronounced where there is frequent and close contact. This may be the case in backyard settings, even though they may also involve a much lower use of antibiotics. In larger operations, risks may be related

to poor disposal of animal slurry or waste. This has implications for environmental quality and other cultural uses of environments for drinking, washing and recreation.

Food preparation, storage, distribution, consumption and disposal practices may also influence ABR transmission and constitute a risk to public health (105). In Ethiopia, traditional preparations of camel, cattle and goat milk involve the storage of unpasteurized milk in smoked wooden containers that have natural antimicrobial properties (102). Recently, however, this traditional practice has begun to change, partly in response to the increasing availability of plastic water bottles that can be washed and routinely reused (106). Use of unsterilized water bottles to store milk increases the risk of food poisoning. Therefore, in order to delay the accelerated spoilage process, antibiotics, which are readily available in local clinics and markets, are sometimes added to the milk that is stored in these reused plastic containers. In this case, changes in material culture have affected both antibiotic use and resistance risks.

Changes to food cultures that can impact transmission of resistance are also apparent in higher-income countries. For example, the developing market for probiotics (in human diets as well as livestock feed supplements and treatments) may reduce antibiotic use, but it may also increase resistance risks (105). Unlike short-term colonizing strains of bacteria, probiotics can colonize the intestines for long periods of time. The gastrointestinal tract is a critical site of microbial contact and exchange, known to play a significant role in the development of ABR (108).

Culture and companion animals

Bonds with companion animals are among the most intimate relationships formed between humans and animals in modern society (109). There is an estimated population of over 70 million cats and dogs in EU countries alone (110). Recent studies have noted the “humanization” of pets, with animals being increasingly seen as “kin” (105). In the United States, 62% of small dogs and 62% of cats now sleep in bed with their owners (111). This shifting context marks changes in the frequency and proximity of our everyday interactions not only with domestic animals, but also with their microbes.

The changing status of companion animals is also reflected in veterinary practices, where extending the life of pets and the development of easy-to-administer and long-lasting antibiotics has led to an increase in resistance risk transmission. CIAs are particularly common in treatment of cats (112).

A joint report by the European Centre for Disease Prevention and Control (ECDC), the European Food Safety Authority (EFSA) and the European Medicines Agency (EMA) identified that MRSA infections in companion animals were becoming more common and that the MRSA strains identified were often the same as those observed in nearby hospitals. This was attributed to human transmission to animals, rather than animal transmission to humans, but it was noted that the animals can then become reservoirs for antibiotic-resistant bacteria (113).

European studies point to the ways in which cultural practices in domestic settings contribute to the emergence and accentuation of ABR transmission pathways (Box 4).

Box 4. Companion animals and ABR

Studies in Europe have documented a high occurrence of vancomycin-resistant Enterococci (VRE) in dogs living in urban areas (7–23%) (110). Canine VRE isolates generally exhibit resistance to multiple antimicrobials including macrolides and aminoglycosides (114). In Spain, 23% of surveyed isolates from pets contained VRE. This is considerably higher than the 4% prevalence reported in pigs (114). A consequence of companion animals' status as "kin" in many western societies is an emerging reluctance to euthanize seriously ill or injured pets, with owners favouring treatment instead. Hobby farms are a further example of a shifting cultural trend where human–animal–environment relationships are also being reconfigured. It is possible that the tendency to keep animals alive both at home and on hobby farms for longer will increase the chances of resistance as well as transmission due to more intense animal handling practices.

Hygiene practices, cultural contexts and ABR transmission

In Europe, over 4 million patients each year are affected by hospital-acquired infections (115). Compliance with hand hygiene protocols in hospitals in Europe rarely exceeds 40% (116). High patient workloads and time pressure are routinely cited as key drivers of poor hand hygiene (117). Multidrug-resistant tuberculosis in the WHO European Region has also been linked to structural factors, including poor ventilation systems and overcrowding of prison populations (118). Hand hygiene is a key component of tackling ABR (119), but rising rates of hand hygiene do not always correspond to lower rates of hospital-acquired infections and there are other routes of transmission that have not yet been adequately documented or addressed.

There is some evidence that hygiene practices can be improved by raising self-awareness of working cultures. Upon watching video footage of their own practices, clinicians acknowledged cluttered corridors with computer trolleys that were routinely touched during the transfer of intensive care unit patients. In this instance, a participatory approach to learning allowed clinicians to draw on their own creative competencies and capabilities to change working cultures and practices to limit hospital-acquired infection (120).

ABR transmission can be affected by both domestic and clinical hygiene practices (Box 5).

Box 5. Domestic hygiene and ABR

Infection with antibiotic-resistant organisms in community settings has recently been reported among individuals who are not themselves taking antibiotics or living in proximity to other individuals on a course of antibiotics, which are factors often associated with encouraging ABR (121). This has led researchers to examine the role of domestic antibacterial hygiene and cleaning regimens in contributing to ABR in the community. Researchers have found that antibacterial agents used in cleaning products can confer cross-resistance. This is particularly the case for the antimicrobial triclosan, traditionally found in most liquid hand soaps. The minimum inhibitory concentration for ciprofloxacin increased 94-fold following exposure to triclosan (122). Other antibacterial agents in household products, including pine oil, have also been implicated in conferring cross-resistance (121). In this case, cultures of hygiene and use of particular cleaning products may co-select for resistance and increase community transmission.

The proliferation of antibacterial cleaning products in the domestic setting has been linked to cultural beliefs that all microbes are dangerous or life-threatening, a widespread conviction that can be traced back to the so-called germ panics of the late nineteenth and early twentieth centuries (122). Popular conceptions of microbes as always pathogenic are also reflected in concerns about other dimensions of infectious disease control, such as immunization. Such concerns are shaped by cultural factors, including lack of trust in pharmaceutical companies and fears about potential negative, if unintended, consequences of vaccination against a range of microbial infections. In 2011, in the WHO European Region, there was an unprecedented fourfold increase in cases of measles concentrated in countries with suboptimal vaccine uptake (123). Analysis of qualitative evidence and lived experience can help the interpretation of statistical data of this nature and reveal the cultural contexts in which decisions are made about whether or not to be immunized (123–127). Although many of these studies have focused on viral, rather than bacterial, infections, qualitative research – part historical, part ethnographic – can be utilized to recognize and, where necessary, shift cultural practices and norms in order to reduce ABR and improve health.

Environmental pollution and ABR

Release of antibiotics, antimicrobial-resistant bacteria or antibiotic resistance genes into the environment can exert considerable selection pressures and increase aquatic and terrestrial reservoirs of resistant bacteria (128, 129) (Box 6).

Antibiotics are often discharged directly into receiving environments. Where waste treatment processes do exist, they have not been designed to prevent the release and dissemination of antibiotic resistance genes (134). Cost–benefit analyses of treatment options would need to consider the economics (with the currently high price of initial investment against uncertain and possibly marginal gains in public health), but also the cultures of risk and acceptable levels of pollution. Safe levels of resistance-conferring compounds in the environment are difficult to determine and the evaluation of those risks in terms of acceptability or necessary action make this more than merely a scientific problem – it is an issue of public debate, common concern and budgetary priorities.

Awareness of the political and economic infrastructures that shape waste processing practices and environmental pollution, as well as recognizing how everyday practices influence exposure to drug-resistant bacteria, offers potential pathways for change, particularly by involving those directly affected by ABR. For example, researchers in the United Kingdom are collaborating with the grassroots organization Surfers Against Sewage (SAS) to develop a fuller appreciation of the presence and effects of antibiotic-resistant bacteria in coastal waters (135). By encouraging people to provide microbial swabs, surfers are helping to build a better understanding of how and where ABR transmission occurs. The surfers here are not simply subjects of research. Instead, their experience and expertise of local environments, frequency of ingesting sea water, and their history as an organization that raises awareness of pollution issues, are being utilized to develop insights into the challenge of ABR. This is an example of how participatory research can generate new knowledge about ABR and inspire change.

Box 6. Pharmaceuticals, wastewater and ABR

Many of the antibiotic medicines consumed in the European Region are produced in Hyderabad, India, where antibiotics in wastewater are up to 5500 times higher than the recommended limit (130). High rates of ABR in the environment in India can also be linked to renewed production of fixed dose combination (FDC) medicines that contain two or more active components and have been reported to contribute to the promotion of ABR (131). In 2016, the Delhi High Court overturned an Indian government ban that had prohibited the sale of 344 FDC medicines, pointing to the continuing influence of the pharmaceutical industry.

Environmental pollution occurs not simply from pharmaceutical production facilities, but from other sources, including hospital waste discharge streams. In Europe, it has been estimated that the discharge of antibiotics into wastewater provides conditions for the spread of resistance (132). The quantity of an active substance depends on a variety of factors, including the chemical structure of the antibiotic as well as temperature and pH. The combination of heavy metals present in agricultural environments across Europe has also been implicated in the spread of ABR via co-selection (129). In other parts of the world, treated wastewater irrigation is becoming more popular due to diminishing freshwater resources and growing populations (128).

Policy options

Transmission pathways are complex and shaped by cultural practices, beliefs and attitudes, and by culturally-specific assessments of uncertainty and risk. Similarly to ABR stewardship interventions, ABR transmission and infection control practices may benefit from being co-produced – that is, they can utilize participatory research methods in the humanities and social sciences (outlined in Annex 2) to facilitate understanding of the cultural factors that shape transmission and identify ways of raising awareness and implementing lasting changes.

Research on ABR transmission suggests that:

- antibiotic use is just one part of the ABR challenge;
- recognizing how social and ecological relationships – exemplified in One World, One Health approaches – can affect ABR transmission is likely to result in better health for all;
- cultural contexts can be utilized to generate momentum for change;
- participatory research that facilitates the co-production of knowledge and health interventions can offer new insights into transmission pathways and how they can be interrupted.

Further research is required to:

- understand the complex and multifaceted nature of ABR transmission;
- develop ABR transmission interventions that are flexible and responsive to local cultural contexts;
- determine how qualitative research methods – including the use of history, ethnography and anthropology – can strengthen approaches to ABR transmission.

Section IV. Research and regulatory cultures

Introduction

Tackling complex global health challenges such as ABR requires new forms of interdisciplinary collaborations, technological investment, novel health care practices, and social innovation, in which all relevant sectors of society are involved (136). However, research methods and partnerships, regulatory environments, and health care services are all framed by their own cultures of practice, as well as by specific cultural perceptions of microbes, that can either enhance or impede attempts to address ABR. These cultural values, practices and perceptions need to be understood and challenged – and in some cases reinforced – in order to effect change.

Cultural dynamics of the development of medicines

The decades after the Second World War are widely regarded as a golden age of antibiotic discovery (95). During that time, pharmaceutical companies such as Pfizer, Lederle and Parke-Davis developed and marketed a wide array of so-called antibiotic wonder drugs (21). Since the 1970s, however, only two new classes of antibiotics have been introduced onto the market (95). The development and availability of effective antibiotic medicines is an important part of tackling the ABR challenge. In some parts of the world, especially in some LMICs, the critical challenge is not how to restrict inappropriate use of antibiotics, but how to increase access to and broaden the range of available antibiotics (137). Concerns about ABR should not therefore serve to demonize antibiotics or hinder the development of new antibacterials, but rather address the challenge of encouraging efforts to regulate or restrict antibiotic use in some settings, while promoting the generation of new replacement antibacterial agents and vaccines and expanding appropriate access in other settings in order to enhance health and sustainable development (138). In this context, it is important to recognize that cultural and social factors, including investment in different structures of innovation and an unquestionable faith in science's ability to eradicate disease, have combined to impede the development and production of new antibacterial agents (Box 7).

In recent decades, clinicians, regulators and politicians have been concerned about low rates of development of new antibiotics. More recently, there have been calls for changes to the regulatory and business environment so that replacement and more sustainable therapies and smarter diagnostics can be brought to market (95). Tackling ABR today requires challenging still widespread assumptions about the capacity of medicine to treat infectious diseases and developing new regulatory cultures of pharmaceutical innovation that decouple profits from sales in order to incentivize the development of less lucrative but effective medicines (144). A system of prizes goes some way to address the economic disincentives for research and development, even though recent reports have suggested that price expectations for medicines and diagnostics are too low to sustain development, and that finance or funding from health services is unlikely to be forthcoming. These barriers are particularly pertinent in LMICs, where markets will need to be primed, but all countries may need to provide initial purchase guarantees in order to maintain innovation. In the current cultures of public spending and privatization of services, these conditions may be difficult to foster unless the health impacts of ABR reach certain tipping points. This is in part a matter of cultural awareness and the development of a public mandate for action.

Box 7. Cultures of development and innovation

In 1967, William Stewart, the Surgeon General of the United States of America, famously stated that the “time has come to close the book on infectious diseases” (139). Stewart’s comments reflected a dominant cultural view of the world where nature was thought to be under control and the dangers to health of microbial life forms could be managed through a combination of human ingenuity and increasing scientific knowledge. At that time, many scientists believed that, at least in high- and upper-middle-income countries, infectious diseases were largely under control.

From the late 1960s, beliefs in the capacity of scientific medicine to control, or eradicate, infectious diseases contributed in part to a move away from the development of antibiotic medicines. Companies focused instead on developing antibiotic analogues (95), and on the production of more lucrative patent-protected medicines used over prolonged periods of time. Antibiotic analogue development was a low-risk innovation strategy compared to the development of new antibiotic classes, which were not only deemed more and more unnecessary but were also subject to expensive and increasingly regulated clinical trial processes (95, 141). In this climate, antibiotic development laboratories and research programmes were shut down (142), which led to a loss of scientific and technological infrastructure and skills (95).

“Treat hard, treat long” as culturally contingent knowledge

The injunction to treat bacterial infections “hard” and “long” has been a central dogma of modern Western medical practice throughout the twentieth century (145). However, it is important to recognize that such medical orthodoxy was established in a very different historical and cultural context and is no longer necessarily supported by evidence or appropriate to the complex health challenges posed by ABR (Box 8).

Although there is considerable uncertainty about the appropriate length of antibiotic treatment regimens, ensuring adherence to treatment regimens also requires an engagement with cultural and social factors that can be deployed to improve compliance and mitigate the risk of ABR. Partners in Health (PIH) and Tomsk TB Services in the Russian Federation have engaged explicitly with sociocultural factors in their work to tackle multidrug-resistant tuberculosis. The success of the “Sputnik” programme in Tomsk, which aims to enhance adherence and improve outcomes in the treatment of drug-resistant tuberculosis, can be attributed in part to its attentiveness to the social and cultural factors that can prevent compliance, including unemployment, lack

Box 8. Scientific knowledge and clinical trials in cultural context

In the early 1900s, German scientist and physician Paul Ehrlich, whose work led to the introduction of Salvarsan as a “magic bullet” to treat syphilis, believed that the best way to treat bacterial infection was to eradicate the causative organism through a long and powerful course of treatment (146).

Ehrlich’s “treat hard, treat long” mantra has been contested for some years (147). Research has found that treatments lasting 2, 3, 5 and 10 days can be equally effective in treating otitis media in children (145). However, contemporary clinical trials and practices still rely on assumptions stemming from Ehrlich’s earlier understanding of infection. For example, inflammatory markers are used to measure the presence of causal organisms and to assess the subsequent effectiveness of an antibiotic regimen (145). However, inflammatory reactions can continue well after the infection has been countered (145), which means that overreliance on inflammatory markers can result in unnecessarily long durations, increasing the risk of ABR. This culturally contingent understanding of microbes, eradication and inflammation became embedded within early clinical trial programmes, which stipulated that new antibiotics must be compared to already existing treatment regimens (64).

of family support and limited access to health care services. The programme encouraged adherence to the treatment regimen by ensuring that patients had sufficient food to take their medications and sufficient support to access health care facilities (143). Both qualitative and quantitative evidence from the studies indicated that compliance and recovery rates could be improved by closer alignment of medical advice and health care services with the cultural contexts of those most at risk of drug-resistant infections (144).

There is a public health implication to this differentiation of treatment regimens. The standard public health advice to complete a course, and to treat hard and long, should not necessarily be changed. However, as this viewpoint is publicly questioned and becomes a matter of debate within wider culture in light of ABR, a more refined message that stipulates treatment regimens in relation to specific conditions or diseases will be needed.

Cultures of science communication

Many contemporary health challenges are characterized by complexity and scientific uncertainty. In the case of infectious diseases, for example, the appropriate treatment course for many upper and lower respiratory tract infections is not entirely clear, partly because those infections are caused by a variety of different organisms and vary in severity under different social conditions (140). As a result, there is rarely a definitive answer as to what constitutes the appropriate or best course of antibiotics. One specific challenge relating to complex health issues of this nature is communicating complexity and indeterminacy in specific cultural contexts that are often marked by diminishing public trust in science. It has long been presumed that public health messages must be simple, clear and instructive, a presumption that is based on prominent cultural beliefs that uncertainty creates anxiety and mistrust and may drive irrational and unhealthy behaviour (145, 146). Research suggests that this presumption may be counter-productive as attempts to deny uncertainty may in fact increase feelings of mistrust in certain forms of knowledge and expertise (Box 9).

Developing effective and affirmative health campaigns and educational messages requires acknowledging: (a) the limits of scientific knowledge; and (b) the ways in which scientific indeterminacy is utilized to serve specific social, political and professional agendas. Cultural contexts and preferences influence which types of knowledge and expertise are trusted (150). Understanding cultural contexts is a critical part of designing effective ABR communication strategies and enhancing cooperation and collaboration.

Changing cultural norms: microbes and antibiotics

Belief in the need to kill bacteria with antibiotics in order to treat infections has been a defining pillar of microbiology for over a century (141). However, tackling ABR effectively requires both a reconsideration of what antibiotics are and a greater understanding of attitudes to microbial life forms. Developing new cultures of collaboration, questioning pre-existing forms of knowledge, and shielding research from purely commercial determinants can help to create novel understandings of human–microbe relationships and, in the process, generate fresh strategies for tackling ABR. Researchers

Box 9. Trust and scientific expertise: cultural determinants

Controversies such as the bovine spongiform encephalopathy crisis in France and the United Kingdom have contributed to a growing lack of trust in scientific institutions and expert figures (147). During disputes about appropriate methods of managing the crisis, scientific complexity was intentionally downplayed, generating distrust in authority figures and institutions.

We are, more recently, entering into what has been described as an era of misinformation or post-truth (148), when scientific uncertainty and emotional insecurities are being exploited to support conflicting and contested courses of action (149). This shifting cultural context is exacerbating already fraught relationships between publics, scientists, organizations, and institutions.

Studies of the cultural contexts that shape public trust in science suggest that health education campaigns should move away from cultural preferences for scientific closure towards an explicit and careful engagement with the limits of scientific knowledge.

at the New York University School of Medicine, for example, are developing molecules which interfere with the ability of bacteria to communicate and cluster together into biofilms (141). In addition, research increasingly reveals that antibiotic use cannot be understood as an individual intervention that attacks a target infection in a single body, but that infections and their treatment are often collective social events (151, 152). If one member of a household is prescribed an antibiotic, other members of that household are likely to have higher levels of antibiotic-resistant bacteria on their skin (151, 152). ABR is thus calling into question scientific understandings of biological relations and genetic variation and highlighting the need to evaluate cultural norms and practices more rigorously.

Prevalent beliefs that all so-called germs are harmful are being challenged by scientific and clinical evidence, as well as by shifting cultural attitudes, beliefs, and practices. Some studies have emphasized the role of germs in aiding and boosting our immune systems (31, 153, 154), a phenomenon that is evident in debates about the part played by hygiene, vaccination and overuse of antibiotics in driving rising levels of allergic diseases (155, 156, 157). This shift towards recognizing the value, rather than the threat, of bacteria is apparent in accounts of the ways in which human life is dependent on the human microbiome, which comprises the genes of the 10–100 trillion microbial cells in each person (158). It is also suggested by the rising popularity of practices such as faecal transplants (159). These examples suggest that shifting cultural norms and social values can help to redefine human–microbe relationships and might be used as a resource to open up new understandings of microbial life in order to address the challenge of ABR.

Reorienting research to reconfigure understandings of the roles of microbes, ecological relations, hygiene practices and antibacterial agents in shaping ABR requires flexible funding strategies that encourage multidisciplinary collaboration across the humanities, social sciences and biomedicine. This approach is already driving some research strategies and funding schemes: researchers working within the One Health paradigm, for example, are already working across disciplines to reconfigure research questions and create pathways for novel solutions (160); and the United Kingdom Medical Research Council has made multidisciplinary collaboration one of the key criteria of its recent research funding (161).

Policy options

Addressing ABR effectively requires acknowledging that scientific knowledge and regulatory policies are produced, communicated and evaluated within particular cultural contexts and that understandings of both microbes and antibiotics are open to challenge and change.

Research findings suggest that:

- tackling ABR effectively requires innovative forms of research and funding that allow new evidence, understandings, and interventions to emerge;
- multidisciplinary collaboration is essential to tackling ABR; collaborative research can pose new questions, generate new methods, and evaluate new forms of both qualitative and quantitative evidence.

Further research is needed to understand:

- how cultural factors determine the feasibility of multidisciplinary collaborative research in practice;
- how cultural contexts influence relationships between public, scientific, communication, and policy communities.

Conclusion

ABR constitutes a formidable threat to global health and sustainable development as set out by the 2030 Agenda and the Sustainable Development Goals. It has been estimated that, without an effective response, resistance to antimicrobial compounds might result in approximately 10 million deaths per year worldwide by 2050. Over recent years, mounting concerns about ABR have resulted in national, regional, and global action plans aimed at improving awareness, promoting research, and optimizing the current use of and access to antibacterial medicines. Global initiatives have also stressed the importance of investing more effectively and sustainably in technological development and cross-sectoral interventions.

This policy brief has examined how cultural factors shape antibiotic use, the transmission of ABR, and the protocols that define how ABR is researched and regulated. Drawing inspiration from Health 2020, which focuses on the importance of understanding subjective experiences of health and illness, gathering and disseminating new forms of qualitative evidence, and addressing the cultural contexts of health and well-being, the case studies presented here suggest that a cultural perspective should be considered a critical component of ABR research. In particular, the policy brief advances several arguments that policy-makers should consider when formulating strategies to address ABR.

- Scholarship within the humanities and social sciences – with a focus on participatory research, the co-production of knowledge and practice, and the generation and analysis of qualitative evidence – can effectively complement and enhance scientific, technological and regulatory approaches to ABR.
- Culturally-informed interventions can lead to greater rates of commitment and compliance and better health outcomes. ABS schemes should be extended to engage with cultural factors by developing training and tools that raise awareness and encourage practitioners to reflect on the cultural norms that influence their prescribing decisions. Efforts to prevent and control the transmission of ABR need to take account of social and ecological relations and make use of participatory research to produce new insights into transmission pathways and how to interrupt them.
- Scientific knowledge and regulatory policies are produced, communicated and evaluated within particular cultural contexts.

In other words, how microbes and antibiotics are understood is open to challenge and change. By posing new questions, generating new methods, and evaluating new forms of both qualitative and quantitative evidence, multidisciplinary collaboration is an essential part of tackling ABR.

The policy brief also acknowledges, however, that further research is needed to:

- understand how cultural factors impact differently in different health care settings;
- elaborate how cultural contexts contribute to the diagnosis and treatment of specific infectious diseases;
- show how cultural factors – such as peer pressure, the perceived charm of antibiotics, or the taste and cost of medicines – shape adherence to antibiotic prescriptions and create the conditions for change;
- better conceptualize the complex and multifaceted nature of ABR transmission in order to develop ABR transmission interventions that are flexible and responsive to local cultural contexts;
- determine how narrative evidence, participatory research and co-produced knowledge can help to strengthen approaches to ABR transmission; and
- understand the cultural factors that determine the feasibility of multidisciplinary collaborative research in practice, and the cultural contexts that influence relationships between public, scientific, communication, and policy communities.

Although this policy brief has focused on ABR, the approaches presented here can be translated to other challenges to global health and sustainable development. Addressing complex health challenges involves understanding beliefs, values and norms across many sites. It also requires the involvement of people affected by the challenge in designing, implementing and evaluating changes in practice. Through specific case studies, this report has highlighted how interventions that are poorly in tune with the cultural contexts and social dynamics within which they operate, or which exclude those affected from the research, are unlikely to achieve desirable outcomes. Taking social and cultural factors into account can help to develop more effective and sustainable practices and policies and facilitate better health outcomes for all.

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Annex 1. Research Methodology

The recommendations and conceptual model developed in this report are based on an extensive review of multiple bodies of relevant literature. Leading databases, including EBSCO and the Cochrane Library, were searched with a combination of specific and free text terms including “antibiotic resistance”, “social” and “cultural”. Searches were also conducted through Google Scholar. Experimental search terms such as “guideline implementation limitations” and “social relations” were utilized to identify and retrieve relevant publications. Over 450 publications were downloaded and read as part of the review process. These publications were then grouped into 27 categories, including AB Clinical Environments, AB Policy and Research, AB Transmission, and AB Low-Income Countries & Global Health. Documents were coded and analysed through an iterative process, which enabled key sensibilities to be identified and integrated into the cultural contexts of health conceptual framework.

Annex 2. Participatory research methods

Components of the ABR challenge in need of addressing	Desired end-goals	What are the key challenges and issues that should be considered?	What and how can social science methods help?	What are the outcomes that emerge from utilizing these approaches?
<p>Awareness of and engagement with ABR as a critical health concern</p>	<ul style="list-style-type: none"> • Informed publics • Greater awareness • Attitude change • Willingness to engage with issue and contribute to change • Participation in ABR interventions 	<ul style="list-style-type: none"> • Technicality of subject matter. There is, to some extent, a lack of understanding among individuals and publics regarding what ABR is and how it occurs. At the same time, it is important not to assume that there is always a knowledge deficit. Assuming that there is a knowledge deficit leads to an emphasis on top-down biomedical guidelines and instruction. This report has demonstrated that top-down biomedical guidelines and instruction are routinely diffracted in practice because they have to compete with other sociocultural norms and knowledges – for example, social hierarchies, cultures of mistrust • Contemporary cultures of scepticism surrounding science and government • Scientific indeterminacy – we do not have all the answers and the answers are likely to change over time due to the complexity of ABR and the emergence of ABR at the shifting intersection of biological and social relations • Beliefs do not always translate into practice – high physician awareness of ABR and physician belief in the need to take action is often diffracted in practice as physicians navigate and juggle patient demands and the need to provide care. Immediate concerns take priority and the threat of ABR has been found to be externalized or attributed to other physicians, practitioners and actors. 	<ul style="list-style-type: none"> • Video-reflexive ethnography, for example, during GP consultations, enables practitioners to reflect on what they do and why. It can help to shed light on why there exists a beliefs/ awareness–practice gap – that is, why, in spite of awareness of ABR amongst some GPs, antibiotic medicines are still prescribed. This might be in response to perceived patient pressure. It might also be in response to the pressures of high patient–doctor ratios and an acknowledgement of poor living conditions faced by patients in specific communities • Home video diaries can help to shed light on shifting cultural understandings of and relations to microbial life (Wood, 2016) • Focus groups can open up an engagement with attitude differences • Q methods help to identify and group together different subjectivities • Note: Interviews alone are insufficient tools to develop an understanding of ABR awareness amongst diverse publics and stakeholders. This is because interviews predominantly access beliefs. Beliefs rarely translate seamlessly into practice. 	<ul style="list-style-type: none"> • ABR interventions which utilize an approach that makes sense to target audiences can help to prevent the externalization of the ABR threat – that is, its attribution to other people and practices • Better relations between ABR stakeholders – for example, publics, government, health practitioners, are likely to emerge through approaches which recognize cultures of mistrust, and acknowledge that practitioners are often experts in their own practices • A shift away from the predominant emphasis that is placed on knowledge campaigns (which are limited in their effect and longevity) to more collaborative engagement with diverse publics and bottom-up solutions

Components of the ABR challenge in need of addressing	Desired end-goals	What are the key challenges and issues that should be considered?	What and how can social science methods help?	What are the outcomes that emerge from utilizing these approaches?
<p>Long-term changes to prescribing practices in diverse settings – for example, hospitals, GP clinics, on the farm</p>	<ul style="list-style-type: none"> • Ongoing commitment to change • Ownership of issue • Iterative, flexible and responsive practice • Appreciation of diverse actors and influences on practice 	<ul style="list-style-type: none"> • Top-down interventions miss the social norms and cultural contexts of working as well as the diverse influences which shape practice – all of these must be taken into account if change is to be sustained and implemented effectively • Interventions unlikely to be implemented if they violate social norms and cultural contexts • Changes to practice can generate unintended consequences, exacerbating mistrust and ambivalence 	<ul style="list-style-type: none"> • Participatory mapping – helps to identify the multiple dimensions and influences on practice which external and top-down interventions cannot access • Video-reflexive ethnography can help practitioners to reflect on why they do what they do – for example, junior doctors overusing broad-spectrum antibiotics because they are reluctant to ask for help in a competitive and hierarchical work environment • Focus groups – these can allow stakeholders to bring up issues that matter to them, offering an insight into the realities of their practices • Interviews – see details in box above 	<ul style="list-style-type: none"> • Novel strategies for change – for example, development of training mechanisms which empower GPs to engage in challenging conversations with their patients; training mechanisms which empower junior hospital staff to question the practices of their superiors • Resonance and compatibility of ABR interventions – preventing externalization of the ABR threat • Effective engagement with key knowledge brokers and intermediaries that matter – for example, in the hospital, top-down stewardship interventions have been found to miss the influences on prescribing exerted by non-prescribers such as nurses (Broom et al., 2017). In some farm settings, farmers have been found to be more responsive to knowledge and information when relayed by fellow farmers and trusted veterinarians rather than government bodies (Lam et al., 2011).
<p>Long-term changes to transmission practices; modification of transmission pathways</p>	<ul style="list-style-type: none"> • Ongoing commitment to change • Ownership of issue • Iterative, flexible and responsive practice • Appreciation of diverse actors and influences on practice 	<ul style="list-style-type: none"> • Scientific uncertainties and indeterminacies pervade transmission pathways – they can be used by diverse bodies and publics to either call for action to be taken or for no action to be taken • Changes to practice can generate unintended consequences, exacerbating mistrust and ambivalence 	<ul style="list-style-type: none"> • Video-reflexive ethnography has been usefully applied in hospitals, enabling practitioners to reflect on their practices (for example, handwashing, touching of patient) and to identify previously unconsidered transmission pathways (Ledema et al, 2015). • Participatory mapping – similarly to video-reflexive ethnography, can visualize the full range of processes and practices which shape transmission 	<ul style="list-style-type: none"> • Contextually specific strategies for action which position diverse practitioners as knowledgeable experts
<p>Policy and innovation frameworks</p>	<ul style="list-style-type: none"> • Iterative and novel approaches to addressing ABR 	<ul style="list-style-type: none"> • Entrenched norms of organizational and policy work • Taken-for-grantedness of specific assumptions • Need to cultivate new skills • Benefits of experimental approaches to policy-making can be hard to articulate 	<ul style="list-style-type: none"> • Cross-institutional and multidisciplinary competency groups can help to expose assumptions and encourage novel approaches • Scenario development and creative foresight thinking 	<ul style="list-style-type: none"> • Legitimization of experimental approaches • Moving beyond confines of rigid and economic approaches to evidence and cost-benefit analysis

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