When the Drugs Don't Work

Antibiotic Resistance as a Global Development Problem

Dag Hammarskjöld Foundation

ReAct

Authors
Maarten van der Heijden, ReAct
Andreas Sandgren, ReAct
Maria Pränting, ReAct
Matti Karvanen, ReAct
Helle Aagaard, ReAct
Anna Zorzet, ReAct
Mengying Ren, ReAct
Otto Cars, ReAct

Production Lead
Maarten van der Heijden, ReAct
Karin Abbor-Svensson, Dag Hammarskjöld Foundation

Graphic design
Kristin Blom, Dag Hammarskjöld Foundation

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Photos
The Swedish award-winning photographer Paul Hansen takes on the threat of multiresistant bacteria in the exhibition *Hand to Hand* at Fotografiska, a museum in Sweden. 'These images are not confined by countries or nationality for the simple reason that diseases and bacteria do not know any borders', says Paul Hansen. ReAct and the Dag Hammarskjöld Foundation are most grateful to photographer Paul Hansen and Fotografiska for letting us include these photos.

Paul Hansen is a Swedish multi-award winner and one of the world's most respected photojournalists. He has won the prestigious award World Press Photo, POYI's Photographer of the Year twice and the Photographer of the Year in Sweden eight times. Paul Hansen tries to convey a message that everything in the world interlinks, bringing his camera to war zones and countries in crisis, as well as taking snapshots of everyday life.

This publication builds on the Dag Hammarskjöld Foundation's Development Dialogue paper 'Antimicrobial Resistance - a Threat to the World's Sustainable Development' connecting antimicrobial resistance (AMR) and the Sustainable Development Goals (SDGs) from 2016.

This paper provides a more detailed analysis of the negative impact of antibiotic resistance on global and national efforts in order to:

- *eradicate poverty (SDG 1)*
- *spur economic growth (SDG 8 and 12)*
- *reduce inequality (SDG 5 and 10)*
- *improve global public health (SDG 3)*
- *reduce hunger (SDG 2), and*
- *protect the environment (SDG 6, 14 and 15).*

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Antibiotic Resistance as a Global Development Problem

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Executive summary

Why is there a need to address antibiotic resistance in the context of the Sustainable Development Goals? Because antibiotics play a crucial role in many more areas of life than most people imagine. However, antibiotics are starting to lose their effectiveness due to resistant infections, and the consequences will be far-reaching if decisive and rapid action is not taken globally and systematically. Antibiotic resistance would seriously jeopardise the achievement of several of the Sustainable Development Goals (SDGs). Therefore, antibiotic resistance must be included in the work on sustainable development, and should be seen as a strong additional reason to urgently increase the work on the Sustainable Development Goals.

Urgent solutions needed

There is a belief that innovation of new antibiotics will out-pace the development and spread of resistant bacteria. However, without rapidly addressing the way antibiotics are currently over- and mis-used, there is no chance of winning this race. Novel antibiotics will continue to play an important role, but they will not be enough. Antibiotics must be seen as a non-renewable resource. And just like in climate change, if this natural resource is exhausted, there will be nothing left for future generations. Managing antibiotic resistance relies on limiting use of antibiotics, discovery of new antibiotics or alternative ways to treat infectious diseases, but also on preventing infections and limiting spread of resistance. There are no quick fixes – antibiotic resistance is a systems failure and thus all sectors need to contribute to a change and jointly securing that antibiotics remain effective.

This report focuses on the Sustainable Development Goals related to poverty, economic growth, inequality, health, food production and the environment:

Economic growth – Poverty

Economic growth is strongly linked to the achievement of many of the Sustainable Development Goals and is currently the main force that lifts people out of poverty.

People living in poverty are not only more susceptible to resistant infections but are also less able to prevent or respond to them. Antibiotic resistance can breed poverty, while poverty feeds the problem of antibiotic resistance. This negatively impacts the efforts of countries and donors to eradicate poverty.

Health – Inequality
Keeping antibiotics effective for treating infectious diseases relies heavily on the work on the Sustainable Development Goals. At the same time as many areas of modern medicine, including cancer treatments, surgery, transplantations, complicated deliveries and treatment of preterm babies, are largely reliant on effective antibiotic treatments. Antibiotic resistance risks furthering inequalities within societies. To prevent deeper inequality through infectious diseases, groups that are extra vulnerable to antibiotic resistance should receive increased attention.

Food – Food production – Environment
Antibiotic resistance in animals threatens the sustainability of food production, the livelihood of farmers and therefore food security as well as food safety, and indirectly harms economic growth. Work on antibiotic resistance should become an essential element in the work towards sustainable food production systems and resilient agricultural practices. Antibiotics and resistant bacteria enter the environment along the supply chain from manufacturer to the end user, both in human and animal consumption. Antibiotics in the environment are a driver of resistance in microbial ecosystems.

Clean water and appropriate sanitation are major drivers of change and reduce the spread of pathogens to humans and animals.

Because of its urgency, antibiotic resistance should receive special attention on the national and global levels as a systems failure both in healthcare and agriculture. To limit the effects of antibiotic resistance, it must be considered a critical sustainable development issue. To achieve progress to meet this challenge, political will and action is urgently needed. This paper aims to support decisionmakers in taking appropriate and informed actions for lasting impact across sectors in the work to implement Agenda 2030 and National Action Plans on Antimicrobial Resistance.

Introduction

Antibiotics have paved the way for development

One hundred years ago, infectious diseases accounted for high morbidity and mortality worldwide. The average life expectancy at birth was often less than 50 years in countries with the best healthcare systems. Infectious diseases such as cholera, diphtheria, pneumonia, typhoid fever, tuberculosis (TB) and typhus were widespread. The antibiotic era revolutionised the treatment of infectious diseases worldwide. Antibiotics are however not used only for treatment of disease in humans, they are also crucial in treating sick animals, and thus resistance seriously threatens food security of populations and the income of those reliant on agriculture.

Effective antibiotics are critically important cornerstones of all health systems, but bacteria becoming resistant threatens their continued lifesaving value. Entering a post-antibiotic era could have devastating impacts on global public health as well as the global economy.

Antibiotic resistance alone, including drug-resistant tuberculosis already claims more than 750,000 lives* every year. Low- and middle-income countries will likely bear the brunt of the negative consequences. They would bear the combination of the greatest burden of infectious diseases and the weakest health care and agricultural systems.

This report focuses on the Sustainable Development Goals (SDGs) related to poverty, economic growth, inequality, health, food production and the environment. Additional Goals can also be affected or tied to the issue. For instance, Goal 4 related to education should cover education on health, infectious disease

Antibiotics vs antimicrobials

Antibiotics are a type of antimicrobial medicine alongside antivirals, antifungals and antiparasitic agents. Resistance development to all of these medicines is what is known as antimicrobial resistance, whereas resistance development in bacteria only is known as antibiotic resistance. Sometimes however, these terms are used interchangeably. This report focuses on antibiotic resistance, unless where specifically noted. However, many of the problems and potential solutions are shared between the two.

and the use of medicines; and Goal 9 on industry and innovation is affected through the need for antibiotics, diagnostics, vaccines and other innovative solutions across different sectors. Another big challenge posed by antibiotic resistance is that of Goal 17, related to forming global partnerships.

The Sustainable Development Goals are deeply interconnected and many goals and targets rely on one another to achieve the envisioned state of wellbeing and sustainability. Antibiotic resistance knows no sectorial limits, country borders or other divisions and therefore requires a level of cooperation that other challenges have not demanded before.

*A conservative estimate that includes resistance to antibiotics (also in tuberculosis), but which excludes drug resistant HIV, extrapolated from four data sources:
1. Phumart, P. *et al*. Health and Economic Impacts of Antimicrobial Resistant Infections in Thailand:
A Preliminary Study. *J. Health Sys. Res.*. 6, 352–360 (2012).
2. Centers for Disease Control and Prevention - CDC. Antibiotic resistance threats in the United States. (2013).
3. European Centre for Disease Prevention and Control - ECDC, European Medicines Agency - EMA. The bacterial challenge: time to react. A call to narrow the gap between multidrug-resistant bacteria in the EU and development of new antibacterial agents Luxembourg: EUR-OP. (2009).
4. World Health Organization - WHO. Global Tuberculosis report. (2017).

People living in poverty are more likely to get sick from resistant infections and are also less able to prevent or get well from them. Antibiotic resistance can breed poverty, while poverty feeds the problem of antibiotic resistance. Photo: Paul Hansen

Poverty

Goal 1: Eradicate extreme poverty

1 NO POVERTY

- People living in poverty are not only more vulnerable to antibiotic resistance, but are also less able to prevent or treat antibiotic-resistant infections.
- The World Bank projects that 24.1 million people could fall into extreme poverty by 2050 because of antimicrobial resistance, most of these people would come from low- and middle-income countries.
- Antibiotic resistance can breed poverty, while poverty feeds the problem of antibiotic resistance. This negatively impacts the efforts of countries and donors to eradicate poverty.
- Poverty alleviation strategies can contribute to addressing antibiotic resistance.

The high burden of infectious diseases among people living below the poverty line

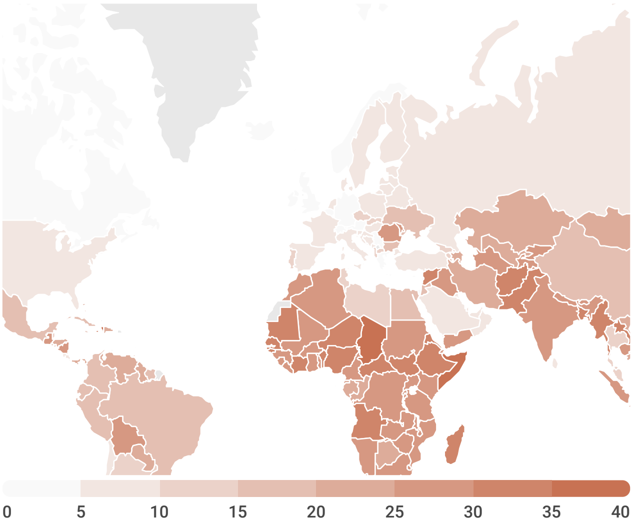
Antibiotic resistance worsens an already high burden of infectious diseases in low- and middle-income countries. According to the World Health Organization (WHO), infectious diseases (including HIV, tuberculosis (TB) and parasitic diseases) were together responsible for the death of more than 8.4 million people worldwide in 2016.[1] Economically disadvantaged people living in low- and middle-income countries suffered the majority of these deaths. Lower-respiratory infections and diarrheal infections are the leading causes followed by TB and HIV/AIDS.[1] In addition, roughly 3 million newborns and 1.2 million children under five suffer from sepsis every year, which causes over half a million deaths.[2–5]

'If we fail [to address antibiotic resistance], we will pay for it through our wallets, but the poor will pay for it with their lives'

Participant speaking on antibiotic resistance at the World Health Organization's Primary Healthcare Meeting (Alma Ata 2.0, 25-26 October 2018 - Astana, Kazakhstan)

Impact of infectious diseases on death of children

The role of sepsis, pneumonia and diarrhoea
in deaths of children under 5 (percentage per country)



Figures are extracted from data gathered in 2016 by WHO, mortality estimates for sepsis, pneumonia and diarrhoea have been summed and rounded.

Several factors affect people living in poverty: One in three people do not have a basic toilet; 2.1 billion people do not have access to safely managed drinking water and one in every eight people – an estimated 890 million people – currently defecate in the open.[6–8] This leads to infections spreading faster which in turn results in an increased consumption of antibiotics. This, in combination with poor nutrition and suboptimal housing conditions, puts populations living in poverty at greater risk of contracting infectious diseases. It also increases their exposure to resistant bacteria and in that way could increase the stigma of infectious disease being diseases of the poor and marginalised.[9,10] Health inequalities are strongly interlinked with other inequalities in society and place individuals or populations already vulnerable at a further disadvantage in terms of infections.[11]

In low- and middle-income countries many people lack access to basic healthcare facilities. In the cases where they do have access, people are often required to pay out-of-pocket for healthcare services and commodities, including for periods of hospitalisation. Poverty may therefore lead to people attempting to self-medicate or see traditional or unqualified practitioners, rather than seeking the help of qualified healthcare professionals. This increases the risk of inappropriate use of antibiotics, which drives resistance.

A recent report from the World Bank projects that 24.1 million people could fall into extreme poverty by 2050 because of antimicrobial resistance (including resistance in malaria and HIV).[13] A vast majority of these would live in low- and middle-income countries. The devastating impact this would have both at the individual household level and for the countries' economies would endanger efforts made to reach SDG 1 – to end poverty in all its forms by 2030.

The crucial role of affordable and effective medical care

Access to affordable and effective medical care and treatment plays a crucial role in addressing the burden of bacterial infectious diseases. Antibiotics have generally been relatively affordable compared to other medicines over the last decades. Recently however, many old generic antibiotics have undergone price hikes up to 400% and new antibiotics entering the market have proven very expensive, also for high-income countries.[14–17] Pharmaceutical companies are calling for increased prices or longer monopolies on their antibiotics through patents or other mechanisms, but are not committing to ensure local registration, wide availability and affordability of medicines in low- and middle-income countries.[16,18]

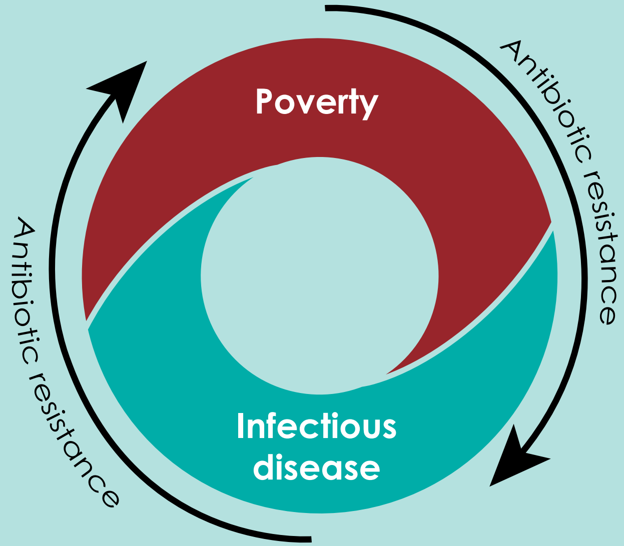
At the same time, up to 90% of the population in low-income countries are paying for their medicines out-of-pocket.[19–21] This already translates to around 25%–70% of total income being spent on healthcare, making medicines the largest family cost after food.[21]

Antibiotic resistance adds to these costs in several ways. Treatment of resistant infections may:

1. depend upon second and third line antibiotics that often are far more expensive,
2. take longer and have less chances of success, and
3. require hospitalisation that with alternative antibiotics would not have been necessary.

All of this puts an additional strain on household incomes. For example, one study points to the relationship of user fees and antibiotic resistance, noting that: 'Out-of-pocket health expenditures were strongly correlated with antibiotic resistance in low- and middle-income countries' and in particular that '[t]his relationship was driven by countries that require co-payments on medications in the public sector.'[22]

Antibiotic resistance accelerates the vicious circle of poverty and infectious disease



People living in poverty are more prone to infectious diseases

Circumstances of poverty increase the spread of antibiotic resistance

The cost of having an infectious disease drives people into poverty

Antibiotic resistance significantly increases cost of treatment driving people into poverty or making treatment inaccessible

Poverty alleviation as a strategy to reduce antibiotic resistance

WHO's report on the social determinants of health emphasises that actions that eradicate poverty are essential for health and wellbeing.[29] This includes improvement in primary healthcare, universal health coverage and quality of care. Similarly, a recently published study makes the argument that poverty reduction and social protection coverage are key to sustainably addressing TB.[30]

Over the last decades there has been a large increase in the use of antibiotics in low- and middle-income countries and consumption rates are rapidly converging to rates in high-income countries.[31] While these numbers are silent on how much of this increase is appropriate, at least some of the increase can be explained by previous underuse and lack of access in these countries.

There is no doubt that access to working antibiotics has played an important role in the overall reduced rates of mortality and morbidity from infectious diseases in low- and middle-income countries over the last decades. Affordable and working antibiotics are essential to those most marginalised and impoverished to live healthier and more productive lives. Poverty alleviation strategies that are sensitive to antibiotic resistance could reduce the vicious circle of infectious disease and poverty.

The expansion of vaccine plans to prevent antibiotic resistance

Prevention of disease will play a huge role in limiting the effects of antibiotic resistance and reducing antibiotic use. Pneumonia, for instance, is a disease from which all children across the world suffer, but nearly all deaths occur in low- and middle-income countries. Pneumonia is a leading cause of vaccine-preventable illness and death among children under five years old in India and many other countries, so expanding access to vaccination can have a major impact on deaths from pneumonia caused by resistant bacteria.[30] In addition, more than 11 million antibiotic days could be avoided annually as a result of universal pneumococcal conjugate vaccine availability.[31]

The economic consequences of antibiotic resistance may be devastating due to increased treatment costs which drain funds, increased morbidity and mortality which affect the possibility to make a living and lead to decreased productivity and labour supply. Photo: Paul Hansen

Sustainable economic growth

Goal 8: Promote sustained, inclusive and sustainable economic growth, full and productive employment and decent work for all

8 DECENT WORK AND ECONOMIC GROWTH

Goal 12: Ensure sustainable consumption and production patterns

12 RESPONSIBLE CONSUMPTION AND PRODUCTION

- Economic growth is strongly linked to the achievement of many of the sustainable development goals and is currently the main force that lifts people out of poverty.
- Economic growth will lead to increased antibiotic consumption in low- and middle-income countries when more people are able to afford diagnostics and treatment.
- The World Bank estimates that between 1.1% and 3.8% of global GDP could be lost due to antimicrobial resistance if left unchecked, which is roughly the same as the global economic impact of climate change.

How does antibiotic resistance impact economic growth?

Economic growth (SDG 8) is strongly linked to the achievement of many of the SDGs and is currently the main force that lifts people out of poverty, but can be undermined by antibiotic resistance in many ways. The macro-economic consequences may be devastating due to:

1. increased treatment costs which drain funds,
2. increased morbidity and mortality which affect the possibility to make a living and leading to decreased productivity and labour supply.

At the household level, the increased costs of treatment and loss of income places a heavy burden on household economies, which in turn can reduce tax revenues while creating an additional need for social services.[34]

According to the World Bank, antimicrobial resistance 'could reduce GDP substantially – but unlike in the recent financial crisis, the damage could last longer and affect low-income countries the most'. The cost of inaction could cause between a 1.1% and 3.8% decrease of global GDP by 2050.[13] By comparison, the consequences of climate change are predicted to cause a drop in global GDP by 2060 of between 1% and 3.3%.[35]

> **The cost of inaction has been calculated to be a 1.1% to 3.8% decrease of global GDP by 2050. By comparison, the consequences of climate change are predicted to cause a drop of 1.0% to 3.3% global GDP by 2060.**
>
> The World Bank
> 'Drug-resistant infections: a threat to our economic future', (2017)
> and OECD, 'Economic Consequences of Climate Change' (2015)

Access, overuse and sustainable consumption of antibiotics

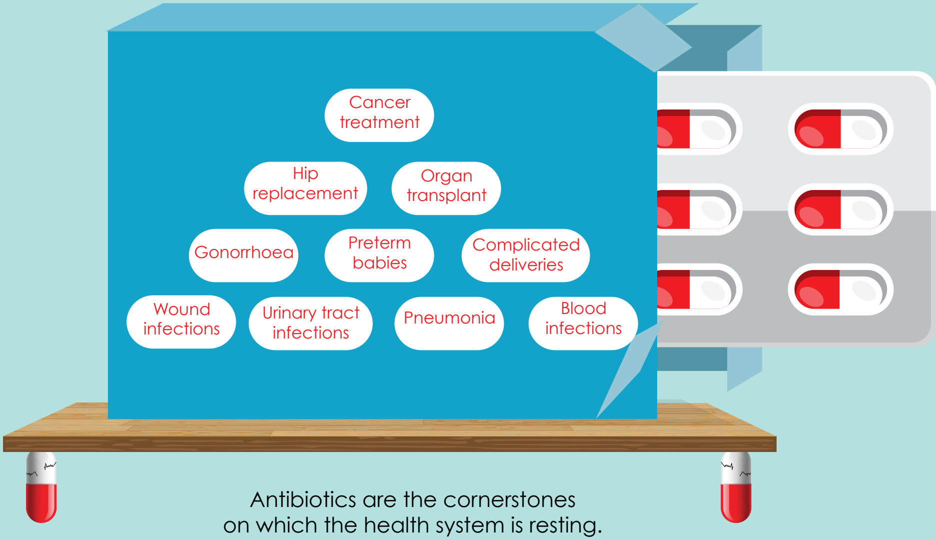
It is important to note that economic growth and increased individual financial means will lead to increased consumption of antibiotics. A recent study on global consumption of antibiotics showed that in low- and middle-income countries with a growing GDP per capita, antibiotic use by humans was also rising.[36] One reason for the increased use is that people can afford the antibiotics they need for good health. Also, some of the increased use is necessary due to a higher burden of infectious diseases.

However, another reason for the increased use is the overuse of antibiotics. The increase in consumption stresses the need to create solutions for increasing sustainable access to antibiotics for those in need, while reducing current misuse and overuse. Sustainable consumption and production of antibiotics needs to be included in sustainability work across human health, animals and food-producing sectors, as antibiotics can be viewed as a global public good and a non-renewable natural resource (SDG Targets 12.1 and 12.2).

Antibiotics are not just the cornerstones of basic medicine, modern medicine and medicinal procedures, such as cancer therapy, organ transplants and care for preterm babies rely on a strong foundation of effective and functioning antibiotics. The antibiotic pyramid shows a number of diseases and surgical procedures that rely on effective antibiotics.

The antibiotics pyramid

Diseases and procedures relying on effective antibiotics



Antibiotics are the cornerstones
on which the health system is resting.

Consequences of losing antibiotic effectiveness for modern healthcare:

- Common infections, such as wound infections, urinary tract infections and pneumonia will increasingly be associated with severe complications and increased risk of death.
- Many childhood and maternal infections such as pneumonia and childbed fever could become fatal once again – as they still are in many countries with limited access to antibiotics.
- Non-vital surgeries would become difficult to justify due to the risk of infection.
- Most cancer therapies would become substantially more risky as chemotherapy causes immune suppression, which increases the risk of even uncomplicated infections becoming fatal.
- Other therapies that require immune suppression, such as organ transplants will be untenable.

The World Bank noted that the costs of unrestricted and increasing resistance would increase the costs of antibiotic resistance even further, but highlighted the difficulty in fully capturing all aspects and consequences of resistance development. Thus far, there are no complete estimates of the indirect costs of antimicrobial resistance. The World Bank estimate that 3.8% of global GDP could be lost due to antimicrobial resistance is therefore likely an underestimate.[13]

To try to fully understand the consequences, cancer therapy is a good example. A recent study by WHO's International Agency for Research on Cancer showed that productivity loss due to cancer deaths in Brazil, the Russian Federation, India, China and South Africa – the BRICS countries – amounted to US$ 46.3 billion in 2012.[37] These countries account for more than 40% of the world's population, 25% of the global GDP and 42% of the world's cancer deaths. The consequence of losing effective antibiotics would make it substantially more difficult to treat and cure cancer patients and would therefore add to the already massive economic burden that cancer places on these countries.

Antimicrobial resistance as an ideal investment case

The World Bank considers funding antimicrobial resistance an exceptional economic and health investment for countries. It projected a high rate of return of 88% per year, if 75% of negative effects of antimicrobial resistance could be avoided.

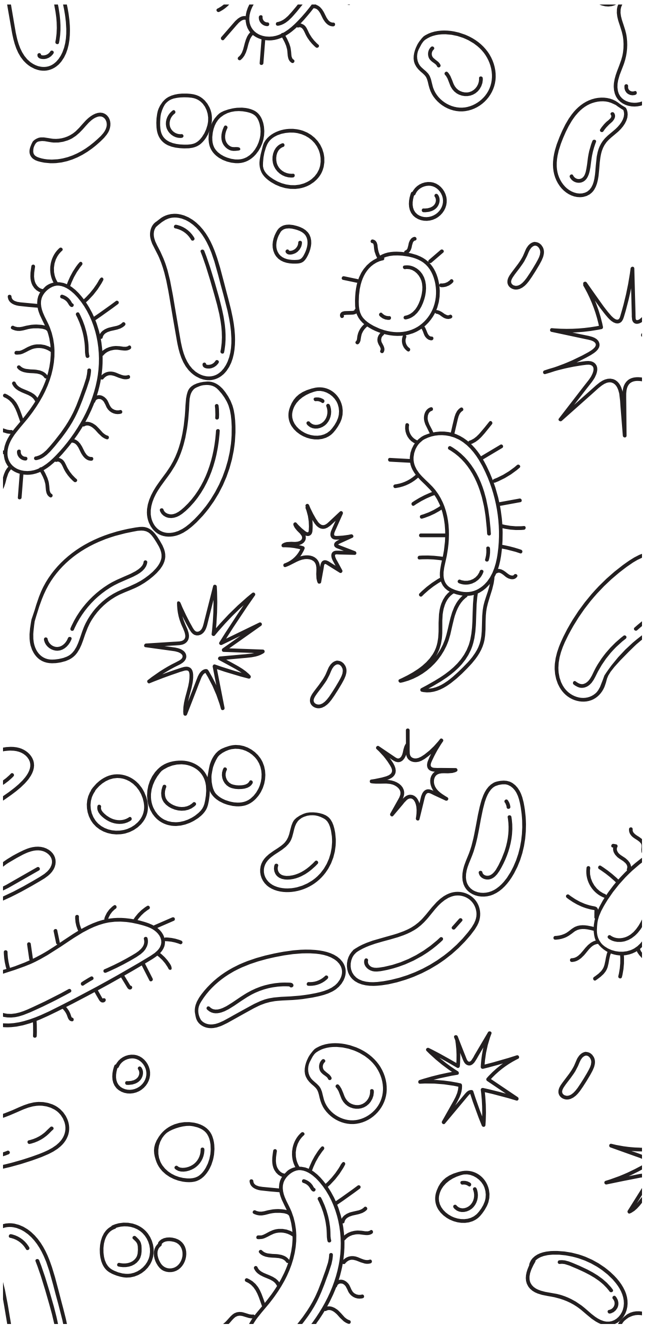
A recent Organisation for Economic Co-operation and Development (OECD) report on antimicrobial resistance also highlights that investing in public health actions to tackle antimicrobial resistance is a good investment. Additional savings and substantial health gains are produced by investing in building capacity, changing practices, scaling up stewardship programmes, awareness and knowledge sharing, improving hand washing and water, sanitation and hygiene.

The impact of antibiotic resistance on epidemics or pandemics

The global spread of resistant bacteria should be considered an ongoing, slow pandemic. Antibiotic resistance is complicating the treatment and outcomes of multiple bacterial infections across the world.

In addition to the effects of antibiotic resistance on poverty and economic growth, bacterial coinfection can also worsen outcomes of viral infections. In the pandemic of the Spanish flu of 1918, which killed approximately 40-50 million people worldwide, the major cause of death was bacterial pneumonia.[38,39] For the related swine flu in 2009, the United States Centers for Disease Control and Prevention (CDC) reported that 22 of 77 fatal cases also had a bacterial infection.[40] Antibiotics play a crucial role in limiting deaths during an influenza pandemic.[41]

Investing in reducing antibiotic resistance would be a good buffer against a scenario in which antibiotics no longer work to effectively control the negative effects of epidemics on human health and wellbeing as well as to ensure global sustainable economic growth.



Antibiotic resistance risks furthering inequalities within societies. To prevent deeper inequality through resistant infections, groups that are extra vulnerable should receive increased attention. Photo: Paul Hansen

Inequality

Goal 10: Reduce inequality within and among countries

Goal 5: Achieve gender equality and empower all women and girls

10 REDUCED INEQUALITIES

5 GENDER EQUALITY

- Antibiotic resistance risks increasing inequalities within societies.
- Groups that are extra vulnerable to antibiotic resistance include women and children, migrants and refugees.
- Antibiotic resistance can increase stigmatisation of people with infectious diseases that already drives inequality.

How does antibiotic resistance drive inequality?

Allowing people 'to reach their potential in dignity and equality and in a healthy environment' is a cross-cutting aim of all the Sustainable Development Goals.[42] Equality is specifically spelled out in relation to economic outcomes (SDG 10) and gender equality (SDG 5) within the SDG framework. Antibiotic resistance – like most infectious diseases – will impact different groups differently and risks furthering inequality within societies.[43]

Since global and national surveillance data on antibiotic resistance continues to be limited in most countries, analysing its implications on specific vulnerable and marginalised societal groups is difficult. The links between poverty and antibiotic resistance are complex and suggest that the two are mutually reinforcing (SDG 1). Increasing attention is also being put on the potential impact of antibiotic resistance on gender equality.[44] Women risk being affected more by diseases because of, for instance, lesser access to healthcare or structural discrimination. Other groups particularly vulnerable to resistant bacteria are migrants and refugees, due to displacement, movement and poor living conditions, but also persons working in jobs that require little or no formal education in the healthcare sector or in agriculture and food production who are more exposed to such bacteria.[44]

Stigmatisation of people with infectious diseases

Stigmatisation of certain infectious diseases has a long history of driving inequality and has been well documented in the field of TB.[45] For antibiotic resistant infections, the effect of stigma adds an extra burden on the disease. The South African Red Cross has identified social exclusion as a serious problem for multi-drug resistant (MDR)-TB patients, resistant to multiple antibiotics, when returning to continue their treatment at home.[46] In Nepal, MDR-TB has been associated with a significant increase in social stigma compared to antibiotic susceptible TB.[47] For sexually transmitted infections (STIs), disease already has a strong impact on people's lives and stigma is a barrier to care for many, resistance in STIs could make stigmatisation even worse.[48]

Such health inequalities place already vulnerable individuals or groups at a further disadvantage in terms of infections. When infections become more difficult or even impossible to treat, there is a risk of increased stigmatisation and an additional barrier to care, thus creating a double burden.

> 'In environments with such rampant spread of tuberculosis, disease-related stigma becomes increasingly visible, especially towards women whose economic and social foundations are shattered by the disease. [...] additional stigmatisation could lead to further social isolation, reduced health-seeking behaviour, and poor adherence to therapy, and could contribute to a continued rise in the number of tuberculosis cases and compound the problem of drug resistance.'
>
> Christodoulou, M. The stigma of tuberculosis.[45]

Devastating impact on the poorest

Socially or economically vulnerable individuals and groups are not only more susceptible to antibiotic resistance, but are also less able to prevent or respond to it as they generally do not have access to adequate healthcare and treatment. Treatment of multidrug resistant diseases is unaffordable for many, and the economic burden due to more expensive treatments will be greater for the poorer.[12] This will not only be the case on a country-level and not only in low- and middle-income countries: the impact on the poorest 40% of the world population will also affect the poor living in high-income contexts where access to, for instance, healthcare and medicines, good housing or education about health and antibiotics is also more limited.

For high-income countries, antibiotic resistance as a consequence of inequality is more easily documented due to more data being available and more research performed. At country-level, housing conditions, lack of education and low income is linked to increased antibiotic resistance.[23]

Impact of antibiotic resistance on women

While sex-disaggregated data is largely lacking in the field of antibiotic resistance, some data does exist. This data indicates that further exploring the gender perspective would be needed in order to develop appropriate solutions which address gender disparities. Urinary tract infections (UTIs), for example, are the second most common treated infectious disease in community practice and mainly affect women.[49] Chlamydia and gonorrhoea are major causes of morbidity among women in low- and middle-income countries. Both infections have been associated with infertility and pregnancy-related complications. Case detection and treatment are essential parts of reproductive health, but it is a problem for women to get a timely diagnosis.[50] In the case of gonorrhoea, some strains are already completely resistant to all existing antibiotics.

The role of antibiotics to prevent infection after a caesarean section (C-section) – in situations in which proper infection prevention control measures are lacking – can have consequences of infertility and wound infections.[51] In addition to the medical effects of infertility, it can cause loss of social status and stigmatisation of women. Finally, women constitute a large majority (67%) of people working in healthcare settings globally.[52] Their exposure to antibiotic resistance in these settings will likely make them more susceptible to contracting resistant pathogens.

Womb loss in Malawi

'Florence was very sick. After a prolonged labour on May 10 she gave birth to a stillborn baby by C-section. The wound [...] became infected and her stomach started to swell. She was in a lot of pain. The infection then spread to her uterus and doctors were forced to perform an operation to remove it. She was given two types of antibiotics but the infection persisted.'

Madlen Davies, Womb Loss in Malawi – An Unfolding Tragedy, The Bureau of Investigative Journalism (September 2018)[51]

- In Klebsiella, a common cause of bloodstream infections, resistance to the two major classes of antibiotics available in the hospital (penicillins and cephalosporins) rose from 12% to 2003 to 90% in 2016. In E. coli, a leading cause of sepsis, resistance rose from under 1% to 30% in the same time period.
- Dr Martha Makwero, Queen Elizabeth Central Hospital, said that in her maternity ward 36 women had undergone hysterectomies due to infection between March and May in 2018 alone.

Impact of antibiotic resistance in armed conflict

In the context of armed conflicts, antibiotic resistance has notably reared its head over the last decades. Recent reports from Iraq, Syria, Yemen, Afghanistan and Palestinian territories point to extreme rates of antibiotic resistance in bacteria causing wound infections in trauma patients.[53–56]

Studies have also identified that refugees frequently are carriers of resistant bacteria. This is mainly because of the circumstances they have been through such as harsh travelling conditions; crowded conditions in refugee camps or settlements; and the lack of regular medical care. All of these are major causes of the spread of infections, including resistant forms.[58]

Programmes that address vulnerable groups should therefore also take into account the effect of antibiotic resistance. Especially the further stigmatisation of these groups as diseases become less or untreatable should be prevented. On the other hand work on antibiotic resistance should be more inclusive and focus on groups that are extra vulnerable to antibiotic resistance like for instance women and children, migrants and refugees, or those suffering from armed conflict.

Including equality in programmes on antibiotic resistance: The example of GARDP

While there are many initiatives on antibiotic resistance that develop new treatments, GARDP (Global Antibiotic Research & Development Partnership) stands out selecting its development focusing on underserved priority patient populations. Their initial work focuses on antibiotics for newborns, children and for sexually transmittable diseases like gonorrhea.

‘Almost 40%
of patients admitted to
MSF’s post-operative care facility
in East Mosul arrive with
multidrug-resistant infections,
and antibiotic resistance is a problem
throughout the country.
While the incidence of antibiotic resistance
is particularly high in Iraq and across
the Middle East, it also occurs in many of
the countries around the world
where MSF works.’

Médecins Sans Frontières
(Doctors Without Borders),
Voices from the Field
(January 2019)[57]

Many areas of modern medicine, including cancer treatments, surgery, transplantations, complicated deliveries and treatment of preterm babies, are largely reliant on effective antibiotic treatments. Photo: Paul Hansen

Health

Goal 3: Good Health and Wellbeing

3 GOOD HEALTH AND WELL-BEING

- Antibiotic resistance is a problem right now and claims over 750,000 lives annually.
- Pneumonia and resistant bloodstream infections causing sepsis are huge contributors to mortality of children under five.
- Modern medicine, including cancer treatments, surgery, transplantations, complicated deliveries and treatment of preterm babies, largely relies on effective antibiotic treatments.
- Work on infection prevention and control is crucial for reducing the number of infections and spread of antibiotic resistance.

How does antibiotic resistance impact health?

Bacterial infections have plagued humans throughout history. In the past 70 years, antibiotics have changed the world by saving and improving countless lives, establishing antibiotics as the cornerstones of all modern health systems. Penicillin, for example, increased the chance of survival from approximately 10% to 90% for patients with pneumonia and bacteria in the blood.[59]

Entering a post-antibiotic era – in which common infections and minor injuries can kill – would have a devastating impact on global public health. Antimicrobial resistance, including malaria and HIV, already claims more than 750,000 lives annually. It is projected that antimicrobial resistance could cause up to 10 million deaths in 2050. Low- and middle-income countries will likely bear the brunt of these as they continue to carry the greatest burden of infectious diseases and the weakest health systems to address them.[60]

Antimicrobial resistance was mentioned in the adopting declaration for the SDGs, 'Transforming our world: the 2030 Agenda for Sustainable Development' in that the new agenda will 'accelerate the pace of progress made in fighting malaria, HIV/AIDS, TB, hepatitis, Ebola and other communicable diseases and epidemics, including by addressing growing antimicrobial resistance'.[42] Although antimicrobial resistance is not specifically mentioned in SDG 3, losing effective antibiotics would seriously compromise the achievement of several targets for both communicable and non-communicable diseases.

Impact of antibiotic resistance on maternal and child health

The number of children dying has halved since 2000 and deaths caused by pneumonia and diarrhoea have been reduced from 2.95 million in 2000 to 1.45 million in 2015.[63] Even though great progress has been made in maternal and child health, the maternal mortality rate in low- and middle-income countries is still 19 times higher than in the rest of the world.[64] Recent estimates found that 35%-40% of deaths of newborns in south Asia and sub-Saharan Africa were caused by severe bacterial infections.[65,66]

Antibiotic resistance and lack of access to effective antibiotics threaten further improvements or even undo these important achievements.[64] It is estimated that 30% of sepsis cases in newborns – the equal of 214,000 babies – die due to bacteria that are resistant to available antibiotics. At the same time, 75% (445,000) children under five with pneumonia could be saved every year by providing access to effective antibiotics.[4]

Impact of antibiotic resistance on communicable diseases

Antibiotic resistance could reverse the falling global mortality rates from communicable diseases.[4] The world already faces untreatable or difficult to treat infections that contribute to a large burden of illness, mortality and severe complications including long-term disability. New data from Europe has shown that the burden of infections with antibiotic-resistant bacteria in the European Union and European Economic Area is similar to the combined burden of three major infectious diseases (TB, HIV and influenza).[67] A study in India showed that people with multi-drug resistant bacterial infections face a two to three times greater risk of dying.[68]

Sepsis in newborn children in India

In 2016 it was estimated that resistant infections kill more than 58,000 babies in India every year.[61]
'Five years ago, we almost never saw these kinds of infections,' said Dr. Neelam Kler, chairwoman of the department of neonatology at New Delhi's Sir Ganga Ram Hospital, one of India's most prestigious private hospitals. 'Now, close to 100 percent of the babies referred to us have multi-drug resistant infections. It's scary.'

Gardiner Harris, 'Superbugs' Kill India's Babies and Pose an Overseas Threat, New York Times (3 December 2014).[62]

Typhoid fever is a life-threatening disease caused by lack of clean water and sanitation and is a major contributor to illness in the world. The global burden is estimated to be 20.6 million cases and 223,000 deaths.[69] In Pakistan, 5,274 cases of extensively antibiotic resistant typhoid were identified between November 2016 and December 2018, with reported spread to the United Kingdom and the United States. In this outbreak, azithromycin is the only reliable and affordable oral antibiotic remaining for treatment.

Sexually transmitted infections (STIs), are also a major cause for concern with an estimated 357 million new cases annually.[72] Some of these infections are becoming increasingly resistant to antibiotics. Access to care and treatment for STIs is an important part of reaching the goals of SDG Target 3.7 on sexual and reproductive healthcare. Gonorrhoea, one of the most common STIs with about 78 million new cases every year, has already started to become untreatable because of resistance to last-resort antibiotics.[72] Furthermore, untreated STIs are also well-known risk factors for HIV transmission which could impact the efforts to prevent and control HIV.[73–75]

Emerging resistance to treatments for TB, HIV and malaria, pose significant obstacles for the achievement of SDG Target 3.3. In the case of TB, treatment saved around 54 million lives between 2000 and 2017. Globally in 2017, 560,000 people developed TB that was resistant to rifampicin, the most effective first-line treatment. 460,000 of these had multi-drug resistant (MDR)-TB. Overall about 230,000 people died from antibiotic resistance through MDR and rifampicin resistant TB in 2017. Extensively drug-resistant TB has been reported by 127 countries.[76]

Impact of antibiotic resistance on non-communicable diseases

Modern medicine, including cancer treatments, surgery, transplantations, complicated deliveries and treatment of preterm babies, relies largely on effective antibiotic treatments to prevent or treat infections that often are life-threatening.[61] Access to effective antibiotics is therefore vital to meet SDG Target 3.4 – to reduce premature mortality from non-communicable diseases by one third.

Both radiotherapy and chemotherapy in cancer treatment weaken the immune system and put patients at increased risk for infections and rely on preventive or curative treatment by antibiotics. In the United States, one in ten cancer patients undergoing treatment is hospitalised due to infection. Every fourth infection in cancer patients is caused by pathogens resistant to commonly used prophylactic antibiotics, used to prevent infections.[77] Patients that have undergone transplantations or have HIV or AIDS are also more vulnerable to resistant infections due to the ensuing suppression of the immune system.

Surgery relies on antibiotics to prevent wound infections and sepsis. Trauma surgery is also relevant for achieving SDG Target 3.6 – to reduce global deaths from road traffic accidents. Up to 50% of bacteria causing surgical site infections are resistant to standard prophylactic antibiotics used in the United States.[77]

Healthcare associated infections and infection prevention and control

In the European Union, approximately 4 million patients per year get an infection during a hospital stay, resulting in around 37,000 deaths. More than 60% of these deaths are due to bacteria resistant to antibiotics.[67] Thorough estimates from low- and middle-income countries are more scarce, but WHO notes that about 10% of hospitalised patients will get at least one healthcare-associated infection. The burden of these infections is particularly high in intensive care units and in newborn children.[78]

One of the primary ways to address healthcare associated infections and prevent harm to patients and health workers is through infection prevention and control. While hand hygiene remains a cornerstone of infection prevention, there are many interventions that have proven beneficial and which are relatively inexpensive. Even though infection prevention and control can effectively and inexpensively reduce the spread of resistant bacteria, and hence the use of antibiotics, it is still not adequately prioritised in many places. Guidelines, where they exist, are often not adhered to.[79–81] Preventing infections, creating and implementing infection prevention control guidelines, would be one of the cheapest and most effective ways to reduce the effects of antibiotic resistance.

Hospitals are well-known hotspots for resistant bacteria and many patients will also become carriers during their hospital stay. The situation in a Greek hospital paints an illustrative picture: more than 40% of critically ill patients became colonised with carbapenem-resistant Klebsiella pneumonia during their hospital stay. Of these patients, 20% suffered a bloodstream infection caused by the same bacteria.[82] Most of these infections would be preventable through improved infection prevention and control measures.

The impact of antibiotic resistance on universal health coverage

Achieving universal health coverage is directly linked to access to safe, effective, quality and affordable essential medicines and vaccines for all. Given the global distribution of infectious diseases, the emergence of antibiotic resistance creates bottlenecks for establishing universal health coverage globally. No health system will be sustainable without working antibiotics.

One of the main reasons would be the increased healthcare and treatment costs due to resistance.[83] Several studies around the world have demonstrated the high costs of treating and caring for a single patient with MDR-TB, for example £60,000 in the United Kingdom, US$ 134,000 in the United States, US$ 2,571 in Zimbabwe and US$ 5,723 in India.[84,85] For extensively drug-resistant TB, this increases to a staggering US$ 430,000 per patient in the United States, US$ 31,000 in Zimbabwe and US$ 8,401 in India.[84–86] The magnitude with which antibiotics of poor quality contribute to treatment failures and global resistance development rates is difficult-to-measure, but indisputable.[87] The increased cost caused by antibiotic resistance would form a barrier to finance and achieving universal health coverage.

The ground-breaking Antibiotic Smart Use community approach in Thailand

The Thai Antibiotic Smart Use approach to lowering antibiotic use has been one of the most successful, using a bottom-up rather than a top-down approach.

The Antibiotic Smart Use project's idea of focusing its campaign on three common ailments – upper respiratory tract infections, especially common cold with sore throat; acute diarrhoea and simple wounds – for which antibiotics are not needed has helped bring focus to the issue in an effective manner.

The Thai programme has sought to improve the rational use of these medicines through a step-wise approach, beginning by improving education on antibiotic use locally and lowering barriers to behavioural change by offering alternative treatments for non-bacterial infections.

Data collected between 2013 and 2016 from around 900 hospitals showed that the rates of unnecessary prescription of antibiotics in upper respiratory infections and acute diarrhoea decreased from 50% to 40% and from 47% to 34%, respectively.

Antibiotic resistance in animals threatens the sustainability of food production, the livelihood of farmers and in the end food security, and indirectly harms economic growth. Such a decline will likely impact the poorest and most vulnerable groups hard, as any increase in food prices will affect them first. Photo: Paul Hansen

Food production, hunger and food security

Goal 2:
End hunger, achieve food security and improved nutrition and promote sustainable agriculture

2 ZERO HUNGER

- Antibiotic resistance in animals threatens the sustainability and security of food production and the livelihood of farmers.
- The target of SDG 2 will require urgently addressing current uses and misuses of antibiotics in agriculture.
- Phasing out routine use of antibiotics has been shown to be feasible without economic harm and decreased output of the farm, but may involve transition costs and investment such as in the improvement of farm hygiene.

What role do antibiotics play in food production?

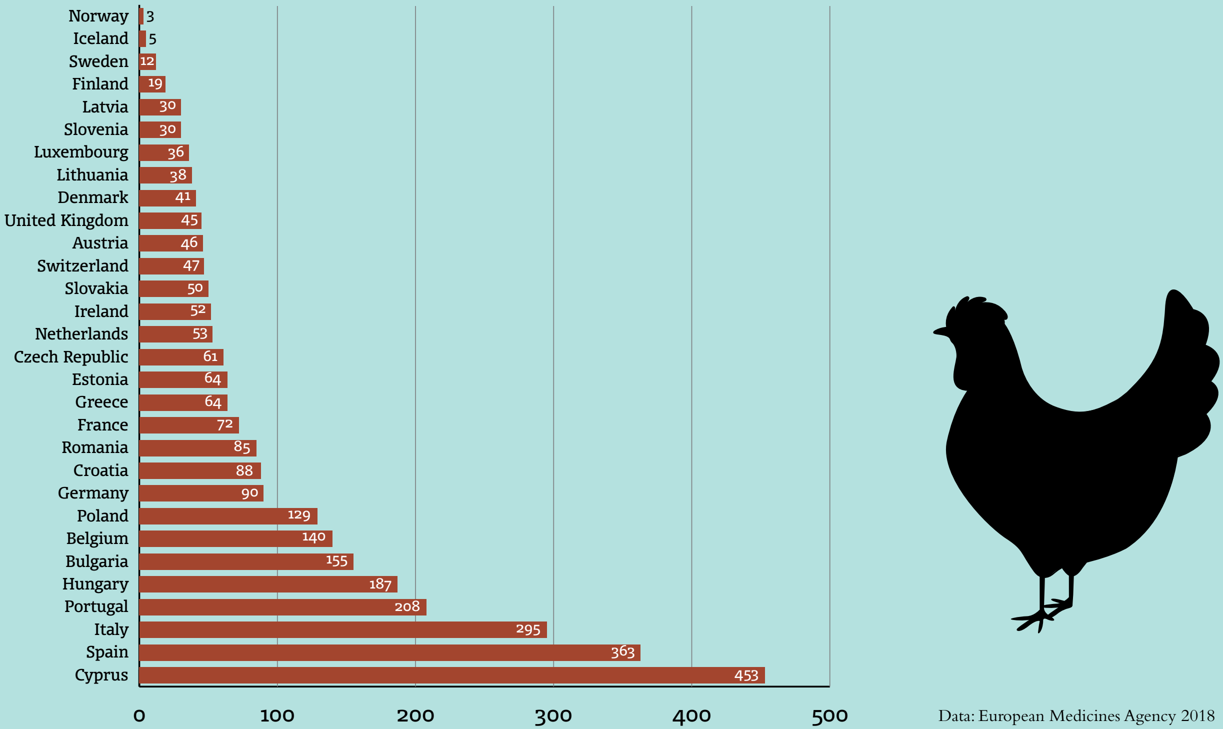
The target of SDG 2 to 'double the agricultural productivity by 2030 and to ensure the implementation of sustainable food production systems and resilient agricultural practices' will require addressing the current uses and misuses of antibiotics in agriculture.[42] The Food and Agricultural Organization (FAO) has warned about the impact of resistance development on rural livelihoods and food security, and emphasised the important role agriculture and farmers will play in this.[88] Globally and regionally, there are large differences in the amounts of antibiotics used.[89] In Europe, practices for the use of antibiotics vary dramatically from country to country (see figure below). Antibiotics make up for bad or inadequate farming practices in many cases, despite increasing evidence that farming without the routine use of antibiotics can be just as cost-effective.

Effective antibiotics play an important role in food animal production for treatment and control of diseases. The use of antibiotics creates a legitimate conflict of interest. On the one hand, there is the interest of farmers to make a living, and the perception that routine antibiotic use is necessary for production. One the other hand, there is the global interest to reduce antibiotic use to limit antibiotic resistance. This tension needs to be resolved as in the long-term, preservation of antibiotic

Antibiotic use in agriculture varies greatly per country

Sales in mg/PCU in 2016

(PCU takes into account a country's animal population over a year, along with the estimated weight of each particular species at the time of treatment with antibiotics)



Data: European Medicines Agency 2018

effectiveness is central to both food security and food safety.

Global antibiotic consumption in livestock was in 2010 estimated to be over 63,000 tonnes.[89] With increasing human population and rising demand for meat, the Organisation for Economic Co-operation and Development (OECD) estimates that antibiotic use in food animals will increase by 67% globally from 2010 to 2030 if nothing is done.[90] To accommodate the growing demand for meat products, there is an increase in the industrial production of food animals. In many circumstances this method of production leads to high use of antibiotics.[91] In that sense the increasing demand for meat is a driver of antibiotic use and resistance. Misuse and overuse is often due to bad animal living conditions, lack of education and awareness about how to use antibiotics as well as a lack of understanding of antibiotic resistance.[92]

Addressing routine use of antibiotics and use for growth promotion

Low-level doses of antibiotics have been used for a long time to promote growth of food animals and to prevent diseases. Antibiotics are readily available for a low price and are often mixed into animal feed. Since profit margins are very small, any measure perceived to increase productivity is likely to incentivise farmers to use it. However, phasing out the routine use of antibiotics in for example growth promotion is feasible without economic harm and decreased output of the farm, but could demand structural changes and investments such as in the improvement of farm hygiene.[93–97] Moreover, restricted financial capacity to change farming practices is an important driver of use of antibiotics.

Sweden was the first country to ban antibiotics for growth promotion already in 1986.[96] Studies conducted in Denmark, Sweden and the Netherlands by government and industry have reported minimal impacts on poultry industries' productivity, as well as for other animals, when removing antibiotics for growth promotion.[93,96–98] Researchers have predicted a similar effect for poultry production in the United States.[99] Since 2006 a ban is in place within the European Union and similar bans exist in, for example, Taiwan and Mexico. WHO also recommends restrictions of antibiotic use for routine use, especially those drugs that are important to human health. In addition, many large producers have voluntarily started to phase out antibiotics, influenced by consumer demand. In the Guidelines on Use of Medically Important Antimicrobials in Food-Producing Animals, WHO recommends restrictions on routine use of antibiotics, especially those drugs that are important to human health.

Routine use of antibiotics is mostly effective in situations with bad infection prevention and control and

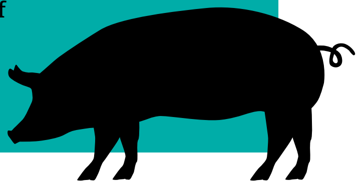
Antibiotic resistance in animals – the example of swine dysentery

Swine dysentery is a bacterial disease that can be found worldwide in up to 40% of pig herds at farms. At present, not many treatment options remain for outbreaks of swine dysentery.

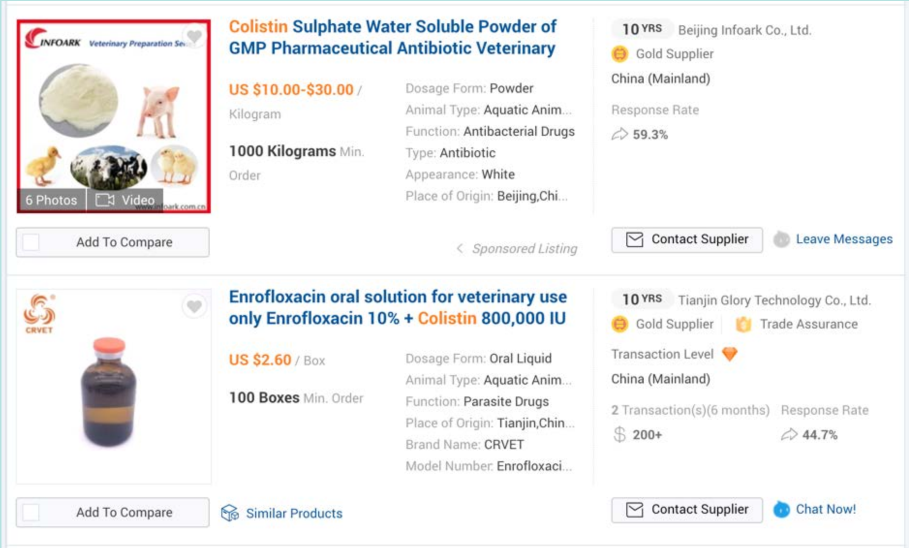
In the European Union, the only effective choice of antibiotics are pleuromutilins, but during the last decades resistance to them has increased. In Italy, one study reported resistance in more than 50% of tested bacteria from infected pigs.

As swine dysentery causes impaired growth and severe forms of the disease can lead to the death of 50-90% of the pigs that get it, lack of effective treatment would have considerable impact on food production and animal health.

E. van Duijkeren et al. 'Pleuromutilins: use in food-producing animals in the European Union, development of resistance and impact on human and animal health', J Antimicrob Chemother 69, (2014): 2022–2031



where there is intensive use of small spaces to house animals.[61,100] A reduction of antibiotic use will only be commercially viable for many farmers if it is coupled with improvements of farming practices and technologies. To reduce the risk of the introduction and spread of infections in modern animal production, common procedures are vaccination, limited co-mingling, adequate ventilation and temperature controls, biosecurity, appropriate nutrition as well as housing and quality-assurance programmes. Other measures that can be taken often overlap with work that can be done on animal welfare. Some of these, however, require significant work and investment or larger farm sizes.[101]



Antibiotics are readily available for a very low price for agricultural use in every corner of the world, but also in bulk online. Very often farmers are not aware they are using antibiotics, or antibiotics are even mixed into animal feed.

Image source: aliexpress.com

The impact of antibiotic resistance on food security and hunger

In addition to the routine and growth promoting use of antibiotics, large portions of the reported use in animals is inappropriate. However, when animals get sick, antibiotics are needed to treat infections, as untreatable infections in animals threaten sustainable food production for the growing world population. If infections cannot be treated, production capacity will be limited and animals may not be suitable for use as human food.[61]

Antibiotic resistance in animals will therefore threaten the sustainability of food production, the livelihood of farmers and in the end food security, and indirectly harm economic growth.[102] Such a decline will likely impact the poorest and most vulnerable groups hard, as any increase in food prices will affect them first.

Antibiotics and foodborne diseases

Infectious foodborne diseases acquired from contaminated raw or cooked food are major causes of mortality and morbidity globally. WHO reports that 600 million people fall ill globally as a result of foodborne diseases with over 91 million people affected in Africa alone each year.[95] Diarrhoeal diseases remain a leading cause of death in low- and middle-income countries and safe food is therefore critical in these countries.[95] According to WHO, the majority of foodborne illnesses are caused by microbes, including bacteria. Resistance in animals would make foodborne infections that require antibiotics more difficult to treat, meaning that more people will die from them.

The majority of acute diarrhoeal diseases however, like for instance Salmonella infection, are self-limiting and do not require antibiotic treatment.[103] Treatment with

'Antibiotic resistance has immense economic consequences and immense implications for food. [...] If we lose that ability [of antibiotics] we begin to perhaps lose the ability to have adequate food supplies in the world.'

Keiji Fukuda, 2016,
Assistant Director-General for Health, Security and Environment

Source: U.N. Pledges To Fight Antibiotic Resistance In Historic Agreement. NPR.org

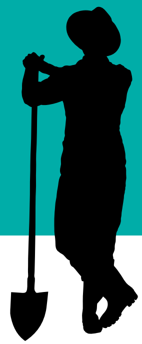
antibiotics is recommended only for severe bacterial diarrhoea. However, inappropriate use of antibiotics is still common in clinical practice for treatment of food-borne diseases worldwide. Foodborne diseases are therefore likely a big driver of irrational use of antibiotics in human health.[104] However, for severe cases and certain groups including the very young, elderly and immuno-compromised individuals, treatment of salmonellosis with antibiotics can save lives. Because treatment options for children and pregnant women are already very limited due to toxicity or contraindications of some antibiotics, every antibiotic that becomes ineffective due to resistance has great impact on mortality.[105]

Farmers united and empowered to deal with antibiotic resistance

In the Netherlands farmers went above and beyond government regulations in limiting antibiotics with the future generations and the safety of their own families in mind.

Gerbert Oosterlaken, a pig farmer from the Netherlands who was leading farmer acting on antibiotic resistance:

'Now, I know that for a lot of countries agriculture is a major economic pillar. I know there is the fear of economic losses. I know from experience. You may not realise it, but the Netherlands, small as we are, is a world player in this field. We are the second largest exporter of agricultural products, next to the United States [...] We were the number one of heavy users of antibiotics in Europe. We too made the mistake of using antibiotics rather than optimising the living conditions of our livestock. Only in three years' time we managed to change the course drastically. And: without ruining the sector! We are still the number two in agricultural export!'[106]



Clean water and appropriate sanitation are major drivers of change and reduce the spread of bacteria that cause infections to humans and animals. Photo: Paul Hansen

The environment

Goal 6: Ensure availability and sustainable management of water and sanitation for all

Goal 14: Conserve and sustainably use the oceans, seas and marine resources for sustainable development

Goal 15: Protect, restore and promote sustainable use of terrestrial ecosystems, sustainably manage forests, combat desertification, and halt and reverse land degradation and halt biodiversity loss

- Resistant bacteria in human and animal waste end up in soil and water systems.
- Antibiotics in the environment are a driver of resistance in bacteria and have disruptive effects on ecosystems.
- Humans, animals and microbes are linked together by the environment we live in.
- Improving water and sanitation services reduces the need for antibiotics and reduces spread of resistant bacteria.

How do resistant bacteria enter the environment?

Antibiotic resistance is a natural process, so antibiotic resistant bacteria are essentially found wherever bacteria are found. However, humans and animals reared by humans are major contributors to antibiotic resistant bacteria in the environment. Resistant bacteria can spread into the environment through untreated waste or sewage, or through wastewater treatment facilities that are incapable of removing them from the wastewater.[107] In this way, resistant bacteria contaminate soil and water sources used by humans and animals. Resistant bacteria exposed to antibiotics in the environment are able to multiply and spread because they have an advantage over non-resistant bacteria. The spread of resistant bacteria is illustrated by studies finding an abundance of antibiotic resistance genes related to human activity flowing from rivers into the sea or ocean.[108] Resistance is more common in wildlife adjacent to human activity, but has also spread very far away from human populations, like the Antarctic.[109,110]

How do antibiotic residues enter the environment?

Across the chain from manufacturer to user, antibiotics enter the environment in multiple ways. Wastewater from hospitals and municipalities, open defecation, waste from animal farms, manure runoff from crop fields, discharge from aquaculture farms and wastewater from pharmaceutical manufacturing plants are all sources of antibiotic pollution in the environment.

When humans or animals consume antibiotics they are only partially metabolised, which means that antibiotics are excreted unchanged by humans and animals through urine or faeces. According to the Food and Agricultural Organization, between 70% and 80% of antibiotics given to fish end up in the environment and are able to spread rapidly through water systems.[111] In the case of waste from food producing animals, which consume the absolute majority of antibiotics globally, the manure is rich in nutrients and is often used as fertiliser on crop fields, leading to the direct contamination of the environment with antibiotic residues. Wastewater treatment facilities are so far never capable of removing antibiotics from the water. As a consequence, antibiotics and other pharmaceuticals used for humans and animals end up in the water flowing into the environment from these facilities.[112–114]

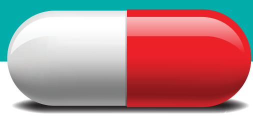
No regulations for antibiotic release into the environment

Antibiotics are currently not considered a priority chemical contamination in UN guidelines, such as WHO's guidelines for quality of drinking water.[120]

Antibiotic waste from pharmaceutical companies

The production of antibiotics is a major cause of antibiotics in the environment.[115,116] While most pharmaceutical products are procured and consumed by high-income countries, the production of antibiotics and the active pharmaceutical ingredients (APIs) mainly takes place in India and China.

In a study from a wastewater treatment plant serving around 90 drug manufacturers in the industrial hub Patancheru in Hyderabad, India, researchers found that 45 kg of ciprofloxacin was released into the environment daily, which is five times the daily consumption of the drug in Sweden.[116,117] Four big pharmaceutical companies have applied limits to their suppliers' sites (GSK, Johnson & Johnson, Pfizer and Roche) but no company has committed to publish its environmental audit results or its discharge levels.[118,119] For generic companies, information on environmental pollution has so far not been made public.



In many countries, including in the European Union, the removal of antibiotics in wastewater treatment is not regulated in current environmental water quality standards.[121] Civil society groups in India and Europe have suggested the inclusion of environmental standards in the rules for good manufacturing practices and researchers have proposed discharge limits, but to date no regulations have been put in place.[122]

The effect of antibiotics in the environment

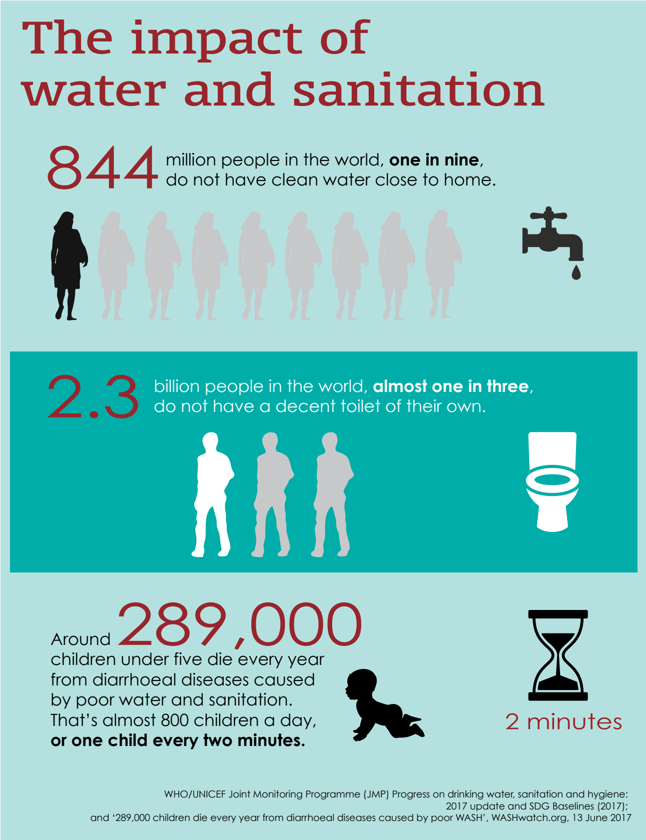
It is clear that antibiotics at concentrations found in the environment are capable of killing or inhibiting growth of non-resistant bacteria, therefore leaving space for resistant bacteria to thrive.[108,109,123] These resistant bacteria can then spread and share their resistance genes with other species. New research even suggests synergies between antibiotic and microplastic pollutants.[124] Interestingly, the amount of antibiotic resistant bacteria that cause disease is connected to environmental factors such as higher local temperatures and increasing population density.[125] There thus is a strong link between antibiotic resistance and almost all work on the environment, ranging from pollution of water and oceans to climate change.

In addition to their role in resistance development, studies have shown that antibiotics have toxic effects on ecosystems and cause a reduction in microbial biodiversity.[126] The negative effect of antibiotics on natural microbial communities could be the disappearance or inhibition of microbial groups that play a key role in ecosystem functions. Several studies have also shown that antibiotics are toxic to animals.[127,128] Such toxic effects may have severe repercussions for biodiversity and the whole ecosystem.

Effects on humans of resistant bacteria in the environment

Humans, animals and the environment are connected by the ecosystems we live in, and the health of one cannot be separated from the health of the other. The presence of resistant bacteria in the environment also has direct implications for humans. First of all, humans may get directly ill with infections that are difficult to treat such as multidrug resistant typhoid fever. But people can also acquire antibiotic resistant bacteria from the environment without becoming ill – they become a part of our normal microbiome in for example the gut. Already more than 60% of the populations in some areas of the world are carriers of multidrug-resistant bacteria.[129,130] As many infections are caused by bacteria from our microbiomes, carriage increases the risk for future infections with resistant bacteria.

Carriage of resistant bacteria can also be the result of exposure to for example livestock, food or environmental sources contaminated with resistant bacteria. People working on farms are for example more exposed to antibiotic resistant bacteria, such as livestock-associated methicillin-resistant Staphylococcus aureus (MRSA).[131] A recent study with healthy children from eight villages in a sparsely populated region in eastern Bolivia showed that 38% of the children carried bacteria resistant to the last-resort antibiotic colistin. Only four of the 337 children had previous exposure to any antibiotics. The researchers hypothesise that the source is use of colistin in the raising of food animals, or in the production of imported food from countries with high use of colistin, like Brazil.[132]



The importance of water and sanitation

Water and appropriate sanitation, part of SDG 6, reduce the need for antibiotics through reducing the incidence of infections. It is estimated that 494 million cases of diarrhoea are treated with antibiotics each year in Brazil, Indonesia, India and Nigeria alone. Universal access to improved water and sanitation in these four countries could reduce this number by a staggering 60%.[133]

A study looking at 130,000 healthcare facilities across 78 low- and middle-income countries found that 50% lacked access to piped water, while a third were without access to toilets. Almost 40% did not have facilities for washing hands with soap.[134] Water and sanitation are therefore crucial elements in addressing bacterial resistance development and spread because it breaks the chain of spreading resistance between humans, animals and the environment.

Clean water in hospitals helps reducing antibiotic use in Sierra Leone

Clean water in hospitals has a huge impact on reducing infections and the spread of antibiotic resistance. One study from a district hospital in Sierra Leone reported that more than half of women who had caesarean sections would contract sepsis. After the operating theatre and labour rooms got better water supply and staff were trained on proper hygienic practices through a one-time investment, cases of sepsis dropped to less than 1 in 10 women. Within six months, admission for deliveries at the hospital doubled as patients learned that the services at the maternity unit had improved and the hospital became self-sustaining. This success was later replicated in eight other district hospitals in Sierra Leone.[135]

Conclusion

Since the Global Action Plan was adopted in 2015, antibiotic resistance has increasingly been recognised as a threat to achieving many of the Sustainable Development Goals. In 2016, the UN General Assembly adopted a Political Declaration on Antimicrobial Resistance which highlighted that antimicrobial resistance challenges both gains in health and development and the attainment of the 2030 Agenda for Sustainable Development.

This paper has presented concrete examples of the underlying and complex aspects of antibiotic resistance and its impacts across different Sustainable Development Goals. Keeping antibiotics effective for treating infectious diseases is essential for the work on achieving the Goals. At the same time, achieving the Goals is important to reduce antibiotic resistance. Antibiotic resistance should therefore be considered a sustainable development issue.

This paper is intended to inform and stimulate discussions on how to further advance the implementation of 2030 Agenda for Sustainable Development, the Global Action Plan on Antimicrobial Resistance, National Action plans on Antimicrobial Resistance, as well as work within all sectors that affect and are affected by antibiotic resistance. These discussions must lead to decisions and concrete action on this urgent challenge, for which solutions must build on a systems perspective across sectors. Antibiotic resistance is a consequence of systems failures and should therefore be seen and addressed through a systems perspective.

Antibiotic resistance is not a problem of the future, it already has major consequences for the lives and livelihoods of people around the globe as seen in this paper. However, looking into the close future there are many actions that can be taken by different actors at different levels to mitigate the effects of antibiotic resistance.


PHARMACY
HOSPITAL
SCHOOL
UNIVERSITY

Actions that can now be taken include:

Integrating antibiotic resistance into the development agenda
To limit its impact on the Sustainable Development Goals, antibiotic resistance needs a place in the development agenda. Work on antibiotic resistance should be integrated into the implementation of the 2030 Agenda for Sustainable Development.

Developing indicators
To give antibiotic resistance a concrete role in measuring sustainable development, antibiotic resistance should be included in national or regional target setting to reach the Sustainable Development Goals. This would give antibiotic the place it needs and acknowledges that without addressing antibiotic resistance it will be difficult to achieve the Goals.

Strengthening governance
Stakeholders in sectors beyond health and agriculture need to engage in the work on antibiotic resistance. United Nations agencies, governments, development partners, professional organisations, civil society and other stakeholders should work together to take action.

Stepping up awareness-raising
Relevant stakeholders that can contribute to change need to be made aware of the consequences of antibiotic resistance. Governments are responsible for dissemination of information to stakeholders across sectors regarding antibiotic resistance to in relation to implementing 2030 Agenda for Sustainable Development and National Action Plans. Multi-sector stakeholder engagement and collaboration on action on antibiotic resistance both at the national and international level is essential.

Implementing interventions with known effect
Concrete actions that have already proven to reduce antibiotic resistance within areas such as Infection Prevention and Control (IPC), Water, Sanitation and Hygiene (WASH), maternal and child health and immunisation should be implemented. More complex interventions that have proven effective, like setting up stewardship programmes and moving towards ending routine use of antibiotics in animals should be started up as soon as possible, looking at examples of other countries' successes in reducing antibiotic resistance.

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ReAct – Action on Antibiotic Resistance is an international network established in 2005 to address antibiotic resistance, with offices in Ecuador, Kenya, India, Sweden, and the United States. ReAct believes that access to affordable and effective treatment and prevention of bacterial infections is a core component of everyone's right to health. ReAct therefore aims to ensure sustainable and equitable access to effective antibiotics for all. The core focus of ReAct's work is on developing sustainable solutions to tackle antibiotic resistance in low- and middle-income countries.

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