



## Review

## Global economic impact of antibiotic resistance: A review

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## ARTICLE INFO

## Article history:

Received 25 October 2018  
 Received in revised form 9 May 2019  
 Accepted 25 May 2019  
 Available online 5 June 2019

## Keywords:

Economic impact  
 Antibiotic resistance  
 Human capital  
 Negative externality

## ABSTRACT

The pandemic of antibiotic resistance has become a serious threat to the therapeutic efficacy of the available antibiotics and their prescribed regimens. The problem is multifaceted as it encompasses medical, social, economic and anthropogenic spheres. The present review reports the global economic impact of antibiotic resistance among humans on the basis of published research as well as reports of national and international organisations. The impact is catastrophic because it includes patients, healthcare providers, researchers, pharmaceutical organisations, healthcare businesses and, moreover, national and international policy-makers. We found very serious economic impacts of the existing and emerging antibiotic resistance conditions. This study is divided into geographical regions to see the total impact. The risk of medical poverty trap is more significant in low-resource settings.

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## 1. Introduction

The discovery of antibiotics was one of the greatest achievements of mankind in the 20th century. The success of antibiotics revolutionised modern biomedicine, which continues to define, shape and expand its future as well as its limits. Unfortunately, the success of any therapeutic agent is limited to the potential development of resistance. The compromise in efficacy (therapeutic effect) owing to resistance compels the development of the next generation of antimicrobials. Resistance to an antimicrobial (here antibiotic) refers to the increased tolerance to the set therapeutic

regimen to which the pathogen was susceptible before the emergence of resistance. This article presents the economic prognosis in the resistant and susceptible population both nationally and globally. The short- and long-term economic impact on attributable hospital costs are also discussed. The 'costs' or 'economic impacts' are not only in monetary terms but also include the social and labour-loss effects. The RAND Corporation estimated in their research that "failing to tackle Antimicrobial Resistance (AMR) will mean that the world population by 2050 will be between 11 million to 444 million lower than it would otherwise be in the absence of AMR" [1]. The World Bank report of 2014 [2] gives the expenditure gaps in health care and related infrastructure.

In economic terminology, resistance is a negative externality, i.e. it has an undesirable effect on people other than the immediate consumer of the antibiotic. This external cost is cross-sectional as it is

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imposed on multiple people other than the consumer itself, but also temporal in the sense that when the consequences of resistance have appeared, the cost is also borne by the consumer [3].

The risk of medical poverty trap is more visible among the poor, illiterate and ignorant populations of underdeveloped and developing nations with low to medium resources at their disposal.

World Health Organization (WHO) data also suggest that there is lack of resources and infrastructure in middle- and lower-middle-income countries [4]. This prevailing differential is in availability of health care at all levels (primary, secondary and tertiary). The loss of human life is acute despite the fact that antibiotic resistance is a pan-global phenomenon affecting all social and income groups in community-acquired and nosocomial infections. The high cost of health care leads to risk of long-term impoverishment, untreated morbidity and mortality. This phenomenon ultimately leads to the loss of human capital.

It seems pertinent to list the organisations working to tackle the 'silent epidemic' of antibiotic resistance. However, it is not possible to reproduce all such endeavours worldwide, therefore only a few policy proposals and congressional hearings are given below.

- During the hearing of the Antibiotic Development to Advance Patient Treatment Act (ADAPT), Boston University Law Professor Kevin Outterson said, "In the movies, heroic research scientists discover the cure before the credits roll; in real life, research programs require at least a decade and generally longer to deliver an effective antibiotic" [5].
- The British Prime Minister David Cameron warned in July 2014 that "If we do not confront the threat of antibiotic resistance, we could be 'cast back into the dark ages of medicine' where treatable infections and injuries will kill once again" [6].
- The Stakeholder Forum on Antimicrobial Resistance (SFAR) [7] convened by the Infectious Diseases Society of America (IDSA)

[8] opined that US Government policy is sustainable and based on stakeholder needs to combat antibiotic resistance.

- The Faces of Antimicrobial Resistance (FOAR) [8] compiled by the IDSA shows the acquisition of community and nosocomial infections through the stories of patients and the economic hardships they had to face.

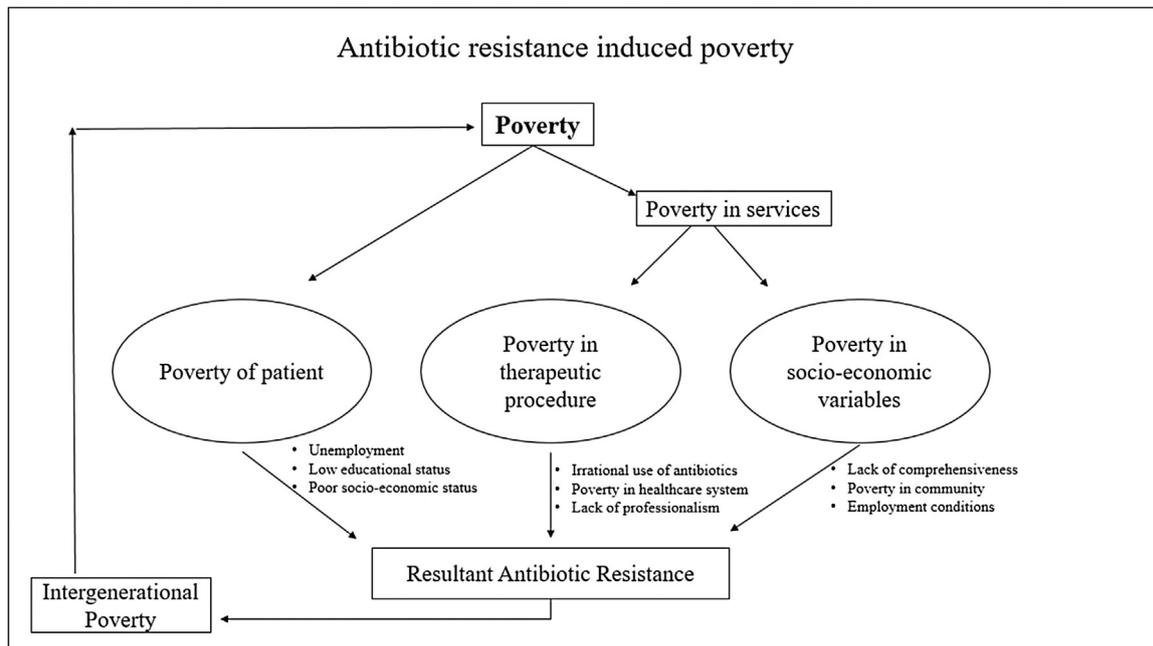
## 2. Medical poverty trap

Medical poverty trap can be explained as the self-reinforcing mechanism that causes poverty to persist both at the service level and the individual level [9]. The said antibiotic resistance causes out-of-pocket medical expenses that contribute significantly to the medical poverty level. A study published by the Institute for Research on Poverty of the University of Wisconsin–Madison (Madison, WI, USA) showed that out-of-pocket medical expenses were a major factor driving the elderly into poverty in the US state of Wisconsin.

## 3. Global economic paradigms

The World Bank defines countries based on income as high-, upper-middle-, lower-middle- and low-income countries based on their Gross National Income (GNI); for the year 2016, high-income countries were defined as those with a GNI per capita of US\$12 476 or more, and low-income countries as those with a GNI per capita of US\$1025 or less [10]. Therefore, the risk of medical poverty trap is highly aggravated in low-resource settings, thus placing vulnerable communities in a generational poverty trap with increased morbidity and mortality (Fig. 1).

In an analysis of expenditure on health care, the World Bank report (2014) mentioned that high-income countries invested 12.26% of their gross domestic product (GDP), whereas upper-middle-income countries invested only 6.17% of GDP and



**Fig. 1.** Relationship between antibiotic resistance and poverty. Antibiotic resistance is one of the major causes of 'situational poverty' and 'intergenerational poverty' in vulnerable socioeconomic groups. Situational poverty is generation-limited and is traceable to a specific situation or incident (here, disease). With the appearance of antibiotic resistance, disease persists and results in poverty, leading to intergenerational poverty. This figure sums up the relationship between three major variables and shows the relationship between them as a function of disease and poverty that, if unattended, untreated and unaddressed, can lead to intergenerational poverty. We want to show how situational poverty and intergenerational poverty are related via antibiotic resistance. The figure also shows that there is a cyclic relationship between them and a possibility of 'chain reaction'.

low-income countries only 5.75%. Global expenditure for health care was 9.9% of total global GDP [11].

The World Bank report (2017) places a thorough focus on all aspects of antibiotic resistance, which is reproduced below [12].

- Impact on GDP: by 2050, annual global GDP would fall by 1.1% in the low-impact antimicrobial resistance (AMR) scenario and by 3.8% in the high-impact AMR scenario. Low-income countries would lose more every year leading up to 2050, with the loss exceeding 5% of GDP in 2050 in the latter scenario.
- Impact on global poverty: there would be a pronounced increase in extreme poverty because of AMR. Of the additional 28.3 million people falling into extreme poverty in 2050 in the high-impact AMR scenario, the vast majority (26.2 million) would live in low-income countries. Currently, the world is broadly on track to eliminate extreme poverty (at US\$1.90/day) by 2030, reaching close to the target of <3% of people living in extreme poverty. AMR risks putting this target out of reach.
- Impact on world trade: in 2050, the volume of global real exports would shrink by 1.1% in the low-case scenario and by 3.8% in the high-case scenario.
- Impact on healthcare costs: global increases in healthcare costs may range from US\$300 billion to more than US\$1 trillion per year by 2050.
- Impact on livestock output: by 2050, the decline in global livestock production could range from a low of 2.6% to a high of 7.5% per year.

The Organization for Economic Co-operation and Development (OECD) report (2017) clearly mentions that patients will require more intensive and expensive care and are more likely to be admitted to hospital. Hospitals will spend, on average, an additional US\$10 000 to US\$40 000 to treat a patient infected by resistant bacteria [13,14].

The North American region, including the USA and Canada, is a resource-rich economic setting with one of the largest economies. Antibiotic resistance first appeared with the start of antibiotic use in the 1950s. The USA spent US\$3.2 trillion on health care and Canada spent US\$228 billion on the same in the year 2014 [15]. But like all other nations, both the nations are challenged by antibiotic resistance. The US Centers for Disease Control and Prevention (CDC) estimates that 23 000 people die each year as a direct result of antibiotic-resistant infections [16]. Thus, the economic burden created by antibiotic resistance in the USA is estimated at US\$55bn, with US\$20 billion in health services costs and US\$35 billion in lost productivity per year [16]. The challenge of resistance is not only limited to humans but also has economic costs for the meat and poultry industries where resistant microbes have been isolated.

Latin America is a low-resource setting, and antibiotic resistance in this region is responsible for significant morbidity and mortality. Reports by the National Nosocomial Infections Surveillance (NNIS) System and the Surveillance and Control of Pathogens of Epidemiologic Importance (SCOPE) highlight the emerging and established AMR in the population through community-acquired and nosocomial infections [17]. Resistant infections were found both in paediatric and adult patients [18]. The SENTRY Antimicrobial Surveillance Program, established by funding from GlaxoSmithKline in collaboration with JMI Laboratories in January 1997, confirms the widespread antibiotic resistance [19]. When considering the economic outlook, in a report published by the RAND Corporation in 2014, it is estimated that countries in this region will see a loss of 1.2% of their GDP with the present levels of resistance compared with the baseline level, which was taken as 0% or no resistance [1]. If AMR is unchecked, its high costs on the population and economy can lead to a situation called medical poverty trap. The OECD countries (including 10 Latin American

countries) will see a cumulative loss of US\$2.9 trillion by 2050 compared with the baseline (AMR-free conditions) [20].

Europe is a resource-rich economic setting. Most countries are either high-income or upper-middle-income countries. The region also suffers from high rates of antibiotic resistance. In a report published by the London School of Hygiene and Tropical Medicine, in the European Union, Iceland and Norway the burden of additional hospital care costs due to antibiotic-resistant infections was estimated to be approximately €1.6 billion in the year 2012 [21].

#### 4. Perspectives suggested to tackle antibiotic resistance

In this section, we briefly explain the policy positions that, if taken into consideration and implemented, can manage the catastrophe of antibiotic resistance. There are now significant approaches that are being taken to combat the situation.

In the USA in March 2015, the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB) was established [22]. The role of PACCARB is to help develop and implement the National Strategy for Combating Antibiotic-Resistant Bacteria and the National Action Plan for Combating Antibiotic-Resistant Bacteria [23].

The following policy positions may yield encouraging results.

- Antibiotic stewardship: the proper use of antibiotic regimens requires an evidence-based approach used in distinct healthcare situations and the individual situation of the patient. Antibiotic stewardship will result in increasingly rational and judicious prescription practices of antibiotics both in private and public healthcare systems [24].
- Antimicrobial surveillance: local, regional and global surveillance of antibiotic resistance patterns are incredibly important to estimate the nature as well as the magnitude of the problem. Antimicrobial surveillance may help in assessing the effectiveness of efforts to combat the problem. Global surveillance programmes include the Antimicrobial Testing Leadership and Surveillance (ATLAS), initiated by Pfizer, and independent surveillance programmes such as LEADER established in 2004 in the USA. ZAPPS and SENTRY need to get more comprehensive and elaborate, engaging more stakeholders nationally and globally [25].
- Regulatory framework: the regulatory framework needs to be made more streamlined to allow greater flexibility in regulation and approval of new drugs in the market. To incentivise new global vaccine and antibiotic research, free-market-based regulations need to be adopted in conjunction with antibiotic stewardship. It is also recommended to develop a global, tiered-based regulatory framework that allows disease-based or pathogen-based labelling and the most appropriate use of new agents in the market [25].
- Novel business model: a new business model is necessary in fostering the development of new vaccines and anti-infectives. It is also crucial to strengthen a sustainable market for increasing R&D investment by companies [26]. World over 'tax credits' to be given to companies working in new anti-infective development.
- A global antibiotic surveillance program, linking medical prescription with a personal identity card, thus making prescription digitalised and auditable.
- Public awareness and education: human endeavour in the form of non-governmental organisations (NGOs) and mass media.
- Infection control and its subsequent spread by separation of infected individuals.
- National and international co-operation in the form of National Action Plans and Global Action Plans.
- Restricting the prophylactic and metaphylactic use of antibiotics in animals, as it ultimately develops resistance among humans.

- Corporate social responsibility funds to be used for awareness programmes. Industry–academia collaborations to conduct research to combat antibiotic resistance. Special funds may be generated for huge corporations for R&D to combat antibiotic resistance.

## 5. Impact of antibiotic use in animals

Antibiotics are an important resource for treating and curing diseased cases of medical importance. Similarly, they are used in animals and livestock to treat diseases and are also administered prophylactically to prevent the occurrence of diseases in animal populations. Non-judicious use of antibiotics or sometimes incomplete regimens cause resistant microbes to survive due to a sublethal dose of the medicine. This is the main cause of drug-induced resistance. This resistance spreads to humans through food, water contaminated by animal gastrointestinal tract waste, and the environment where slaughtered animal gastrointestinal tract waste is disposed of. This leads to drug resistance in the human population, which has huge socioeconomic costs. The non-judicious use of antibiotics leads to alteration of the gut microbiome of animals [27].

## 6. Conclusion

If taken seriously, the human catastrophe of antibiotic resistance can be managed in a better way by involving all stakeholders. Ultimately, these shall alleviate human health, limit morbidity and reduce mortality. The United Nations may initiate measures to mobilise the world community to combat the AMR catastrophe. Nations pledge to AMR research by signing declarations and sound funding. The above facts on the economic impacts of antibiotic resistance lead us to conclude that AMR is a very serious problem for humanity that may cause serious morbidity and mortality. Poor and developing societies and nations shall face the maximum brunt. A joint effort of all stakeholders, from judicious use of antibiotics to serious research to increase the efficacy of existing drugs and develop new-generation antibiotics, is required.

### Funding

None.

### Competing interests

None declared.

### Ethical approval

Not required.

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