Estimating the return on investment from tackling antimicrobial resistance using a package of One Health interventions

With the contribution of the OECD

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Contents

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Key findings

Estimating the return on investment from tackling antimicrobial resistance using a package of One Health interventions

- With the current level of action, it is projected that antimicrobial resistance (AMR) will lead to a reduction in life expectancy of 1.8 years globally by 2035.
- It will be met with significantly higher healthcare costs, with annual expenses for treating resistant bacterial infections estimated to reach US$ 412 billion worldwide.
- The increase in morbidity and mortality resulting from these bacterial infections will impose economic losses of US$ 443 billion from reduced workforce productivity alone.
- Evaluation of a mixed policy of One Health interventions – including awareness raising, surveillance, optimizing antimicrobial use in human and animal health, infection prevention, and new treatments – suggests a potential to avert nearly US$ 7.7 trillion in losses deriving from healthcare expenditure and workforce productivity by 2035. Implemented for longer, these interventions would offset another US$ 615.5 billion in losses per year, resulting in cumulative gains of US$ 19.1 trillion by 2050.
- The One Health intervention package considered in this study is estimated to cost US$ 1,248.1 billion worldwide by 2050, or US$ 40.3 billion per year.
- From this perspective in which the economic impact from AMR is measured through changes in healthcare expenditure and general workforce productivity, for every US$ 1 invested in a mixed policy intervention package, a global net return of between US$ 10.9 and US$ 14.2 is expected (2035 and 2050 scenarios respectively).

1 Background

Untreatable bacterial infections are an increasing worry as we see the growth of antimicrobial resistance (AMR) and the continued lack of access to effective antibiotics in many parts of the world. The Institute for Health Metrics and Evaluation (IHME) estimates that already in 2021 1.14 million deaths were directly caused by bacterial AMR worldwide *(2)*, and between 2025 and 2050 another 39 million deaths from AMR will occur. Despite these staggering estimates, action on prevention and control of infection, surveillance, stewardship, and other basic measures has been very slow. While most countries have National Action Plans (NAPs) in place, only 10% had financial provisions to actually implement these measures (TrACCS 2024) seemingly due to fiscal constraints or lack of affordability.

Clearly, tackling AMR is going to take considerable resources. And crucially, the decision to take action depends in large part how the crisis is perceived relative to other pressing global concerns, and how effective interventions are likely to be in terms of their ability to save lives and prevent catastrophic economic losses deriving from the crisis. Indeed, it is only through comprehensive analyses that we can make informed choices about where, how and when to take action. The analysis presented here was undertaken with the Organization for Economic Co-operation and Development (OECD), with support from several others including members from within the Quadripartite organizations and the World Bank in an effort to construct the investment case for tackling AMR at the global level.

2 Methods

Microsimulation model

The geographical scope of the economic burden analysis covered 182 countries grouped by World Bank income categories (i.e. low, lower-middle, upper-middle, and high-income) (**Table 1**).

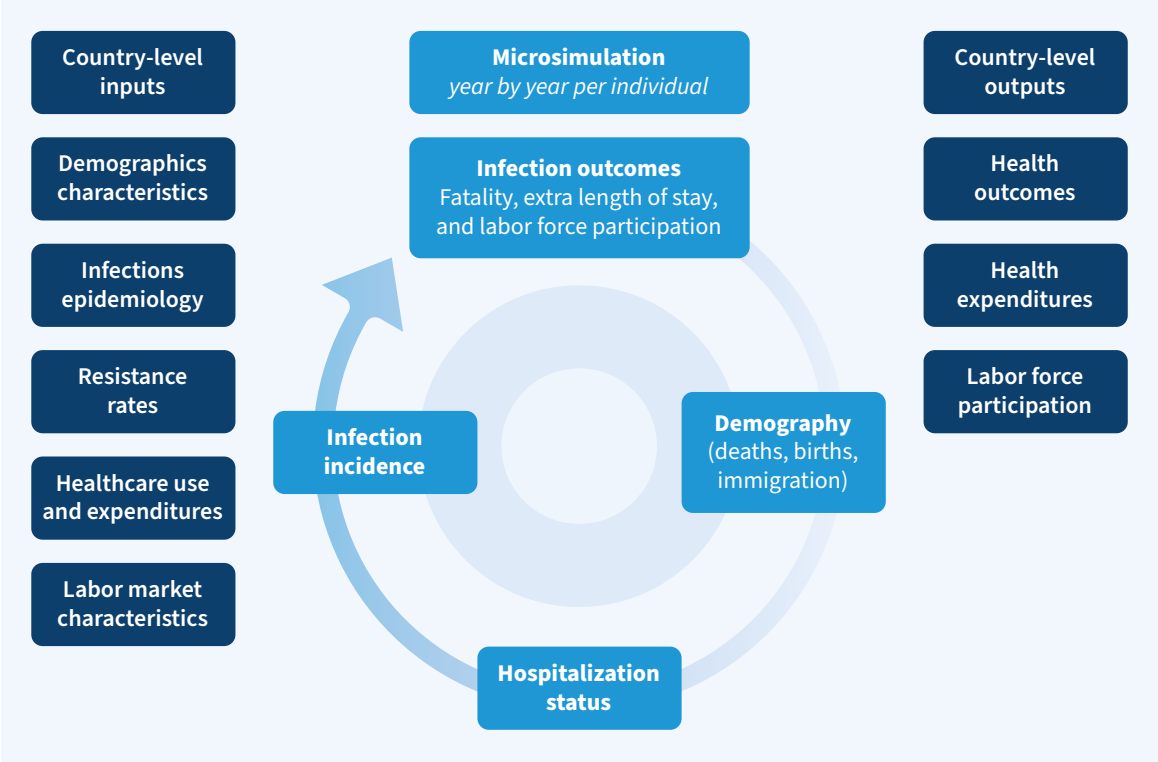
Table 1.
Countries included in this study by World Bank income group classification

Low / Lower middle income				
Afghanistan	Comoros	Kenya	Nicaragua	Syria
Algeria	Congo, Democratic Republic of the	Kiribati	Niger	Tajikistan
Angola	Congo, Rep.	Kyrgyzstan	Nigeria	Tanzania
Bangladesh	Djibouti	Lao	North Korea	Timor-Leste
Benin	Egypt	Lesotho	Pakistan	Togo
Bhutan	Eritrea	Liberia	Philippines	Tunisia
Bolivia	Eswatini	Madagascar	Rwanda	Uganda
Burkina Faso	Ethiopia	Malawi	Samoa	Ukraine
Burundi	Gambia	Mali	Sao Tome and Principe	Uzbekistan
CÃ´te d'Ivoire	Ghana	Mauritania	Senegal	Vanuatu
Cabo Verde	Guinea	Micronesia	Sierra Leone	Viet Nam
Cambodia	Guinea-Bissau	Mongolia	Solomon Islands	Yemen
Cameroon	Haiti	Morocco	Somalia	Zambia
Central African Republic	Honduras	Mozambique	Sri Lanka	Zimbabwe
Chad	India	Myanmar	Sudan	
		Nepal		

Upper middle / High income				
Albania	Colombia	Hungary	Mauritius	Serbia
Antigua and Barbuda	Costa Rica	Iceland	Mexico	Seychelles
Argentina	Croatia	Indonesia	Moldova	Singapore
Armenia	Cuba	Iran	Montenegro	Slovakia
Australia	Cyprus	Iraq	Namibia	Slovenia
Austria	Czechia	Ireland	Netherlands	South Africa
Azerbaijan	Denmark	Israel	New Zealand	South Korea
Bahamas	Dominican Republic	Italy	Norway	Spain
Bahrain	Ecuador	Jamaica	Oman	Suriname
Barbados	El Salvador	Japan	Panama	Sweden
Belarus	Equatorial Guinea	Jordan	Paraguay	Switzerland
Belgium	Estonia	Kazakhstan	Peru	Thailand
Belize	Fiji	Kuwait	Poland	Tonga
Bosnia and Herzegovina	Finland	Latvia	Portugal	Trinidad and Tobago
Botswana	France	Lebanon	Qatar	Turkey
Brazil	Gabon	Libya	Romania	Turkmenistan
Brunei Darussalam	Georgia	Lithuania	Russia	United Arab Emirates
Bulgaria	Germany	Luxembourg	Saint Kitts and Nevis	United Kingdom
Canada	Greece	Macedonia	Saint Lucia	United States
Chile	Grenada	Malaysia	Saint Vincent and the Grenadines	Uruguay
China	Guatemala	Maldives	Saudi Arabia	Venezuela
	Guyana	Malta		

For each country or region, the model uses demographic and risk factor characteristics by age and gender (4). From these inputs, it generates synthetic cohorts in which individuals are assigned demographic characteristics and risk factor profiles (Figure 1). Based on these profiles, individuals have a certain annual risk of developing an infection of interest.

Figure 1.
Model framework



Healthcare costs associated with treating the disease are estimated from a societal perspective, based on an annual cost per case associated with the medical treatment of infections. Medical treatment encompasses both inpatient care and care provided in intensive care units. The cost for medical treatment is calculated by multiplying the number of hospitalizations attributed to the condition for the length of stay in the hospital (accounting for both stay in inpatient and intensive care units) and the estimates of cost of medical treatment, with the analyses relying as much as possible on country-specific and pathogen-specific estimates.

Analyses on human capital and its impact on the economy include both the formal and informal economy and are based on relative risks connecting disease status with the risks of absenteeism, presenteeism and employment rate. Changes in workforce participation are assessed using the human capital approach, employing national average wages to calculate lost labor market outputs. Population growth factors reported by the United Nations (https://population.un.org/wpp/) are considered for each region for future projections. A more detailed description of the model and technical information on how the analyses were carried out are described in detail in the OECD Strategic Public Health Planning (SPHeP) for antimicrobial resistance (4).

Study outcomes

For each year of analysis, a cross-sectional representation of the population is used to calculate health status indicators such as the prevalence of the disease of interest and the associated life expectancy*(4)*. Economic outcomes comprise healthcare costs and workforce productivity costs, the latter as a combination of workforce participation and productivity at work measured as a composite of absenteeism and presenteeism. The study outcomes are calculated by comparing a business as-usual-scenario (BAU) and a scenario entailing the implementation of a package of AMR interventions.

Business as usual scenario. The BAU scenario was analyzed with a cost-of-illness approach using the OECD Strategic Public Health Planning for AMR (SPHeP-AMR) model *(4)*. The BAU scenario estimated the current and projected cost of AMR (in terms of healthcare expenditure and productivity loss) should no additional action be taken and was then used as the benchmark for the development of the investment case.

Defining the package of AMR interventions. The selection of interventions is made through a combination of literature review and expert consultation. To ensure consistency and establish boundaries for the selection process, key terminology and the search scope were as follows:

- ***Definition of key terminology***. A priority AMR intervention is a broadly defined policy intervention that seeks to answer one of the key objectives laid out in the Global Action Plan on AMR *(5)* or the Quadripartite One Health Joint Plan of Action *(6)*. These interventions are also anticipated to be effective and have an economic impact. The "package" is the subset of interventions for which cost and effectiveness data are available, and therefore included in the economic analysis.

- ***Definition of sectors***: Animal, human, environment, and plant sectors were included. Interventions across sectors (One Health) were also considered.

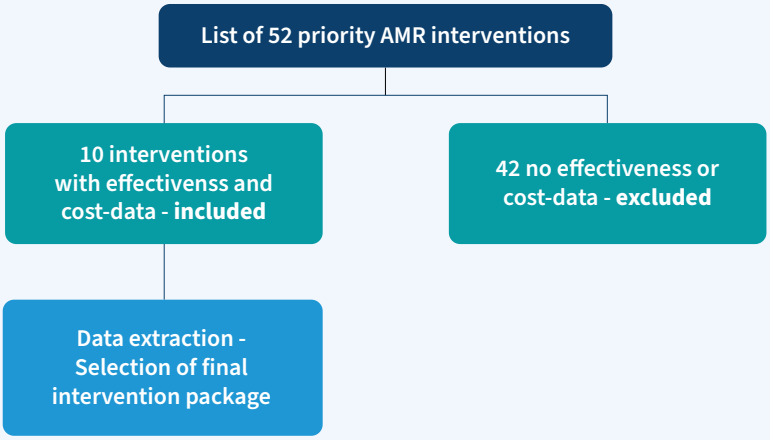
- ***Applicability of interventions***. The list of priority AMR interventions takes a global perspective acknowledging the fact that countries are at different stages of readiness to address AMR. The list of priority AMR interventions is intended to be a menu for countries to consider in making their selection across the sectors. They are in line with the list of priority policy actions highlighted in the Global Action Plan on Antimicrobial Resistance *(5)*. The list does not consider local, regional, or national implementation requirements or variation in healthcare settings.

- ***Selection of interventions***. In order to identify all potential interventions, a literature search was undertaken spanning peer-reviewed articles (in PubMed) and publications from intergovernmental organizations (e.g. FAO, OECD, UNEP, WHO, WOAH, and World Bank), non-governmental organizations and research institutions. Only articles published between 2015 to 2023 in English language were considered. For the human sector, the WHO People-centered framework for addressing AMR was considered *(7)*. A summary of the included literature can be found in **Appendix 1**. The categorization of the interventions was based on the overarching objectives outlined in the Global Action Plan on Antimicrobial Resistance *(5)*. The consolidated list of priority AMR interventions included 52 interventions. **Appendix 2** provides an overview of each identified intervention per sector with a link to the appropriate reference.

In order to identify the interventions with sufficient recent cost and effectiveness evidence to be included in the intervention package for the economic analysis, a further systematic review was undertaken. This included all studies published in English between 2018 – 2023 for each of the 52 interventions, singling out systematic reviews in the first instance. **Appendix 3** gives an overview of the identified studies. Each of the systematic literature reviews identified were then searched for specific primary studies that showed cost-effectiveness or cost-analysis estimates for the interventions of interest. In a second step, a more targeted search for primary studies reporting cost and effectiveness data for each of the 52 priority AMR interventions was conducted-- the aim being to capture any primary studies that were not captured by the previous systematic reviews. A detailed summary of each search strategy per AMR intervention can be found in **Appendix 4**.

The literature searches identified effectiveness and cost information for 10 interventions out of the 52 priority AMR interventions. In some cases, effectiveness and cost data were available for multiple practices within a single intervention category. Ultimately, 13 practices falling within 10 intervention categories were selected. **Figure 2** displays a summary of the methodological approach.

Figure 2.
Methodological approach for selecting the key AMR intervention package



Modelling interventions

Each intervention is modelled across 4 key parameters including intervention effectiveness, effectiveness over time, baseline and target coverage, and cost.

Information on effectiveness and costs were extracted from all identified studies. Of the total 10 interventions included in the package, seven corresponded to the human sector, one to the animal sector, one to the environment sector and one, cutting across all sectors, to One Health. **Table 2** summarizes the main characteristics of the final package of key AMR interventions sub-selected for the return on investment (RoI) analysis. Cost information is included in **Appendix 5**.

Table 2.
Final package of key AMR interventions for the RoI analysis

Category	Intervention	Identified practice	Sector
Improve awareness and understanding of AMR	1. AMR awareness raising, education and behavior change of health workers and the community	1. a. Enhance health worker training 1. b. Scale up mass media campaigns	Human
Improve surveillance AMR/AMU	2. Enhance food-handling practices / biosecurity practices to reduce the risk of AMR spread between humans and animals	2. a. Improve food handling practices	One Health
Invest in new drugs, diagnostic tools, vaccines, and other interventions (R&D)	3. Research into new antimicrobials, diagnostics and vaccines for AMR and behavioral and implementation science	3. a. New antibiotic incentive program	Human

Category	Intervention	Identified practice	Sector
Effective sanitation, hygiene, and infection prevention measures	4. Implementation of biosecurity measures to prevent the introduction and spread of disease in farms	4. a. Improve farm hygiene	Animal
	5. Implementation of infection, prevention, and control core components to mitigate AMR	5. a Enhance hand hygiene	Human
	6. Universal access to improved WASH and waste management to mitigate AMR	6. a. Strengthen access to latrines / improved latrines for children aged 0-5	Human
	7. Ensure safe and sustainable disposal and treatment of antimicrobials and hazardous waste	7. a. Enhance environmental hygiene	Environment
Optimize the use of antimicrobial medicines in human and animal health (Antibiotic stewardship)	8. Quality laboratory system and diagnostic stewardship to enable clinical bacteriology and mycology testing.	8. a. Implementation or scale up of Rapid diagnostic tests (RDTs)	Human
	9. Access to vaccines and expanded immunization to manage AMR.	9. a. Improve vaccination coverage for children aged 0-5	Human
	10. Up-to-date evidence-based treatment guidelines and antimicrobial stewardship programs	10. a. Strengthening antimicrobial stewardship programs 10. b. Delayed antimicrobial prescribing 10. c. Financial incentives for prescribing targets	Human

Baseline and target coverage values for each intervention were applied in the model. Baseline coverage was taken to vary in line with values reported in the 2023 Tracking AMR Country Self-assessment Survey (TrACSS), as well as the WHO first global survey on infection prevention and control in healthcare facilities[1] reflecting the level of implementation of the various interventions as self-assessed by national focal points and varying from no implementation to full implementation of the intervention. Target intervention coverage was assumed to be the same for all regions and, depending on the intervention, may reflect agreed targets for similar types of interventions or a pragmatic and achievable target that would help countries make a significant step towards achieving universal health coverage for AMR-related interventions. **Appendix 6** reports information on the target coverage selected for each intervention (**Table A6.1**), as well as information about the effectiveness, population target, and impact for each intervention included in the package (**Table A6.2**).

Finally, to estimate the present values for investment (intervention costs), and in light of the complexity of conducting a micro costing approach for each intervention and each country/region, costs identified from 2023 TrACCs survey responses and from the literature were extrapolated where missing and adjusted for purchasing power parity (PPP) index values from the World Bank. **Appendix 7** shows detailed information on costs for each intervention included in the analysis.

1 https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00809-4/fulltext

Expert consultation was undertaken to validate the approach and to identify any missing parameters. In 2022, each organization of the Quadripartite, in addition to the World Bank, nominated an expert to participate in the meetings of the Core Group on the economics of AMR. The Core Group had oversight of each stage of the work. Additionally, the Quadripartite Technical Group on the economics of AMR (QTG-EA) was formed in June 2023, bringing together twenty selected experts across the globe to advise the Quadripartite organizations on the economic implications of tackling AMR across sectors. Members of QTG-EA provided feedback about the main assumptions, methodology, and inputs of the BAU scenario, the selection of key AMR interventions, and investment case over 2023 and early 2024. Finally, the regional offices of the Quadripartite organizations provided feedback in relation to the list of priority key AMR interventions and the methodology used to select them.

Calculating the return on investment from implementing a package of interventions

The SPHeP-AMR model was run to simulate the impact of the policy package on AMR-related health and cost outcomes. The package is assumed to be implemented from 2020 and its effect is calculated for the period spanning 2020-2035. A societal perspective is considered in the analysis, accounting for healthcare expenditures avoided and improved productivity from lower levels of AMR from the intervention package. A multiplicative approach is used to combine intervention effectiveness for the package of interventions. No inflation factors are used. Income groups are weighted by population. Undiscounted and discounted (3% and 6% annual discount rate starting in the second year) results are presented for both investments and benefits. The following formula is used to estimate the return on investment (RoI) from implementing the intervention package.

$$ROI = \left(\frac{\text{Present values (benefits)}}{\text{Present values (investment)}} - 1 \right)$$

Where:

RoI represents the net return on investment. Values > 0 show that each invested unit gives a positive return, while values < 0 show a negative return.

Present values (benefits) represent the present values for the intervention benefits (returns), throughout the analysis.

Present values (investment) represent the present values for investments (implementation costs of interventions) throughout the analysis.

Additional analyses

Scenario analysis was conducted to provide additional information to decision makers and to incorporate uncertainty into the analysis:

Alternative intervention cost structure. While the base case assumes an equal distribution of investment for all years of analysis, a more conservative scenario is also considered, which assumes that 50% of the total investment occurs during the first year, and the rest (maintenance costs) are incurred in the remaining years. The value of 50% was chosen based on the information reported for the Water, Sanitation and Hygiene (WASH) intervention investment *(39)* and could reasonably be assumed for interventions requiring large initial (e.g. infrastructural) outlays.

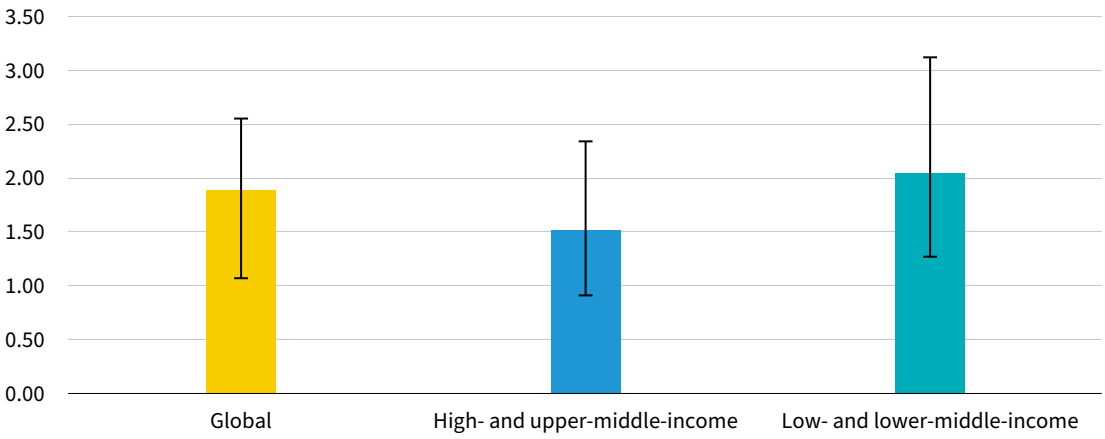
Alternative time period. The analysis is also run for a longer time horizon period, spanning 2020 to 2050.

3 Results

3.1. Business as usual scenario

On average, a loss of 1.8 years in life expectancy could be attributed to AMR globally by 2035 if the current levels of activity continue. Low- and lower-middle income countries are expected to see a greater loss, estimated at an average of 2.04 years while high- and upper-middle income countries are expected to face losses closer to 1.5 years (**Figure 3**).

Figure 3.
Loss in average life expectancy (years) attributed to AMR by 2035



Error bars represent 95% confidence intervals

Overall, the healthcare systems across the globe are estimated to spend approximately US$ 412 billion per year by 2035 as direct of consequences of AMR (**Figure 4**).

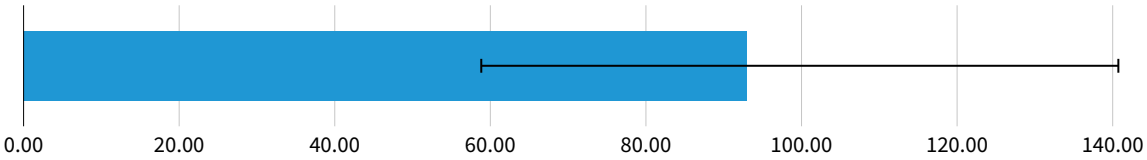
Figure 4.
Estimated yearly global healthcare expenditure on AMR by 2035 (US$ 2020)

There is great variability across regions, reflecting the differences in the levels of access to health care services and the cost of delivering health care services. In low- and lower-middle income countries costs are expected to be approximately US$ 6 per capita (**Figure 5a**), while in high-income countries expenditure is expected to be approximately US$ 93 per capita (**Figure 5b**).

Figure 5a.
Estimated healthcare expenditure attributed to AMR by 2035 (2020 US$ per capita)
Low- and lower middle-income countries

Error bars represent 95% confidence intervals

Figure 5b.
Estimated healthcare expenditure attributed to AMR by 2035 (2020 US$ per capita)
High- and upper middle-income countries

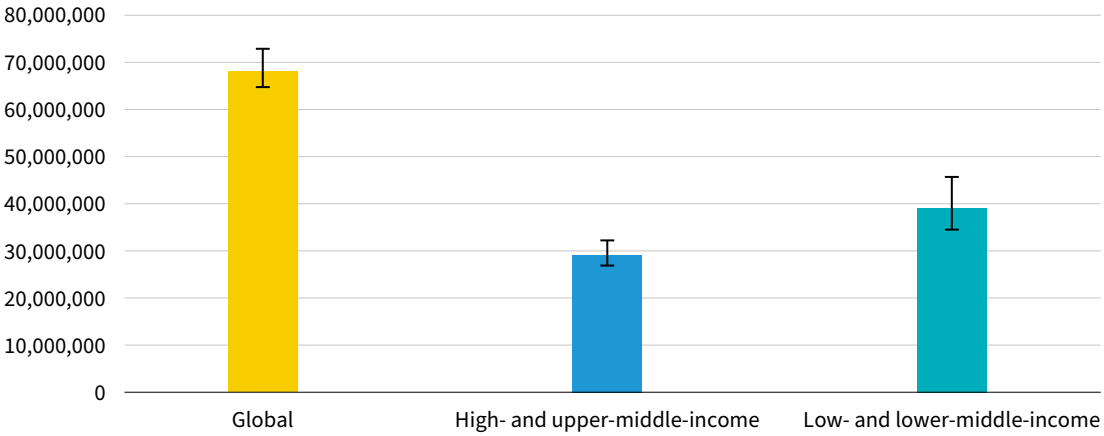


Error bars represent 95% confidence intervals

Globally, AMR is expected to depress the workforce by the equivalent of more than 68 million full-time equivalents (FTEs) every year, which can be considered as the number of people with a full-time job contributing to the formal or informal economy.[2] Cross-regional variability is determined by various factors such as the total number of individuals in each region as well as demography and workforce participation.

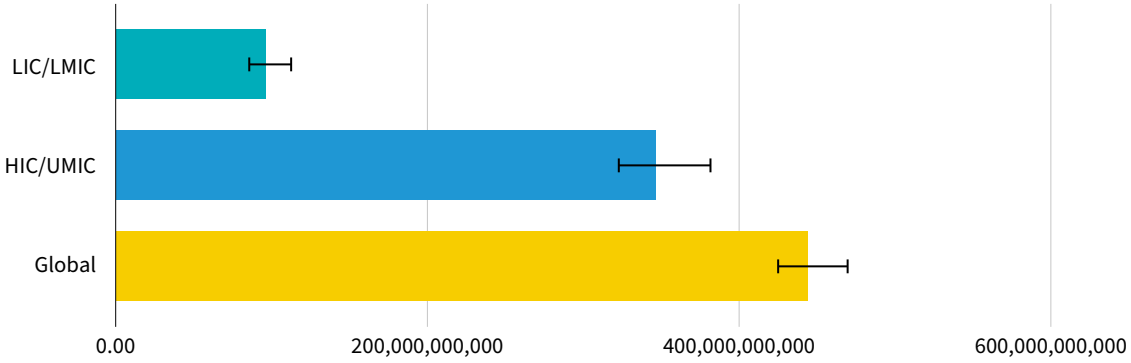
Figure 6 shows the average yearly losses in workforce participation attributed to AMR by 2035 in terms of full-time equivalents.

Figure 6.
Losses in workforce participation
Full-time equivalents per year: 2035 scenario



Average annual losses from reduced workforce participation between by 2035 are estimated to be 443 billion US$, with 78% of these losses occurring in high- and upper-middle income countries (**See Figure 7**).

Figure 7.
Yearly losses in average labor output by 2035 based on average wages (US$ 2020)



Note. US$ 2020, error bars depict 95% confidence interval

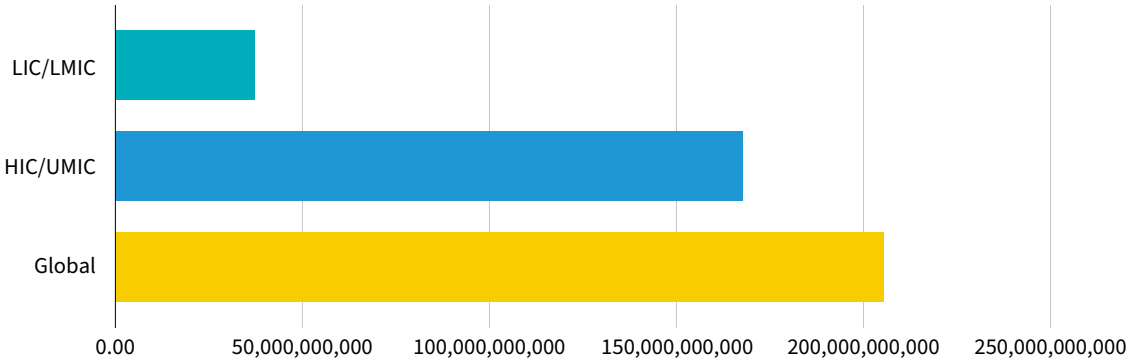
2 Informal workforce is accounted for to the extent that it is captured in official national estimates.

3.2. Benefits due to the Intervention package

The implementation of the package is estimated to produce significant savings to the healthcare systems. The SPHeP-AMR model predicts that every year, countries could save an average of US$ 4,390 billion by 2035 and about US$ 9,141 billion by 2050.

The reduction in morbidity and mortality produced by the package also favorably impacts workforce participation. Across the regions included in the analysis the total gains produced by the package in terms of workforce participation, would be approximately US$ 3,293 billion by 2035 and US$ 9,939 billion by 2050. **Figure 8** shows the average annual gains that would be produced by the implementation of the package.

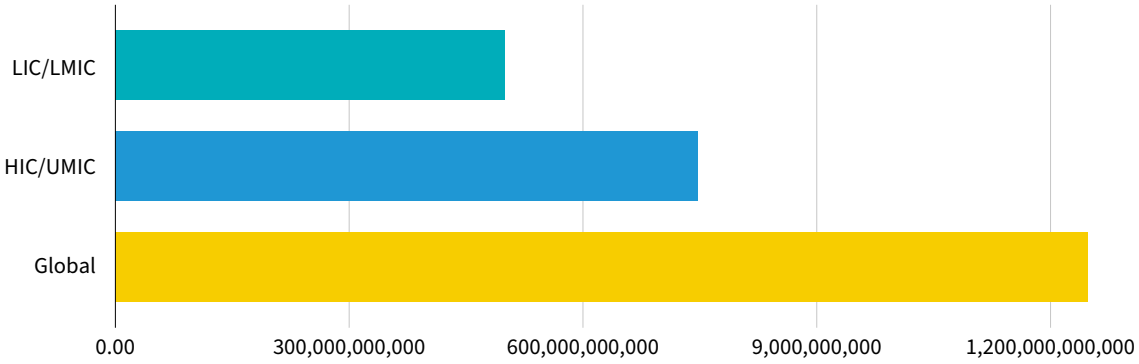
Figure 8.
Gains in average labor market output based on average wages per year produced by the package 2020 to 2035 (US$ 2020)



3.3. Total investment

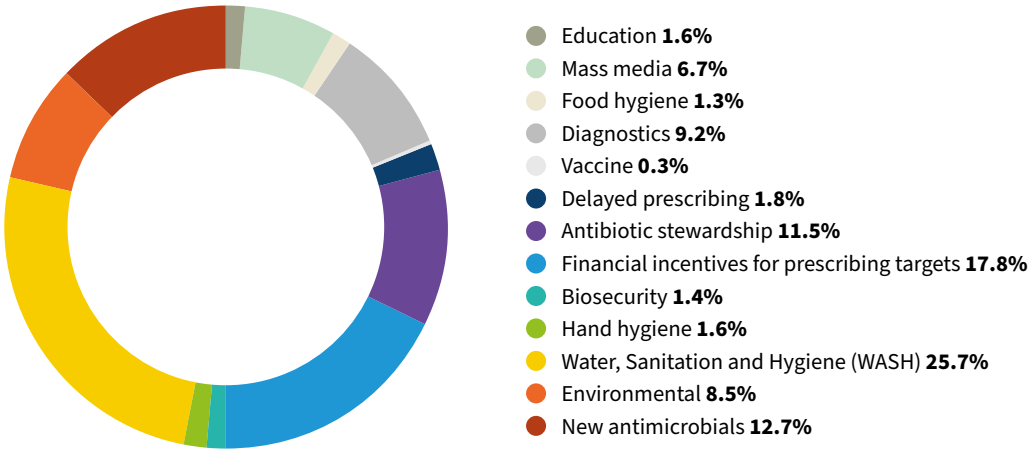
For the period 2020-2035 full implementation of the package of interventions globally is estimated to cost USD 614.9 billion. **Figure 9** shows the total investment required for longer time horizon.

Figure 9.
Total investment required for the period of analysis 2020-2050 per income category (US$ 2020)



Additionally, **Figure 10** shows the distribution of total costs for the 13 practices included in the analysis.

Figure 10.
Intervention package cost distribution

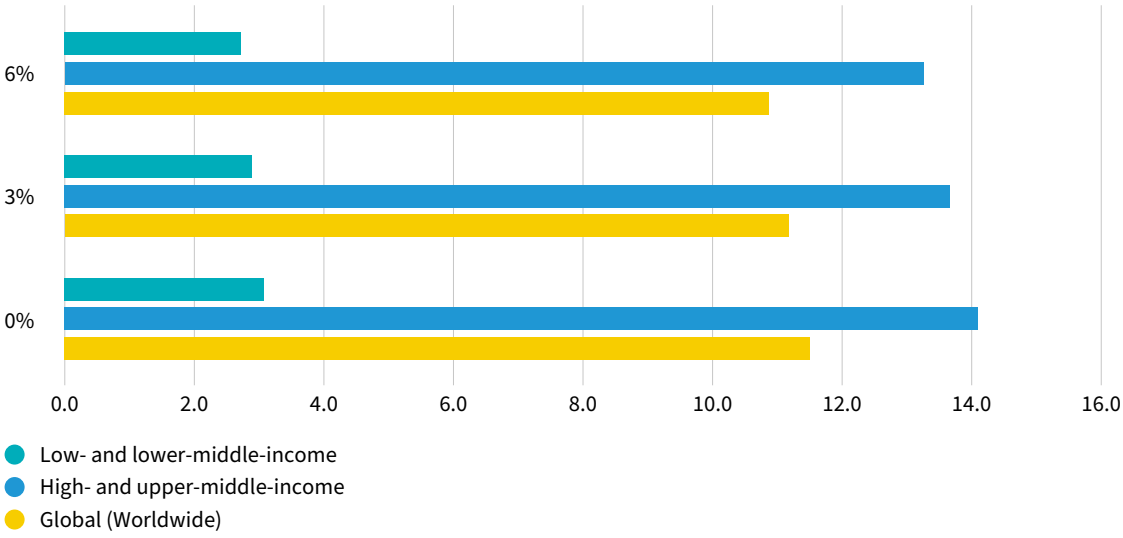


It should be noted that relative costs across the intervention package are partially driven by the estimated differential between the current and target coverage level. So, for example, whereas WASH interventions are generally not costly to implement, the overall relative cost burden of WASH within the One Health package is considerable.

3.4. Return-on-investment

Return-on-investment results are presented for the base case and scenario analysis. When the analysis period (2020-2035) was considered, the global RoI, including all regions, was estimated to be between 10.9 and 11.5, applying an annual discount rate of 6% and 0% respectively (**See Figure 11**).

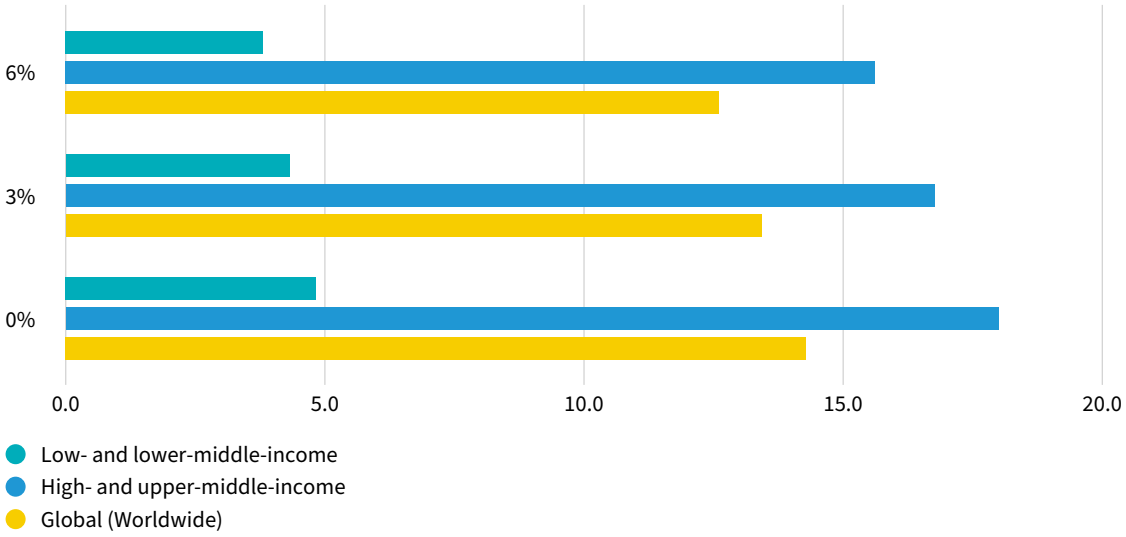
Figure 11.
RoI values for the 2020-2035 analysis period, considering different annual discount rates (%)



Note. Interpretation: For every US$ 1 invested in a mixed policy AMR package, countries in high and higher-middle income regions can expect a net return of US$ 11.2 (3% discount rate analysis)

When a longer period was considered (2020-2050), the global RoI was estimated to be 12.6 and 14.3, applying an annual discount rate of 6 and 0% respectively (**Figure 12**).

Figure 12.
RoI values across all the regions (2020-2050) considering different annual discount rates (%)



An alternative cost structure that assumed 50% of intervention costs occur in the first year produced slightly different RoI estimates. When the base case period was considered (2020-2035), the global RoI was estimated to be between 8.9 and 11.8, applying an annual discount rate of 6% and 0% respectively. When the extended analysis period (2020-2050) was considered, the global RoI was estimated to be between 7.4 and 15.2, applying an annual discount rate of 6% and 0% respectively. (See **Appendix 8**)

4 Discussion

The work presented here reports quantitative findings on the disease burden attributable to AMR, its economic implications, and returns that can be expected from implementing a package of One Health interventions globally. Even with the conservative approach taken, findings suggest that the economic burden of AMR will be staggering and that the effects will be felt well beyond the healthcare sector. Indeed the long-term costs associated with increased healthcare use, and decreased economic productivity due to resistant infection are substantial. However, if greater action is taken, it is expected that the returns made from investing in suitable AMR interventions are likely to pay for themselves, and in most regions this will be several times over. The omission of economic ripple effects from AMR in this study (e.g. reduction in travel, dampening of wider production-related parameters, etc.) suggest these results may be conservative, underestimating savings over time, especially in regions that rely on tourism and other sensitive sectors. It should also be noted that studies such as this one, that account for the full cost of broad infection prevention interventions while only capturing benefits related to AMR, will underestimate the full cost-effectiveness of such interventions to the health sector, and to society more broadly.

This is not the first study to estimate the economic burden of AMR. A World Bank publication previously concluded that by 2050, the financial cost of AMR would be in the order of magnitude of US$ 1 trillion annually at the global level, when measured in terms of losses in global GDP *(3)*. Considering the differences in methodologies and assumptions, the findings from the current study are relatively comparable, given that the SPHeP-AMR model suggests worldwide costs would amount to approximately US$ 0.86 trillion annually by 2035, with higher annual costs in the final phases of the simulation.

Moreover, a WHO publication *(8)* reported that between 2020-2030, the AMR burden in the Western Pacific Region amounts to 5.2 million deaths (i.e., about 473 000 deaths per year) with an associated cost of 148 billion US$ (i.e., 13.5 billion US$ per year). This cost was split almost equally between healthcare costs and productivity losses. Conversely, the current study concludes that, by 2035, countries in the region will suffer 1 070 000 deaths per year due to AMR, associated with yearly costs of 246 billion US$, 42% of which will be caused by higher healthcare expenditures. Several methodological differences across the two analyses help explain the varying results. Firstly, the WHO study only focuses on a smaller set of antibiotic-bacterium combinations (for example, tuberculosis is not considered). It also focuses on invasive infections as opposed to a broader set of infections, such as respiratory, urinary tract and soft tissue infections, which are considered in the current study.

The SPHeP-AMR model was calibrated to compare mortality data (i.e. number of deaths) by region and antibiotic-bacterium combinations that were calculated by the IHME in a scenario where all resistant infections are eliminated. **Appendix 9** shows mortality due to AMR by region and depicts those results by antibiotic and bacterium combination, normalizing results to the IHME data, which are considered equal to 100% for each region and antibiotic bacterium combination. Both figures show the IHME confidence intervals and the SPHeP-AMR model outputs as a percentage of the IHME value. Overall, the results from the model match well with the number of deaths calculated by IHME on both of the considered dimensions, with mortality predicted by the SPHeP-AMR model well within the confidence intervals provided by the IHME.

The present analysis reveals that the global RoI of public health interventions for AMR would be particularly high. Even in the most conservative scenarios, a global RoI of 12.6 was estimated for the period of analysis (2020-2050). To the best of our knowledge, there are few RoI values reported in the literature. A publication from the Center for Global Development has reported that the RoI of an initiative to develop new antibiotics could be estimated at 125:1 (benefit: cost ratio) at a Global level for a period of 30 years) *(9)*. OECD has recently reported RoI values for high-income countries only (OECD countries). Although most of the data included in the present analysis mirrors that of the OECD, there were some differences (i.e., different regions involved and addition of new interventions). Despite this, the positive RoI findings of the present analysis remained in line with the previous OECD result reporting for every US$ 1 invested in a mixed policy AMR package across the health and food sectors, US$ 5 in returns can be expected *(10)*.

An analysis of the variation of the outputs over time suggests that extending the simulation time has a relatively small but significant impact. For example, extending the end of the simulation period from 2035 to 2050 increases the average yearly health care expenditure by around 6.6%, from US$ 44 per capita per year to US$ 47 per capita per year. While the result could appear relatively small in absolute terms, it should be noted that the estimated increases in the average yearly health expenditure is the average over each simulation period (i.e. 2015-35, 2015-40, 2015-50), meaning that there is a much steeper increase in average expenditure between 2035 and 2050. Again, some cross-regional variation is observed, with values ranging between 1% in low- and lower middle-income countries in the African region and 13% upper-middle income countries in the Eastern Mediterranean region.

Furthermore, the high RoI identified in higher income countries underscores that no nation is immune to the economic consequences of AMR. As these countries often serve as global hubs, investing in public health interventions becomes not only a national imperative but also a strategic move to safeguard global economic stability and security.

Overall, the findings from this investment case underscore the need for a collaborative, global effort to address AMR, with a focus on equitable distribution of resources to ensure that vulnerable populations countries benefit from these interventions. Developing countries often face resource constraints and are disproportionately affected by infectious diseases. Allocating funds to AMR interventions such as strengthening healthcare infrastructure, promoting antimicrobial stewardship, and Improving awareness and understanding of AMR can yield significant health and financial benefits, and contributing to global health security.

The study also emphasizes the importance of a One Health approach, recognizing the interconnectedness of human, animal, and environmental health. By investing in interventions that promote responsible antimicrobial use in both healthcare and agriculture, we can create a holistic strategy that addresses the root causes of AMR and reduces the emergence and spread of resistant pathogens.

Limitations

The present RoI analysis has limitations. Given the dearth of studies testing interventions in LMIC contexts, much of the information used to conduct this analysis comes from high-income countries. Although adjustments have been made to account for cross-country price level differences related to intervention implementation, the effectiveness values have been assumed to be the same across settings, only varying with region-specific data on the current coverage (BAU intervention coverage) for each intervention. Also, it should be noted that the very limited data from informal economic activity likely distorts findings from regions where such activity is prominent.

Inclusion of interventions in the RoI analysis was dependent on the availability of cost and effectiveness data. There are many interventions for which little evidence of direct effect on morbidity or mortality exists (and therefore have been excluded) but can play an important role in tackling AMR. Integrated surveillance is one such example. Also, evidence on costs and effectiveness of interventions is very unequal across the One Health settings. Little is available from areas related to animal health, and almost none is available from the environment. This imbalance is reflected in the relative abundance of human interventions relative to animal and environment interventions in the final package that is analyzed in this study. This emphasizes the need for greater evidence from the animal health and environment sectors.

5 Conclusions

The findings of this investment case make a compelling argument for the prioritization of public health interventions to tackle antimicrobial resistance on a global scale. The high RoI estimates highlight the transformative potential of targeted interventions in mitigating the financial and health consequences of AMR. The cost of tackling AMR globally is substantial, and indeed it is higher than previously estimated. However, the losses from failing to do more are expected to be immense, likely even catastrophic in some parts of the world.

In absolute terms the cost of tackling antimicrobial resistance will be greatest for higher-income countries but these are also the countries that stand to lose the most economically from the growth of resistance. Policymakers are urged to allocate resources strategically to ensure a sustainable and resilient future in the face of the growing global threat posed by AMR.

In light of global political commitments, including the 2024 UNGA Political Declaration on AMR, there is now a clear mandate for countries to transform their One Health ambitions into tangible interventions aimed at results. The evidence presented in this report can support Member States and global organisations to prioritise action, finance sustainable systems, and deliver on AMR goals by 2030.

Appendix 1.
Overview of evidence – Literature review

Table A1.1:
Overview of evidence.

Study	Title	Overview and Key Findings
OECD & WHO, 2022 *(11)*	Addressing the Burden of Infections and Antimicrobial Resistance Associated with Health Care	The report discussed various interventions suggested by the organization in addressing antimicrobial resistance. Evidence behind the interventions suggested were also provided.
Morel et al, 2020 *(12)*	A one health framework to estimate the cost of antimicrobial resistance	The study created a costing framework that may be utilized by first identifying the most common antimicrobial resistance pathogens and how the epidemiologic pattern of AMR is. This was followed by analyzing the probabilities for each sector (human health, animal health, and others).
World Bank, 2021, unpublished	"Stopping the Silent Epidemic: An Operational Framework for Addressing Antimicrobial Resistance" Working Draft	The document presented a framework in looking at various interventions to address antimicrobial resistance. It divided interventions into AMR-sensitive and AMR-specific.
WHO & World Bank, 2022 *(13)*	Sustaining Action Against Antimicrobial Resistance: A Case Series of Country Experiences	The report presented case series of several countries, mostly from LMICs with their strengths and weaknesses in implementing their national action plan against antimicrobial resistance as pushed by member countries.
WHO, 2019 *(14)*	Global Antimicrobial Resistance Surveillance System (GLASS)	The GLASS report was created to boost AMR surveillance among member countries. This was thus a report describing it and discussing key points on surveillance with regards to national action plans of countries.
FAO, 2022 *(15)*	Tackling Antimicrobial Use and Resistance in Food-producing Animals: Lessons Learned in the United Kingdom	The FAO discussed interventions within the animal health realm in addressing antimicrobial resistance using the United Kingdom as a case study for discussion on national plans for AMR.
OECD & WHO, 2019 *(16)*	Challenges to Tackling Antimicrobial Resistance	The joint report presented interventions aimed at tackling antimicrobial resistance. It provided a good background on infection control and different approaches to address AMR.
WHO, 2021 *(17)*	Comprehensive Review of the WHO Global Action Plan (GAP) on Antimicrobial Resistance	The document presented indicators per GAP objective identified to monitor and evaluate efforts for AMR.
WHO, 2022 *(7)*	People centered framework for addressing AMR ppt	Overview of interventions for human health
Jit et al, 2020 *(18)*	Quantifying the economic cost of antibiotic resistance and the impact of related interventions: rapid methodological review, conceptual framework and recommendations for future studies	The study proposed a conceptual framework for antibiotic resistance.
UNEP, 2022 *(19)*	Environmental Dimensions of Antimicrobial Resistance: Summary for Policymakers	The paper presents environmental impacts of AMR and the causes of the development and spread of resistance in the environment, including the gaps in understanding those impacts and causes.

Study	Title	Overview and Key Findings
FAO, 2021 *(20)*	The FAO Action Plan on Antimicrobial Resistance 2021-2025	This FAO Action Plan on AMR 2021–2025 sets out the five objectives that guide the programming of FAO activities: 1. Increasing stakeholder awareness and engagement 2. Strengthening surveillance and research 3. Enabling good practices 4. Promoting responsible use of antimicrobials 5. Strengthening governance and allocating resources sustainably
OECD, 2018 *(21)*	Stemming the Superbug Tide: Just a Few Dollars More	In this report, OECD used advanced techniques, including machine learning, ensemble modelling and a microsimulation model, to provide support for policy action in the human health sector.
World Bank, 2017 *(3)*	Drug Resistant Infections: A Threat to Our Economic Future	This report examines the economic and development consequences of antimicrobial resistance (AMR), using the World Bank Group economic simulation tools to put a price tag on AMR's destructive impacts on the global economy from 2017 through 2050, if adequate measures aren't taken to contain the AMR threat.
Al-Haboubi et al, 2020 *(22)*	Views of health care professionals and policymakers on the use of surveillance data to combat antimicrobial resistance	Identified the extent of the use of AMR data to the perceived needs of healthcare professionals and policymakers
PIRU RVC, 2019 *(23)*	Impact of guidelines and recommendations on the level and patterns of antimicrobial use in livestock and companion animals: Systematic Review	Explored guidelines in Europe and analyzed their impact on AMR relating to farm animals and companion animals
EFSA and EMA, 2016 *(24)*	EMA and EFSA Joint Scientific Opinion on measures to reduce the need to use antimicrobial agents in animal husbandry in the European Union, and the resulting impacts on food safety (RONAFA)	Assessment and recommendations on AMR interventions in the European region
OECD, 2019 *(25)*	Evaluating the economic benefits and costs of antimicrobial use in food producing animals	Evaluated on an economic perspective and provided interventions to promote AMR action
OECD, 2023 *(10)*	Embracing a One Health Framework to Fight Antimicrobial Resistance	Considers the effectiveness of numerous One Health interventions

Appendix 2.
List of priority AMR interventions

Defining the package of AMR interventions. To reach a consensus-based list of priority AMR interventions to be modelled in the investment case, a multi-step approach was implemented, including evidence generation and expert consultation. First, key terminology and the scope of work were defined, which involved the following elements:

Definition of key terminology: A priority AMR intervention is a broad (policy) intervention that seeks to answer one of the key objectives laid out in the Global Action Plan on AMR *(5)* or the Quadripartite One Health Joint Plan of Action *(6)*. These interventions are also anticipated to be effective and have an economic impact. The "package" is the subset of interventions for which cost and effectiveness data was available, and therefore included in the economic analysis.

Definition of sectors: Animal, human, environment, and plant were included. Interventions across sectors (One Health) were also considered.

Applicability of interventions: The list of priority AMR interventions takes a global perspective acknowledging the fact that countries are at different stages of readiness to address AMR. The list of priority AMR interventions is intended to be a menu for countries to digest and understand which interventions are relevant per sector and across sectors. The list does not consider local, regional, or national implementation requirements or variation in healthcare settings. A targeted literature search of peer-reviewed (in PubMed) articles and publications from intergovernmental organizations (e.g. FAO, OECD, UNEP, WHO, WOAH, and World Bank), non-governmental organizations and research institutions was performed. In addition to the literature search, feedback was received on relevant evidence from the Quadripartite core group as well as from the Quadripartite Technical Group on the Economics of Antimicrobial Resistance (QTG-EA).

The key terms used in the search were the following: "Antimicrobial Resistance / AMR intervention" AND "Animal Health" OR "Plant Health or "Environment" OR "Cross-sector" AND "One Health". Only articles published between 2015 to 2023 in English language were considered. For the human sector, the WHO People-centered framework for addressing AMR were considered *(7)*.

Literature that met the inclusion criteria were selected and their information was extracted using a predesigned data extraction form. The categorization of the interventions was based on the overarching objectives outlined in the Global Action Plan on Antimicrobial Resistance *(5)*.

Table A2.1.
Package of key AMR interventions per sector (long-list): Animal, Human, Environment and Plant sectors.

Objectives	**Animal** *(20–22,26,27)*	**Human** *(28)*	**Environment** *(19,28,29)*	**Plant**
Improve awareness and understanding of AMR	Improve awareness, education, and behavior/ perception change programs incl. learning experiences for farmers, veterinarians, veterinarian students, pet owners, regulators, and the general public.	AMR awareness raising, education and behavior change of health workers and the community.	Education and awareness of key source pollution emitters for appropriate and point-source waste prevention and treatment, and protection of source waters.	Communicate with, educate, and provide training to farmers on AMR, integrated pest management (IPM), and the appropriate use and disposal of pesticides / herbicides/ molluscicides.
			Education and awareness of environmental and other relevant-sector authorities on the role of the environment in AMR development, transmission and spread.	
Strengthen knowledge and evidence-based through surveillance and research	National AMR surveillance to inform development and allow assessment of effectiveness of interventions and policies at national level.	National AMR surveillance network to generate quality data to inform patient care and action on AMR.	Implement systems for transparent and swift collection and reporting of the production, sales, use, and disposal of unused antimicrobials.	National surveillance of AMR data in food and agriculture and AMU data in crops through enrolling in the International FAO Antimicrobial Resistance Monitoring (InFARM).
	National AMU surveillance to inform development and allow assessment of effectiveness of interventions and policies at national level.	Antimicrobial consumption and use surveillance to inform patient care and action on AMR.	Integrate environmental monitoring data (e.g., from monitoring of surface water, solid waste, and airborne particulate matter) with existing AMR surveillance and pollutants data.	
			Document the safety of bioproducts (e.g., biofertilizers, bioplastics, biosolid and manure applications, and plant growth promoters) and novel agricultural practices, as well as key sources of pollution that indicate an impact on AMR in the environment.	
Reduce the incidence of infection through effective sanitation, hygiene, and infection prevention measures.	Implementation of biosecurity measures to prevent the introduction and spread of disease in farms.	Implementation of infection, prevention and control (IPC) core components to mitigate AMR.	Improve integrated water management and promote water, sanitation, and hygiene (WASH) to limit the development and spread of AMR in the environment as well as to reduce infections and need for antimicrobials.	Incentivize farm assurance or certification benchmarking schemes in farms.
	Ensure good animal husbandry and farm management practices linked to the Five Freedoms of animal welfare.	Universal access to improved WASH and waste management to mitigate AMR.	Ensure safe and sustainable disposal and treatment of antimicrobials and hazardous waste from healthcare facilities, pharmacies, veterinarian centers, animal and crop production, and households (e.g., creating, strengthening and promoting take-back programs).	
			Implement an integrated zoonotic disease surveillance system to detect disease emergence in human/animal population.	

Objectives	**Animal** *(20–22,26,27)*	**Human** *(28)*	**Environment** *(19,28,29)*	**Plant**
Optimize the use of antimicrobial medicines in human and animal health	Increase veterinary laboratory capacity (including ability to transport, store and process samples appropriately).	Quality laboratory system and diagnostic stewardship to enable clinical bacteriology and mycology testing.	Optimize strategies and resources, to include minimum standards such that adequate laboratory and human resource capacity can be established to maintain quality integrated surveillance at scale.	Establish regional, central BSL (Biological Safety Level) 3 and 4 laboratories for detection of zoonotic and infectious diseases.
	Promotion of use of viable / natural alternatives (e.g., prebiotic, probiotic) to reduce AMU (e.g., vaccines in salmon farming or alternatives to growth promotion).	Access to vaccines and expanded immunization to manage AMR.		Reduce the secondary use of AMU as growth promoters in agriculture (e.g., avoid mention of this use on labels).
	Create prescribing guidelines and stewardship programs at national level for targeted AMU including indication, line of therapy, dose, administration route and course of treatment of antimicrobials (e.g. switch from broad-spectrum to appropriate narrow-spectrum antimicrobial substances) with no perverse incentives (e.g. delinking prescribing with remuneration).	Up-to-date evidence-based treatment guidelines and antimicrobial stewardship programmes.	Implement management options to prevent and address releases, effluent, and waste from intensive animal and crop production and from healthcare facilities and pharmaceutical manufacturing.	Promote integrated pest management to reduce the use of antimicrobial pesticides.
	Phasing out over-the-counter (OTC) should be coupled with ensuring the availability of quality and affordable antibiotics.	Implementation of regulation to restrict non-prescription antimicrobial sales.		Reduce the need to use antimicrobial pesticides through the Reduce the Need for Antimicrobials on Farms (RENOFARM) initiative.
	Ensure accessibility and affordability of AMR diagnostics.	Uninterrupted supply of essential health products for AMR.		
		AMR diagnosis and management health services are made affordable for all.		
Increase investment in new medicines, diagnostic tools, vaccines and other interventions	Research and development of novel, cost-effective, and affordable vaccines.	Research into new antimicrobials, diagnostics and vaccines for AMR and behavioral and implementation science.	Develop new methods/ technologies to remove antimicrobial residues from the flows of wastewater, manure, and agricultural run-off.	-
	Develop veterinary/ animal/farm-appropriate diagnostics.		Develop soil/water/air-appropriate diagnostics.	

Abbreviations: AMR = Antimicrobial Resistance, AMU = Antimicrobial use, BSL = Biological Safety Level, INFARM = International FAO Antimicrobial Resistance Monitoring, IPC = Infection, Prevention, Control, IPM = integrated pest management, OTC = over-the-counter, RENOFARM = Reduce the Need for Antimicrobials on Farms, WASH = Water, Sanitation and Hygiene

Table A2.2.
Package of key AMR interventions across sectors (One Health, cross-cutting interventions).

Objectives	Cross-cutting interventions
Enhance policy, legislation, advocacy and financing.	Set up a functional multisectoral national coordination group to tackle AMR / One Health national platforms, engaging relevant stakeholders and organizations, and considering inequities associated with gender and vulnerable populations.
	Guarantee financing of AMR National Action Plans (NAPs) including the implementation of the recommended interventions e.g., in national budgets.
	Enhance food-handling practices / biosecurity practices to reduce the risk of AMR spread between humans and animals e.g., appropriate personal protective equipment (PPE) and hand hygiene.
	Address AMR in National and Subnational Emergency Preparedness and Response Plans.
Strengthen organizational development, implementation and sectoral integration	Capacity building in all areas of the above-mentioned interventions as well as in data management.
	Advocacy and education to raise awareness of AMR as a holistic OH issue, which can affect humans, animals, plants, and the environment. In particular, provide information about the interconnection and potential transmission routes between humans, animals, plants and the environment such as through soil, water and food.*
Implement data, evidence, and knowledge	Implement high quality, robust data collection, analysis and reporting and sharing systems to periodically review and analyze data on antimicrobial resistance and antimicrobial use across sectors in an integrated fashion and disseminate findings for sector specific and joint action.
	Implement pollution and residue controls for pharmaceutical production, human health systems, animal health systems (including aquaculture), plant production and protection, and municipal waste and wastewater at scale linked to Environmental, Social, and Governance (ESG) principles and conditionalities.
	Collaborative surveillance that covers human and animals, and where possible plant/environment.

Abbreviations: AMR = Antimicrobial Resistance, ESG = Environmental, Social, and Governance, HP=CIAs = Highest Priority Critically Important Antibiotics (HP-CIAs), JPA = Joint Plan of Action, NAP = National Action Plan, OH = One Health, PPE = Personal Protective Equipment, QJS = Quadripartite

* This includes the intervention "AMR advocacy, governance, and accountability in the human health sector in collaboration with other sectors." As mentioned in the WHO People-Centered Framework

Appendix 3.
Systematic literature reviews reporting cost-effectiveness or cost-analysis information of AMR interventions

Table A3.1.
Overview of systematic literature reviews (2018-2023) reporting cost-effectiveness or cost-analysis information of AMR interventions.

Human	One Health
Ananthakrishnan A, et al. A protocol for a systematic literature review of economic evaluation studies of interventions to address antimicrobial resistance, 2021 *(30)*	Naylor, NR, et al. Quantitatively evaluating the cross-sectoral and One Health impact of interventions: A scoping review and case study of antimicrobial resistance, 2020 *(31)*
Poudel AN, et al. The economic burden of antibiotic resistance: A systematic review and meta-analysis, 2023 *(32)*	Quadripartite One Health Return on Investment *(6)*
Befikadu L Wubishet et al. Economic evaluation of antimicrobial stewardship in primary care: a systematic review and quality assessment, 2022. *(33)*	Aluzaite, K, et al. Economic evaluation of interventions to reduce antimicrobial resistance: a systematic literature review of methods. Unpublished.
Painter, C., Faradiba, D., Chavarina, K.K. et al. A systematic literature review of economic evaluation studies of interventions impacting antimicrobial resistance, 2023. *(34)*	
D'hulster E, et al. Cost-effectiveness of point-of-care interventions to tackle inappropriate prescribing of antibiotics in high- and middle-income countries: a systematic review, 2023. *(35)*	
Carla Cuevas et al., Improving antibiotic use through behaviour change: a systematic review of interventions evaluated in low- and middle-income countries, 2021. *(36)*	
Nathwani, D. et al. Value of hospital antimicrobial stewardship programs [ASPs]: a systematic review, (2019) *(37)*	

Appendix 4.
Search strategies of the targeted review literature conducted

a.1. Systematic reviews

a.1.1.
Systematic literature reviews reporting cost-effectiveness or cost-analysis information of AMR interventions.

Search strategy (PubMed):

(Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab]) AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH]) AND (systematic review[Publication Type])

Filter: Last 5 years;

b.1. Human

b.1.1.
AMR awareness raising, education and behavior change of health workers and the community.

Search strategy (PubMed):

("Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab]) AND (Awareness [tiab] OR Education*[tiab] OR Behavior change[tiab]) AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

b.1.2
National AMR surveillance network to generate quality data to inform patient care and action on AMR.

Search strategy (PubMed):

("Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab]) AND Surveillance [tiab] AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

b.1.3
Antimicrobial consumption and use surveillance to inform patient care and action on AMR.

Search strategy (PubMed):

("Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab]) AND (Surveillance [tiab] OR consumption [tiab]) AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

Results: none met the inclusion criteria.

b.1.4.
Implementation of infection, prevention and control (IPC) core components to mitigate AMR.

Search strategy (PubMed):

("Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab]) AND (infect* control [tiab] OR infect* prevention [tiab]) AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

b.1.5.
Universal access to improved WASH and waste management to mitigate AMR.

Search strategy (PubMed):

("Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab]) AND (WASH [tiab] OR waste [tiab]) AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

b.1.6.
Quality laboratory system and diagnostic stewardship to enable clinical bacteriology and mycology testing.

Search strategy (PubMed):

("Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab]) AND (test* [tiab]) AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

b.1.7.
Access to vaccines and expanded immunization to manage AMR.

Search strategy (PubMed):

("Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab]) AND (vaccin* [tiab] OR immunisation [tiab]) AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

b.1.8.
Up-to-date evidence-based treatment guidelines and antimicrobial stewardship programmes.

Search strategy (PubMed):

("Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab]) AND (evidence-based [tiab] OR guideline* [tiab]) AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

b.1.9.
Implementation of regulation to restrict non-prescription antimicrobial sales.

Search strategy (PubMed):

("Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab]) AND (regulat* [tiab] OR prescription* [tiab]) AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

b.1.10.
Uninterrupted supply of essential health products for AMR.

Search strategy (PubMed):

("Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab]) AND (accessibility [tiab] OR affordability [tiab]) AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

b.1.11.
AMR diagnosis and management health services are made affordable for all.

Search strategy (PubMed):

("Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab]) AND (accessibility [tiab] OR affordab* [tiab]) AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

b.1.12.
Research into new antimicrobials, diagnostics and vaccines for AMR and behavioural and implementation science.

Search strategy (PubMed):

("Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab]) AND (new [tiab] OR novel [tiab]) AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

b.2. Animal

b.2.1.
Improve awareness, education, and behaviour/ perception change programs incl. learning experiences for farmers, veterinarians, veterinarian students, pet owners, regulators, and the general public.

Search strategy (PubMed):

("Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab]) AND (farmer*[tiab] OR veterina*[tiab] OR pet owners[tiab] OR regulators[tiab] OR general public [tiab]) (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

b.2.2.
National AMR surveillance to inform development and allow assessment of effectiveness of interventions and policies at national level.

Search strategy (PubMed):

("Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab]) AND Surveillance [tiab] AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

b.2.3.
National AMU surveillance to inform development and allow assessment of effectiveness of interventions and policies at national level.

Search strategy (PubMed):

("Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab]) AND (Use [tiab]) AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text; Species: Other Animals.

b.2.4.
Implementation of biosecurity measures to prevent the introduction and spread of disease in farms.

Search strategy (PubMed):

biosecurity [tiab] AND farm*[tiab] AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

b.2.5.
Ensure good animal husbandry and farm management practices linked to the Five Freedoms of animal welfare.

Search strategy (PubMed):

("Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab]) AND (farm [tiab] OR animal [tiab]) AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

b.2.6.
Increase veterinary laboratory capacity (including ability to transport, store and process samples appropriately).

Search strategy (PubMed):

("Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab]) AND (veterin* [tiab] OR labo* [tiab]) AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

b.2.7.
Promotion of use of viable / natural alternatives (e.g., prebiotic, probiotic) to reduce AMU (e.g., vaccines in salmon farming or alternatives to growth promotion).

Search strategy (PubMed):

("Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab]) AND (Antimicrobial use [tiab]) AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

b.2.8.
Create prescribing guidelines and stewardship programs at national level for targeted AMU including indication, line of therapy, dose, administration route and course of treatment of antimicrobials (e.g. switch from broad-spectrum to appropriate narrow-spectrum antimicrobial substances) with no perverse incentives (e.g. delinking prescribing with remuneration).

Search strategy (PubMed):

(Antimicrobial use [tiab]) AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

b.2.9.
Phasing out over-the-counter (OTC) should be coupled with ensuring the availability of quality and affordable antibiotics.

Search strategy (PubMed):

("Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab]) AND (accessibility [tiab] OR affordab* [tiab]) AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

b.2.10.
Ensure accessibility and affordability of AMR diagnostics.

Search strategy (PubMed):

("Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab]) AND (accessibility [tiab] OR affordab* [tiab]) AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

b.2.11.
Research and development of novel, cost-effective, and affordable vaccines.

Search strategy (PubMed):

("Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab]) AND (new [tiab] OR novel [tiab]) AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

b.2.12.
Develop veterinary/animal/farm-appropriate diagnostics.

Search strategy (PubMed):

("Drug Resistance, Microbial"[MeSH Terms] OR Antimicrobial resistance* [tiab] OR Antibiotic resistance* [tiab] OR Antimicrobial use[tiab]) AND (diag*[tiab]) AND (animal*[tiab] OR farm*[tiab] OR veterin*[tiab]) AND (costs and cost analysis [MeSH] OR cost savings [MeSH] OR cost-benefit analysis [MeSH] OR economic evaluation [tiab] OR cost analysis [tiab] OR cost-effectiveness [tiab] OR cost control [tiab] OR cost efficiency analysis [tiab] OR cost-effectiveness analysis [MeSH])

Filter: Last 5 years; Full Text.

b.3. Environment

b.3.1.
Education and awareness of key source pollution emitters for appropriate and point-source waste prevention and treatment, and protection of source waters.

Search strategy (grey literature, Google Scholar):

Cost AND pollution emitters AND education OR awareness AND AMR OR AMU

Filter: Lat 5 years; first three pages.

b.3.2.
Education and awareness of environmental and other relevant-sector authorities on the role of the environment t in AMR development, transmission and spread.

Search strategy (grey literature, Google Scholar):

Cost AND environment AND education OR awareness AND AMR OR AMU

Filter: Lat 5 years; first three pages.

b.3.3.
Implement systems for transparent and swift collection and reporting of the production, sales, use, and disposal of unused antimicrobials.

Search strategy (grey literature, Google Scholar):

Cost AND unused antimicrobials AND education OR awareness AND environment

Filter: Lat 5 years; first three pages.

b.3.4.
Integrate environmental monitoring data (e.g., from monitoring of surface water, solid waste, and airborne particulate matter) with existing AMR surveillance and pollutants data.

Search strategy (grey literature, Google Scholar):

Cost AND environment AND data OR surveillance AND AMR OR AMU

Filter: Lat 5 years; first three pages.

b.3.5.
Document the safety of bioproducts (e.g., biofertilizers, bioplastics, biosolid and manure applications, and plant growth promoters) and novel agricultural practices, as well as key sources of pollution that indicate an impact on AMR in the environment.

Search strategy (grey literature, Google Scholar):

Cost AND environment AND safety bioproduct AND AMR OR AMU

Filter: Lat 5 years; first three pages.

b.3.6.
Improve integrated water management and promote water, sanitation, and hygiene (WASH) to limit the development and spread of AMR in the environment as well as to reduce infections and need for antimicrobials.

Search strategy (grey literature, Google Scholar):

Cost AND environment AND WASH OR water AND AMR OR AMU

Filter: Lat 5 years; first three pages.

b.3.7.
Ensure safe and sustainable disposal and treatment of antimicrobials and hazardous waste from healthcare facilities, pharmacies, veterinarian centers, animal and crop production, and households (e.g., creating, strengthening and promoting take-back programs).

Search strategy (grey literature, Google Scholar):

Cost AND environment AND waste AND AMR OR AMU

Filter: Lat 5 years; first three pages.

b.3.8.
Implement an integrated zoonotic disease surveillance system to detect disease emergence in human/animal population.

Search strategy (grey literature, Google Scholar):

Cost AND zoonotic AND disease AND AMR OR AMU

Filter: Lat 5 years; first three pages.

b.3.9.
Optimize strategies and resources, to include minimum standards such that adequate laboratory and human resource capacity can be established to maintain quality integrated surveillance at scale.

Search strategy (grey literature, Google Scholar):

Cost AND capacity OR surveillance AND AMR OR AMU

Filter: Lat 5 years; first three pages.

b.3.10.
Implement management options to prevent and address releases, effluent, and waste from intensive animal and crop production and from healthcare facilities and pharmaceutical manufacturing.

Search strategy (grey literature, Google Scholar):

Cost AND environment AND waste AND AMR OR AMU

Filter: Lat 5 years; first three pages.

b.3.11.
Develop new methods/technologies to remove antimicrobial residues from the flows of wastewater, manure, and agricultural run-off.

Search strategy (grey literature, Google Scholar):

Cost AND residues AND AMR OR AMU

Filter: Lat 5 years; first three pages.

b.3.12.
Develop soil/water/air-appropriate diagnostics.

Search strategy (grey literature, Google Scholar):

Cost AND diagnostic AND AMR OR AMU

Filter: Lat 5 years; first three pages.

b.4. Plants

b.4.1.
Communicate with, educate, and provide training to farmers on AMR, integrated pest management (IPM), and the appropriate use and disposal of pesticides / herbicides/ molluscicides.

Search strategy (grey literature, Google Scholar):

Cost AND pesticide OR herbicide OR molluscicides AND AMR OR AMU

Filter: Lat 5 years; first three pages.

b.4.2.
National surveillance of AMR data in food and agriculture and AMU data in crops through enrolling in the International FAO Antimicrobial Resistance Monitoring (InFARM).

Search strategy (grey literature, Google Scholar):

Cost AND surveillance OR data AND food OR agriculture AND AMR OR AMU

Filter: Lat 5 years; first three pages.

b.4.3.
Incentivize farm assurance or certification benchmarking schemes in farms.

Search strategy (grey literature, Google Scholar):

Cost AND farm AND AMR OR AMU

Filter: Lat 5 years; first three pages.

b.4.4.
Establish regional, central BSL (Biological Safety Level) 3 and 4 laboratories for detection of zoonotic and infectious diseases.

Search strategy (grey literature, Google Scholar):

Cost AND zoonotic AND laborator* AND AMR OR AMU

Filter: Lat 5 years; first three pages.

b.4.5.
Reduce the secondary use of AMU as growth promoters in agriculture (e.g., avoid mention of this use on labels).

Search strategy (grey literature, Google Scholar):

Cost AND agriculture AND AMR OR AMU

Filter: Lat 5 years; first three pages.

b.4.6.
Promote integrated pest management to reduce the use of antimicrobial pesticides.

Search strategy (grey literature, Google Scholar):

Cost AND pest AND AMR OR AMU

Filter: Lat 5 years; first three pages.

b.4.7.
Reduce the need to use antimicrobial pesticides through the Reduce the Need for Antimicrobials on Farms (RENOFARM) initiative.

Search strategy (grey literature, Google Scholar):

Cost AND pesticides AND AMR OR AMU

Filter: Lat 5 years; first three pages.

b.5. Across sector interventions

b.5.1.
Enhance policy, legislation, advocacy and financing.

Search strategy (grey literature, Google Scholar):

Cross-sectoral AND Cost AND policy OR legislation OR advocacy OR financing AND AMR OR AMU

Filter: Lat 5 years; first three pages.

b.5.2.
Strengthen organizational development, implementation and sectoral integration.

Search strategy (grey literature, Google Scholar):

Cross-sectoral AND Cost AND Implement* OR development AND AMR OR AMU

Filter: Lat 5 years; first three pages.

b.5.3.
Implement data, evidence, and knowledge.

Search strategy (grey literature, Google Scholar):

Cross-sectoral AND Cost AND data OR evidence AND AMR OR AMU

Filter: Lat 5 years; first three pages.

Appendix 5.
Intervention cost data

Table A5.1.
Detailed information for each intervention included in the package.

Intervention	Specific practice	Description	Source
1. AMR awareness raising, education and behavior change of health workers and the community	1. a. Enhance health worker training	A training program for health professionals to improve communication skills during consultations with their patients in outpatient care settings.	OECD (2023) *(10)*
	1. b. Scale up mass media campaigns	The modelled intervention is a nationwide mass media campaign involving mass media and social media platforms to raise AMR understanding and awareness across key stakeholders.	
2. Enhance food-handling practices / biosecurity practices to reduce the risk of AMR spread between humans and animals	2. a. Improve food handling practices	A food safety control training program targets food service workers in food establishments, coupled with visual reminders and regular audits based on checklists.	OECD (2023) *(10)*
3. Research into new antimicrobials, diagnostics and vaccines for AMR and behavioral and implementation science	3. a. New antibiotic incentive program	New antibiotic incentive program including 18 new antibiotics. Based on Towse and Silverman (Centre for Global Development, 2022), it was assumed that the costs associated with incentives to produce new antibiotics would be covered solely by high-income countries. However, the costs related to improving access to all three types—Access, Watch, and Reserve antibiotics—were considered for all regions worldwide. According to the SECURE work, an estimate suggests that it will cost approximately $44.3 million per 100 million population using public health services.	Towse and Silverman. Centre for Global Development (2022) *(39)*
4. Implementation of biosecurity measures to prevent the introduction and spread of disease in farms	4. a. Improve farm hygiene	The modelled intervention is a procurement program that facilitates the purchase of PPE in farm settings by farmers and professional visitors like veterinarians.	OECD (2023) *(10)*
5. Implementation of infection, prevention, and control core components to mitigate AMR	5. a. Enhance hand hygiene	A facility-based intervention that aims to enhance hand hygiene practices among health workers.	OECD (2023) *(10)*
6. Universal access to improved WASH and waste management to mitigate AMR	6. a. Strengthen access to latrines and improved latrines	The intervention phase (community-led total sanitation) included bolstering access to latrines/ improved latrines, etc. An improved latrine was defined as a pit-hole of 2 m depth or more, installation of a slab and a pit-hole cover, construction of a wall, door, and roof, and installation of a hand-washing facility with soap within the community-led total sanitation (CLTS) framework.	Cha S et al (2020) *(39)*
7. Ensure safe and sustainable disposal and treatment of antimicrobials and hazardous waste	7. a. Enhance environmental hygiene	A bundled intervention that aims to enhance environmental hygiene practices in hospitals.	OECD (2023) *(10)*

Intervention	Specific practice	Description	Source
8. Quality laboratory system and diagnostic stewardship to enable clinical bacteriology and mycology testing	8. a. Implementation or scale up of Rapid diagnostic tests (RDTs)	A novel program aims to increase the use of rapid diagnostic tests by increasing the availability of point-of-care (POC) CRP in ambulatory care settings in combination with antibiotic treatment guidelines depending on the CRP levels.	OECD (2023) *(10)*
9. Access to vaccines and expanded immunization to manage AMR	9. a. Improve vaccination coverage	Scale up of nationwide campaign of 23-valent pneumococcal polysaccharide (PVV23) targeting older adults.	Lu E (Yiwei) et al (2021) *(40)*
10. Up-to-date evidence-based treatment guidelines and antimicrobial stewardship programmes	10. a. Strengthening antimicrobial stewardship programmes (ASPs)	The modelled intervention entails scaling up a hospital-based program that involves the creation of multi-disciplinary teams that provide antibiotic stewardship and the scale-up of monitoring and surveillance systems.	OECD (2023) *(10)*
	10. b. Delayed antimicrobial prescribing	The model intervention is the rollout of antimicrobial prescribing guidelines that promote delayed prescription in primary healthcare settings.	
	10. c. Financial incentives	A nationwide pay-for-performance (P4P) program that aims to optimize antimicrobial use in community settings by rewarding bonuses to prescribers for achieving pre-set antibiotic prescribing targets.	

Note. (*) New antibiotic intervention targets deaths due to *E. Coli, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumanii, Pseudomonas aeruginosa, Streptococcus pneumoniae.*

Appendix 6.
Target coverage and impact data per intervention

Table A6.1.
Target coverage values for each intervention included in the package.

Intervention	**Target coverage** *(10)*
1. AMR awareness raising, education and behavior change of health workers and the community.	- Enhanced health worker training: 70% - Mass media campaigns: 100%
2. Enhance food-handling practices / biosecurity practices to reduce the risk of AMR spread between humans and animals	70%
3. Quality laboratory system and diagnostic stewardship to enable clinical bacteriology and mycology testing.	70%
4. Access to vaccines and expanded immunization to manage AMR.	90%
5. Up-to-date evidence-based treatment guidelines and antimicrobial stewardship programs.	- Strengthening antimicrobial stewardship programs (ASPs): 80% - Delayed antimicrobial prescription: 40% - Financial incentives: 70%
6. Implementation of biosecurity measures to prevent the introduction and spread of disease in farms.	70%
7. Implementation of infection, prevention, and control (IPC) core components to mitigate AMR.	70%
8. Universal access to improved WASH and waste management to mitigate AMR.	90%
9. Ensure safe and sustainable disposal and treatment of antimicrobials and hazardous waste.	70%
10. Investment in new antimicrobials	100% (*)

(*) Assumption based on Towse and Silverman. Centre for Global Development (2022) *(38)*, in addition to an assumption that an access-geared mechanism similar to GARDP's SECURE program would be utilized to ramp up access to all lines of treatment based on clinical need.

Table A6.2.
Effectiveness data, population target, and impact for each intervention (and practice) within the package.

Intervention	Specific practice	Population target	Impact	Effectiveness value	Source
1. AMR awareness raising, education and behavior change of health workers and the community	1. a. Enhance health worker training	Healthcare workers with impact on patients	Resistant community infections	39% reduction in antibiotic prescription	OECD (2023) *(10)*
	1. b. Scale up mass media campaigns	Whole population	Resistant community infections	7% reduction in antibiotic prescription	
2. Enhance food-handling practices / biosecurity practices to reduce the risk of AMR spread between humans and animals	2. a. Improve food handling practices	Food caterers with impact on the population	Resistant and susceptible enteric infections	28.6% reduction in microbial count	OECD (2023) *(10)*
3. Research into new antimicrobials, diagnostics and vaccines for AMR and behavioral and implementation science	3. a. New antibiotic incentive program	Patients with resistant infections	Resistant set of infections	5% reductions in deaths attributed to AMR each year: starting from year 10 onward (*)	Towse and Silverman. Centre for Global Development (2022) *(38)*
4. Implementation of biosecurity measures to prevent the introduction and spread of disease in farms	4. a. Improve farm hygiene	Farmers with impact on the population	Resistant and susceptible community infections	12% reduction in risk of infection among people who use personal protective equipment (PPE) compared to those who do not	OECD (2023) *(10)*
5. Implementation of infection, prevention, and control core components to mitigate AMR	5. a. Enhance hand hygiene	Healthcare workers with impact on patients	Resistant and susceptible hospital infections	33% reduction in risk of infection among people who comply with enhanced hand hygiene practices compared to those who do not	OECD (2023) *(10)*
6. Universal access to improved WASH and waste management to mitigate AMR	6. a. Strengthen access to latrines and improved latrines	Children aged 0-5	Resistant and susceptible enteric infections	29% reduction in diarrhea cases	Assumption based on Cha S et al (2020) *(39)*
7. Ensure safe and sustainable disposal and treatment of antimicrobials and hazardous waste	7. a. Enhance environmental hygiene	Healthcare workers with impact on patients	Resistant and susceptible hospital infections	26% reduction in risk of infection among people who are exposed to enhanced environmental hygiene practices compared to those who do not	OECD (2023) *(10)*
8. Quality laboratory system and diagnostic stewardship to enable clinical bacteriology and mycology testing	8. a. Implementation or scale up of Rapid diagnostic tests (RDTs)	Antibiotic prescribers in the community with impact on patients	Resistant community infections	32% reduction in immediate antibiotic prescribing in adults and 46% in children < 18 years of age	OECD (2023) *(10)*

Intervention	Specific practice	Population target	Impact	Effectiveness value	Source
9. Access to vaccines and expanded immunization to manage AMR	9. a. Improve vaccination coverage	Children aged 0-5	Resistant and susceptible pneumococcal infections	Reduction in pneumococcal disease cases: Pneumococcal pneumonia 9.41% reduction. Pneumococcal meningitis: 42.46% reduction Pneumococcal acute otitis media (AOM): 8.32% reduction	Lu E (Yiwei) et al (2021) *(40)*
10. Up-to-date evidence-based treatment guidelines and antimicrobial stewardship programmes	10. a. Strengthening antimicrobial stewardship programmes (ASPs)	ATB prescribers in hospitals with impact on patients	Resistant hospital infections	25% reduction in antibiotic use	OECD (2023) *(10)*
	10. b. Delayed antimicrobial prescribing	ATB prescribers in the community with impact on patients	Resistant community infections	60% reduction in antibiotic use	
	10. c. Financial incentives	ATB prescribers in the community with impact on patients	Resistant community infections	8% reduction in antibiotic use	

Note. (*) New antibiotic intervention targets deaths due to *E. Coli, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumanii, Pseudomonas aeruginosa, Streptococcus pneumoniae.*

Appendix 7.
Cost data for each intervention included in the package

Table A7.1.
Cost data for each intervention included in the package.

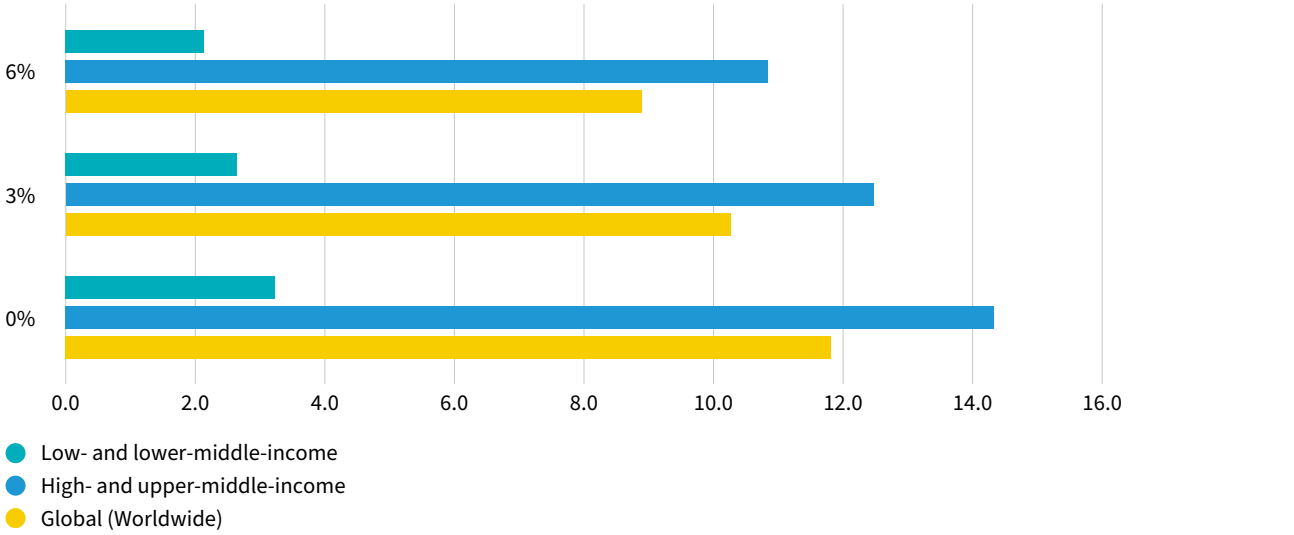
Intervention	Specific practice	Intervention costs	Original currency/ year	Country/ region of reference	Source
1. AMR awareness raising, education and behavior change of health workers and the community	1. a. Enhance health worker training	$0.40 per capita per year	US$ PPP, 2020	OECD countries	OECD (2023) *(10)*
	1. b. Scale up mass media campaigns	$0.69 per capita per year	US$ PPP, 2020		
2. Enhance food-handling practices / biosecurity practices to reduce the risk of AMR spread between humans and animals	2. a. Improve food handling practices	$0.24 per capita per year	US$ PPP, 2020	OECD countries	OECD (2023) *(10)*
3. Research into new antimicrobials, diagnostics and vaccines for AMR and behavioral and implementation science	3. a. New antibiotic incentive program	$ 3.83 billion for total country's costs for a 30-year period (*)	US$, 2020	Japan	Towse and Silverman. Centre for Global Development (2022) *(9)*
4. Implementation of biosecurity measures to prevent the introduction and spread of disease in farms	4. a. Improve farm hygiene	$0.245 per capita per year	US$ PPP, 2020	OECD countries	OECD (2023) *(10)*
5. Implementation of infection, prevention, and control core components to mitigate AMR	5. a. Enhance hand hygiene	$0.48 per capita per year	US$ PPP, 2020	OECD countries	OECD (2023) *(10)*
6. Universal access to improved WASH and waste management to mitigate AMR	6. a. Strengthen access to latrines and improved latrines	$ 45.80 per capita for a 10-year period	US$ PPP, 2016	Ethiopia	Assumption based on Cha S et al (2020) *(39)*
7. Ensure safe and sustainable disposal and treatment of antimicrobials and hazardous waste	7. a. Enhance environmental hygiene	$2.24 per capita per year	US$ PPP, 2020	OECD countries	OECD (2023) *(10)*
8. Quality laboratory system and diagnostic stewardship to enable clinical bacteriology and mycology testing	8. a. Implementation or scale up of Rapid diagnostic tests (RDTs)	$1.34 per capita per year	US$ PPP, 2020	OECD countries	OECD (2023) *(10)*
9. Access to vaccines and expanded immunization to manage AMR	9. a. Improve vaccination coverage	$0.21 per capita per year	US$ PPP, 2020	OECD countries	OECD (2023) *(10)*

Intervention	Specific practice	Intervention costs	Original currency/ year	Country/ region of reference	Source
10. Up-to-date evidence-based treatment guidelines and antimicrobial stewardship programmes	10. a. Strengthening antimicrobial stewardship programmes (ASPs)	$2.3 per capita per year	US$ PPP, 2020	OECD countries	OECD (2023) *(10)*
	10. b. Delayed antimicrobial prescribing	$0.45 per capita per year	US$ PPP, 2020		
	10. c. Financial incentives	$2.58 per capita per year	US$ PPP, 2020		

Note (*) Based on the cited source, it was assumed that the costs associated with incentives to produce new antibiotics would be covered solely by high-income countries. However, the costs related to improving access to all three types—Access, Watch, and Reserve antibiotics—were considered for all regions. According to the SECURE work, an estimate suggests that it will cost approximately $44.3 million per 100 million population using public health services.

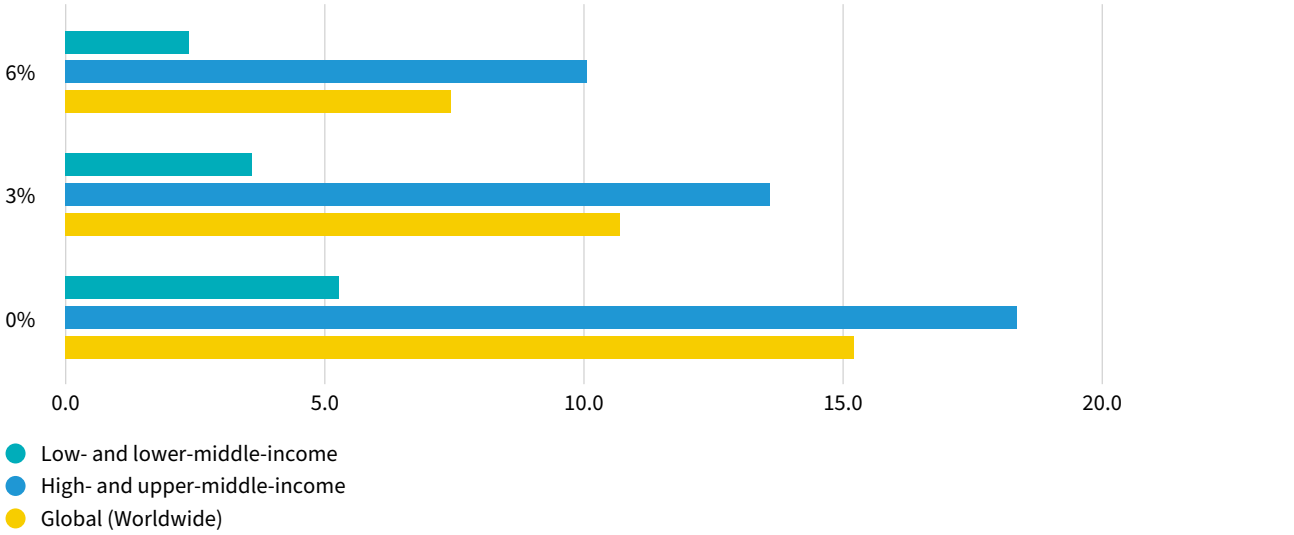
Appendix 8.
Additional RoI results

Figure A8.1.
RoI values if cost structure assumes that 50% of intervention cost occurs in the first year (2020-2035)



Note. Interpretation: Countries from Low and Lower middle-income countries can expect at least double their investment when implementing a package of One Health AMR interventions.

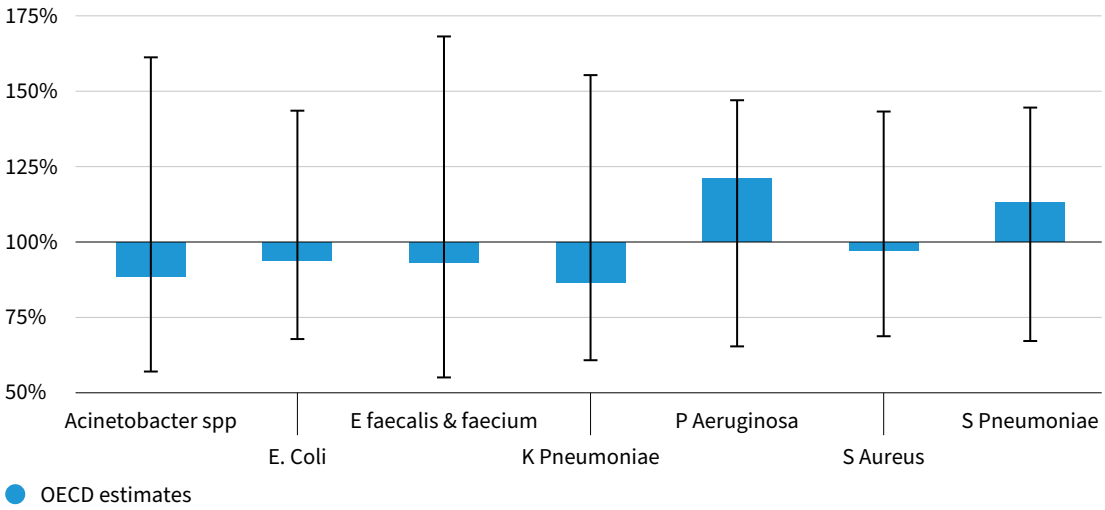
Figure A8.2.
RoI values if cost structure assumes that 50% of intervention cost occurs in the first year (2020-2050)



Note. Interpretation: For every US$ 1 invested in a mixed policy AMR package, countries from low and lower middle-income regions can expect a net return of US$ 3.6 (3% discount rate analysis).

Appendix 9.
Comparison of mortality estimates provided by SPHeP-AMR and IHME

Figure A9.1.
Comparison of the number of deaths due to AMR estimated by the SPHeP-AMR model and by the IHME by antibiotic-bacterium combination



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