Health and Economic Impacts of Antimicrobial Resistance in the Western Pacific Region, 2020–2030

World Health Organization
Western Pacific Region

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Abbreviations

AMR	antimicrobial resistance
AWaRe	access, watch, reserve
COVID-19	coronavirus disease 2019
E. coli	*Escherichia coli*
E. faecalis	*Enterococcus faecalis*
FAO	Food and Agriculture Organization of the United Nations
GBD	global burden of disease
GDP	gross domestic product
H. influenzae	*Haemophilus influenzae*
IPC	infection prevention and control
K. pneumoniae	*Klebsiella pneumoniae*
MRSA	methicillin-resistant *Staphylococcus aureus*
OECD	Organisation for Economic Co-operation and Development
PICs	Pacific island countries and areas
P. aeruginosa	*Pseudomonas aeruginosa*
S. pneumoniae	*Streptococcus pneumoniae*
SDGs	Sustainable Development Goals
UHC	universal health coverage
UNEP	United Nations Environment Programme
WHO	World Health Organization
WOAH	World Organisation for Animal Health

Glossary of terms

Antimicrobial resistance (AMR)	AMR develops when adaptive changes in bacteria and other infectious organisms result in antibiotics and antiviral and antifungal medicines used to treat infections becoming less effective. The emergence of AMR is accelerated by overuse, misuse and poor quality or falsified antimicrobial drugs in the human health, animal health, agricultural and environmental sectors. AMR in this document focuses on antibiotic resistance, that is resistance to medications used to treat bacterial infections. It excludes resistance to other antimicrobial agents such as those that treat viral, fungal or parasitic infections.
Antimicrobial resistance rate	The proportion of laboratory isolates with resistance to antimicrobials. Also known as the antimicrobial resistance proportion or detection rate.
Antibiotic-resistant bacteria	Bacteria that no longer respond to standard antibiotic treatments.
Antibiotic-susceptible bacteria	Bacteria that respond to standard antibiotic treatments.
Incidence rate of infection	The number of new cases of an infection in a population over a specified period.
Health impact of AMR	The impact of AMR on mortality and morbidity.
AMR-related deaths (mortality)	Additional/excess deaths among people infected with an antibiotic-resistant bacterial pathogen compared with people infected with antibiotic-susceptible bacteria of the same species. It is estimated in this study as total cumulative excess deaths from 2020 to 2030.
AMR-related disease (morbidity)	Additional/extra days spent in hospital by people infected with antibiotic-resistant bacteria compared with patients infected with antibiotic-susceptible bacteria. It is estimated in this study as total cumulative extra days spent in hospital from 2020 to 2030.
Economic impact of AMR	The total economic cost – resulting from higher treatment costs (direct costs) and costs related to loss of productivity from premature deaths and prolonged hospitalizations (indirect costs) – related to AMR infections compared with antibiotic-susceptible infections. It is estimated in this study as total cumulative economic cost from 2020 to 2030.

Executive summary

Antimicrobial resistance (AMR) is projected to cause substantial morbidity and mortality in the World Health Organization (WHO) Western Pacific Region over the next decade, at significant economic cost. By endangering people's health, AMR poses a threat to health security and has implications for overall development, particularly in Member States that are more vulnerable to the impacts of AMR.

AMR caused an estimated 700 000 deaths globally in 2014 *(1)* and 1.27 million deaths in 2019, among which 286 040 deaths occurred in regions that include countries in the Western Pacific Region *(2)*.[1] AMR may reduce global gross domestic product (GDP) by as much as 3% by 2030, adding an extra US$ 700 billion globally in health-care costs in 2030 and affecting low-income countries more severely *(1,3,4)*.

Health security including AMR is a thematic priority in *For the Future: Towards the Healthiest and Safest Region*, WHO's vision for work with Member States and partners in the Western Pacific Region *(5)*. The *Framework for Accelerating Action to Fight Antimicrobial Resistance in the Western Pacific Region (6)* embodies this vision and identifies operational shifts needed to mitigate the impact of AMR.

The fight against AMR is hampered by a lack of data. The 2015 WHO *Global Action Plan on Antimicrobial Resistance (7)* and the *Action Agenda for Antimicrobial Resistance in the Western Pacific Region (8)* prioritize strengthening surveillance and research on AMR. The WHO Regional Office for the Western Pacific commissioned the modelling study presented in this document to enhance political agility by providing policy-makers with local intelligence on which to base timely and cost-effective interventions to combat AMR.

The study, conducted by the WHO Collaborating Centre for Infectious Disease Epidemiology and Control at The University of Hong Kong, is the first to quantify the health and economic impacts of AMR for seven priority bacteria in the Western Pacific Region, as well as model the future spread and cost implications of AMR from 2020 to 2030. In the context of this study, AMR refers to antibiotic resistance, that is resistance to medicines which treat bacterial infections.

Data from eight countries and one area in the Region on the health impact and economic cost of infections with antibiotic-resistant compared with antibiotic-sensitive bacteria were obtained through a systematic review covering 2010–2019. Data were extrapolated to other countries and areas in the Region based on the nearest GDP per capita and used to forecast the health impact and economic cost of AMR in each of the 37 countries and areas in the Region from 2020 to 2030.

The study estimated a worst-case scenario of 450 000 AMR-related deaths in 2020 (mortality rate 23.5 deaths per 100 000 population) and projected a cumulative total of 5.2 million AMR-related deaths across the Region from 2020 to 2030. Over the same period, patients with

[1] Also includes deaths in the Democratic People's Republic of Korea, Indonesia, Maldives, Mauritius, Myanmar, Seychelles, Sri Lanka, Thailand and Timor-Leste, and excludes deaths in Mongolia as a result of differences between WHO regions and the regional classification system used by the *Global Burden of Disease* study.

AMR infections were projected to spend 172 million extra days in hospital. The AMR-related economic cost in the Region was forecast to reach a cumulative total of US$ 148 billion.

The 450 000 excess AMR-related deaths estimated in 2020 are comparable to the 286 040 (188 060 to 419 110)[2] deaths attributable to AMR estimated in 2019[3] *(2)*. The regional AMR-related mortality rate is similar to rates for kidney diseases, diabetes mellitus, liver cirrhosis and breast cancer, and it is considerably higher than rates for tuberculosis and HIV/AIDS *(9,10)*.

The projected regional economic cost of AMR of US$ 148 billion from 2020 to 2030 is higher than total health expenditure in 2019 in Australia (US$ 136.8 billion) and the Republic of Korea (US$ 134.4 billion) *(13)* and equal to nearly 10% of total health expenditure in the Western Pacific Region in 2019 (US$ 1.68 trillion). It is nearly two and a half times the annual GDPs projected for 2020 for Cambodia, the Lao People's Democratic Republic and Mongolia combined (US$ 60 billion) *(12)* or of all the Pacific island countries and areas and Papua New Guinea combined (US$ 59.8 billion). The total cost is similar to the total diabetes-related health expenditure in 2019 in the Western Pacific Region (US$ 162.2 billion).

The study brings to light the lack of AMR-related data that meant assumptions had to be made to allow extrapolation to countries and areas in the Region without data. Despite the data limitations, the study provides compelling evidence for the potential health and economic costs of AMR in the Western Pacific Region: AMR has a substantial mortality impact, comparable to many priority diseases; AMR increases health-care costs and comes at a significant total economic cost. The impacts are not distributed equally and AMR is an especially serious threat for some of the poorest people and most marginalized populations in the Region.

Governments must pay policy and financial attention to addressing AMR, proportionate to its impact compared with priority diseases such as diabetes, as an investment in the economy for the future. Money spent now on interventions that mitigate the impacts of AMR will be well spent, saving on future health-care costs and protecting the workforce and economy.

AMR is a cross-cutting, silent pandemic. It threatens maternal, child and reproductive health, infectious disease management, cancer therapy, surgical interventions and health security. Mitigating measures against AMR are an integral component of emergency preparedness and primary health care as part of universal health coverage. Tackling AMR requires an understanding of the threat and of factors that contribute to that threat, and an awareness of the importance and urgency of mitigating actions.

There is an overriding need for more and better-quality data, to understand the trajectory of AMR in the Region, reduce uncertainty around its impacts and monitor interventions. Establishing and strengthening national AMR surveillance systems, integrated in national health information systems, must be a priority. Laboratory and epidemiological surveillance data should be complemented by research on incidence and resistance rates, clinical outcomes of infections, antibiotic prescription and consumption, cost-effectiveness of interventions, as well as by clinical trials of new antibiotics and vaccines.

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[2] 95% uncertainty interval

[3] In regions that include Western Pacific countries and areas (except Mongolia) as well as the Democratic People's Republic of Korea, Indonesia, Maldives, Mauritius, Myanmar, Seychelles, Sri Lanka, Thailand and Timor-Leste.

Introduction

The silent pandemic of rising antimicrobial resistance (AMR) threatens our future health and security and endangers overall development. In 2019 over 7 million deaths, comprising 13.6% of all global deaths, were associated with bacterial infections, making such infections the second-leading cause of death globally *(13)*. Effective antibiotics are critical for preventing and treating bacterial infections. Patients with infections resistant to antibiotics – that is, AMR infections – are more difficult to treat, have longer hospital stays and have worse clinical outcomes. AMR risks undermining health-care systems, rendering childbirth, routine operations and cancer treatment much more dangerous. AMR is expensive, adding strain to health systems and economies through greater health-care costs and the loss of productivity.

AMR jeopardizes universal health coverage (UHC) and progress on many Sustainable Development Goals (SDGs), including those on poverty, health and well-being, inequality, and work and economic growth *(14)*. AMR is a global problem, driven by factors such as overuse and misuse of antibiotics and limited infection prevention and control (IPC) measures in health-care facilities, and is compounded by international trade and travel and by climate change *(15–17)*. AMR has substantial health and economic implications (Fig. 1) and requires coordinated, multisectoral mitigating actions, integrated with those for emergency preparedness and prevention, to be instituted urgently by individual Member States, and by regional and global organizations.

Fig. 1. Impacts of AMR predicted by major studies if trends continue unabated

	O'Neill Review 2014 *(1)*	**World Bank report 2017** *(3)*	**OECD[a] report 2018** *(4)*	**Global AMR burden[b] 2019** *(2)*
	700 000 global deaths in 2014 **10 million people** dying every year by 2050		**2.4 million** deaths in Europe, North America and Australia between 2015 and 2050	**1.27 million** global deaths in 2019 **286 040 deaths** in Asia Pacific in 2019
	Global GDP decline by 2050 **2–3.5%** Global cost by 2050 **US$ 100 trillion**	Global GDP decline by 2050 **1.1–3.8%**	Cost across 33 OECD countries per year **US$ 3.5 billion** between 2015 and 2050	

[a] Organisation for Economic Co-operation and Development
[b] Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis

Source: Health and Economic Impacts of Antimicrobial Resistance in the Western Pacific Region, 2020–2030.

AMR is a focus of concern and attention in the World Health Organization (WHO) Western Pacific Region. Health security including AMR is a thematic priority in *For the Future: Towards the Healthiest and Safest Region*, WHO's vision for work with Member States and partners in the Western Pacific *(5)*. The *Framework for Accelerating Action to Fight Antimicrobial Resistance in the Western Pacific Region (6)* embodies this vision and identifies operational shifts needed to mitigate the impact of AMR. Encouraging actions are being taken by countries and areas in the Region to combat and control AMR, including raising awareness of the threat, developing national AMR action plans and AMR surveillance systems, and conducting capacity-building among health professionals.

The fight against AMR is hampered by the lack of data on AMR and its impacts. The 2015 WHO *Global Action Plan on Antimicrobial Resistance (7)* and the *Action Agenda for Antimicrobial Resistance in the Western Pacific Region (8)* prioritize: (i) improving awareness and understanding of AMR through effective communication; and (ii) strengthening the knowledge- and evidence-base on AMR through surveillance and research. Health policy-makers need evidence on the burden and impact of AMR to inform advocacy and decision-making, and accelerate efforts to contain AMR.

The WHO Regional Office for the Western Pacific commissioned the modelling study presented in this document to enhance political agility by providing policy-makers with local intelligence on which to base timely and cost-effective interventions to combat AMR. The study, conducted by the WHO Collaborating Centre for Infectious Disease Epidemiology and Control at The University of Hong Kong, estimated the health impact of AMR for seven priority bacteria in the Western Pacific Region, and modelled the future spread and economic costs of AMR from 2020 to 2030. In the context of this study, AMR refers to antibiotic resistance, that is resistance to medicines that treat bacterial infections. Resistance to other antimicrobial agents, such as antivirals, antifungals, etc., is not considered. Results from the study are presented in Figs. 3–8 and 11.

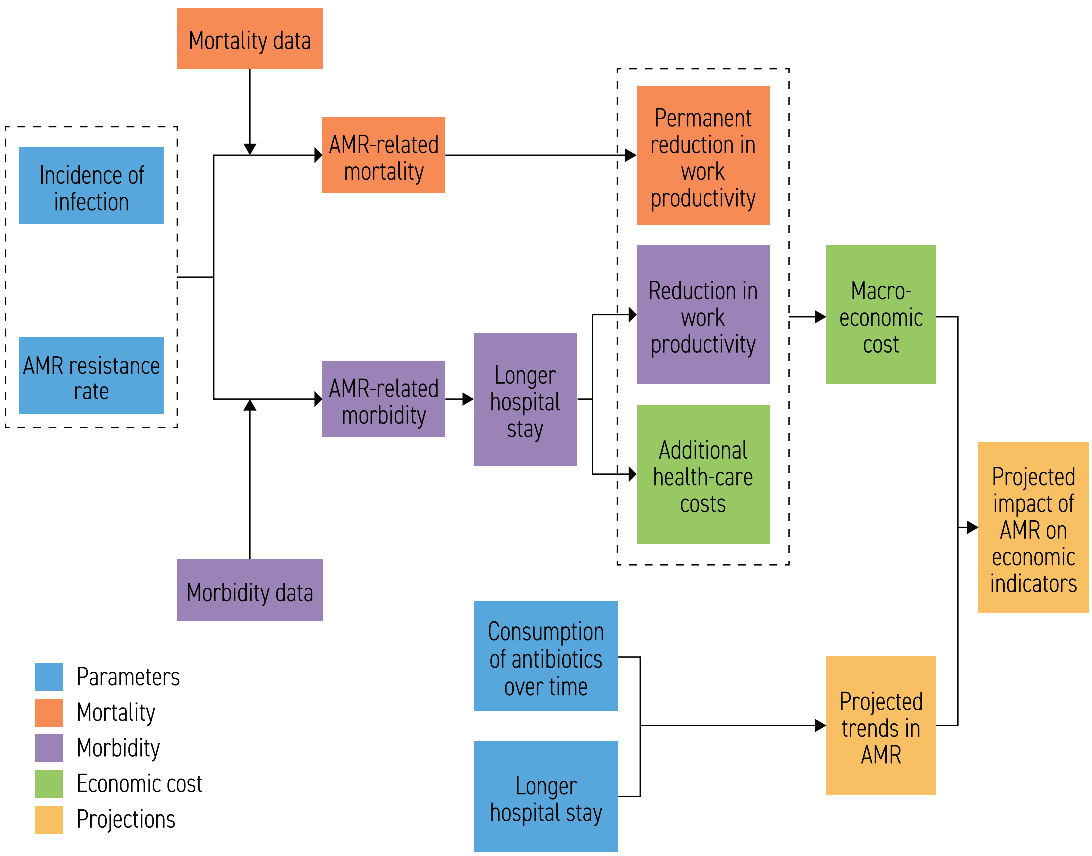
The health impact of AMR was estimated as the excess deaths (mortality) and additional days spent in hospital (disease or morbidity) among people with antibiotic-resistant infections caused by seven priority bacterial pathogens compared with antibiotic-susceptible infections with the same bacteria. The economic costs were estimated as the GDP loss due to decreased work productivity from death and disease and the increased health-care costs of caring for people with AMR infections.

This publication is primarily intended for national and subnational health policy-makers and health professionals, but it may also be useful for other sectors as part of the One Health approach to AMR advocated by WHO, the Food and Agriculture Organization of the United Nations (FAO), the World Organisation for Animal Health (WOAH), the United Nations Environment Programme (UNEP) and others.

Methodology

The study involved conducting a systematic literature review on AMR in the Western Pacific Region covering 2010 to 2019 to obtain information on the health impact and economic cost of infections with antibiotic-resistant bacteria compared with antibiotic-sensitive infections. The researchers then developed a mathematical model using parameters derived from the literature review (Annex 1) and conducted a sensitivity analysis (Annex 2) based on increased AMR resistance rates to forecast the health and economic impacts of AMR in each of the 37 countries and areas in the Western Pacific Region from 2020 to 2030 (Fig. 2) Definitions of terms and key assumptions used to calculate the AMR-related health and economic impact are given in Box 1.

Fig. 2. Methodological framework for projecting AMR-related mortality and economic cost



Source: Health and Economic Impacts of Antimicrobial Resistance in the Western Pacific Region, 2020–2030.

The study focused on seven bacterial pathogens of importance for human health: methicillin-resistant *Staphylococcus aureus* (MRSA), *Escherichia coli (E. coli)*, *Enterococcus faecalis (E. faecalis)*, *Haemophilus influenzae (H. influenzae)*, *Klebsiella pneumoniae (K. pneumoniae)*, *Pseudomonas aeruginosa (P. aeruginosa)* and *Streptococcus pneumoniae (S. pneumoniae)* (Annex 3). The study did not look at antimicrobial-resistant tuberculosis, HIV or malaria to avoid duplication with other work.

The literature review identified pathogen-specific incidence rates, antibiotic resistance rates against four classes of antibiotics (cephalosporins, penicillins, fluroquinolones and carbapenems), and estimates of mortality (excess deaths) and morbidity (additional days spent in hospital) among patients with antibiotic-resistant infections compared to antibiotic-susceptible infections (Annexes 4–7). Data on country and area populations, GDP and GDP per capita from 2010 to 2019 were obtained from national statistics and from the World Bank *(12)* and used to develop linear projections for 2020–2030 (Annex 8).

Due to a lack of data,[4] a single maximum value for pathogen-specific incidence rates, AMR-related mortality and AMR-related morbidity was applied to all countries. Pathogen-specific resistance rates were projected linearly from 2020 to 2030. For the country and area projections, antibiotic resistance rates and/or antibiotic consumption were extrapolated from the countries and areas with data to other countries and areas in the Region based on the nearest GDP per capita (Annex 5).

[4] Countries and areas in the Western Pacific Region with data on incidence rates, resistance rates, antibiotic consumption and AMR-related mortality or morbidity: Australia, China, Hong Kong SAR (China), Japan, Malaysia, the Philippines, the Republic of Korea, Singapore and Viet Nam.

Box 1. Definition of terms and key assumptions used to calculate the AMR-related health and economic impact in the Western Pacific Region, 2020–2030

- **Incidence of infection:** the number of cases of infection in a population in a defined time period.

  The study applied the most recent incidence rate available for each pathogen from any country/area to all calculations, assuming that incidence rates would be similar in all countries/areas across the Western Pacific Region and stable over the next 10 years. Rates were matched for source (community- or hospital-acquired) and anatomical site (bloodstream infection, invasive pneumonia or other invasive disease) of infection where possible (Annex 4).

- **AMR resistance rate:** the proportion of infections that are resistant to antibiotics.

  The maximum reported resistance rate was used to inform linear projections from 2020 to 2030; where data were missing, national antibiotic consumption data were used instead on the assumption that the trend of antibiotic consumption in a country follows the trend of AMR. Data were extrapolated from countries/areas with data to the remaining countries/areas in the Region, based on the closest GDP per capita (Annex 5).

- **Health impact of AMR:** excess mortality and morbidity related to AMR infections.

  The number of deaths and additional days spent in hospital by patients with antibiotic-resistant infections compared with antibiotic-susceptible infections. Data from the literature were pooled and applied to all countries/areas across the Region (Annex 6).

  AMR-related excess mortality = mortality rate among patients with antibiotic-resistant infections – mortality rate among patients with susceptible infections

  AMR related excess morbidity = length of hospitalization of patients with antibiotic-resistant infections (days) – length of hospitalization of patients with susceptible infections (days)

- **Population, GDP and GDP per capita**

  Data were obtained from national statistics and World Bank data for 2010–2019 and used to develop linear projections for 2020–2030 (Annex 8).

- **Economic impact of AMR:** loss of GDP and additional health-care costs related to AMR infections.

  The sum of three cost components arising from infections with antibiotic-resistant compared with antibiotic-susceptible bacteria:

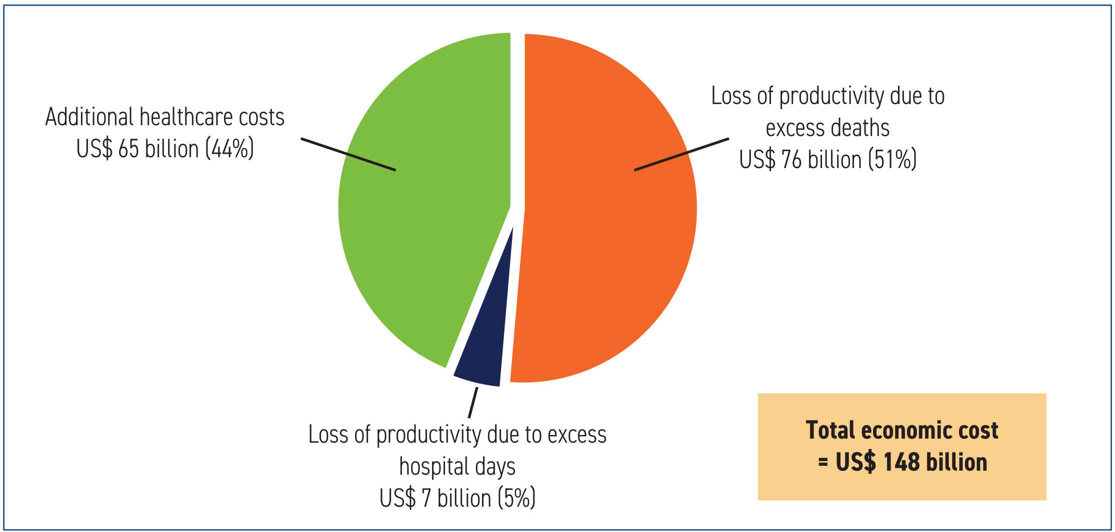
  1. GDP loss resulting from permanent loss of work productivity due to deaths from AMR infections;
  2. GDP loss resulting from reduction in work productivity due to patients with AMR infections spending more days in hospital; and
  3. additional health-care costs arising from extra days spent in hospital by people with antibiotic-resistant pathogens compared to patients with antibiotic-susceptible pathogens.

  Additional indirect costs resulting from complex care needs or increased mortality and costs borne by families of people with antibiotic-resistant infections were not considered in this study.

Results

Based on data from the literature review, the study estimated a worst-case scenario of 450 000 AMR-related deaths in 2020 (mortality rate 23.5 deaths per 100 000 population) and projected a cumulative total of 5.2 million AMR-related deaths across the Western Pacific Region from 2020 to 2030. Over the same period, patients with AMR infections were projected to spend 172 million extra days in hospital. The total AMR-related economic cost in the Region was forecast to reach US$ 148 billion, resulting from an estimated US$ 76 billion in lost productivity due to deaths, US$ 7 billion in lost productivity due to extra days spent in hospital and US$ 65 billion in additional health-care costs due to prolonged hospitalizations (Fig. 3).

Fig. 3. AMR-related economic impact in the Western Pacific Region by cost component, 2020–2030 (US$ billions)

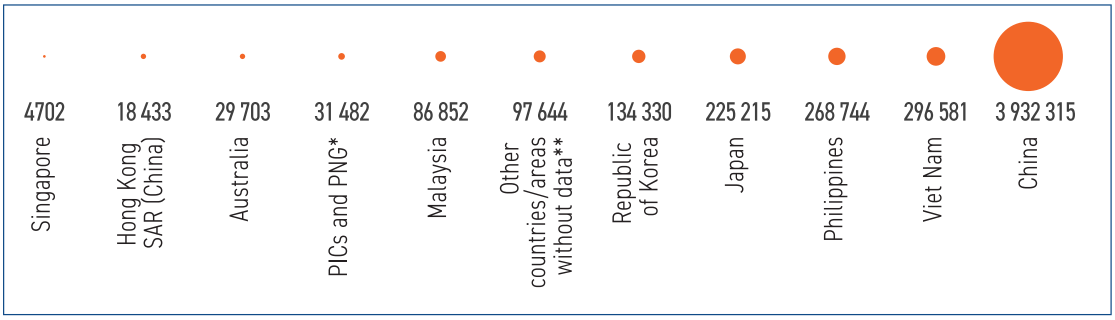


Source: Health and Economic Impacts of Antimicrobial Resistance in the Western Pacific Region, 2020–2030.

The sensitivity analysis looked at projected impacts when AMR resistance rates were increased by 25% and 50%. Estimated AMR-related deaths across the Region from 2020 to 2030 rose, respectively, to 5.7 million and 6.1 million deaths, and the total economic cost increased to US$ 167 billion and US$ 181 billion (Annex 2, Fig. A1).

The absolute number of AMR-related deaths was highest in countries with large populations – namely China (3.9 million) and Viet Nam (297 000) (Fig. 4 and Table A8).

Fig. 4. AMR-related deaths in the Western Pacific Region by country/area, 2020–2030

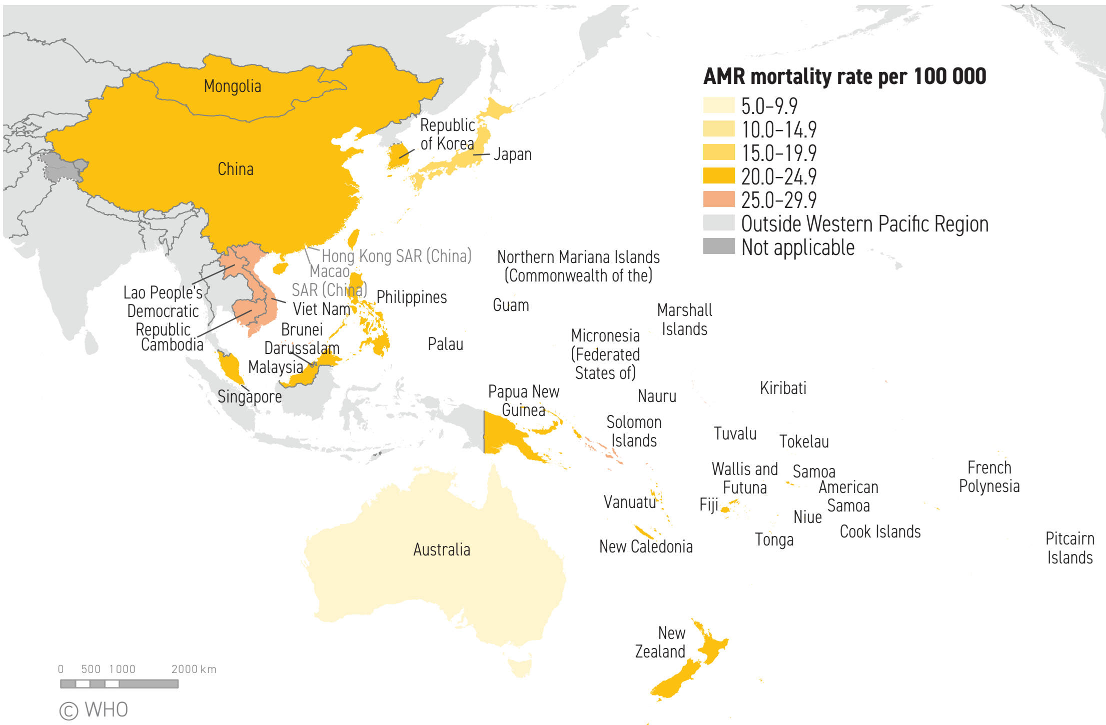


* Pacific island countries and areas and Papua New Guinea
** Brunei Darussalam, Cambodia, the Lao People's Democratic Republic, Macao SAR (China), Mongolia and New Zealand
Source: Health and Economic Impacts of Antimicrobial Resistance in the Western Pacific Region, 2020–2030.

Fig. 5 shows projected AMR-related mortality rates and total economic cost as a percentage of predicted GDP from 2020 to 2030 by country and area in the Western Pacific Region. AMR-related mortality rates range from 7.0 to 26.4 AMR-related deaths per 100 000 population (Fig. 5a) and the total economic cost as a percentage of projected country and area GDP ranges from 0.02% to 0.09% (Fig. 5b).

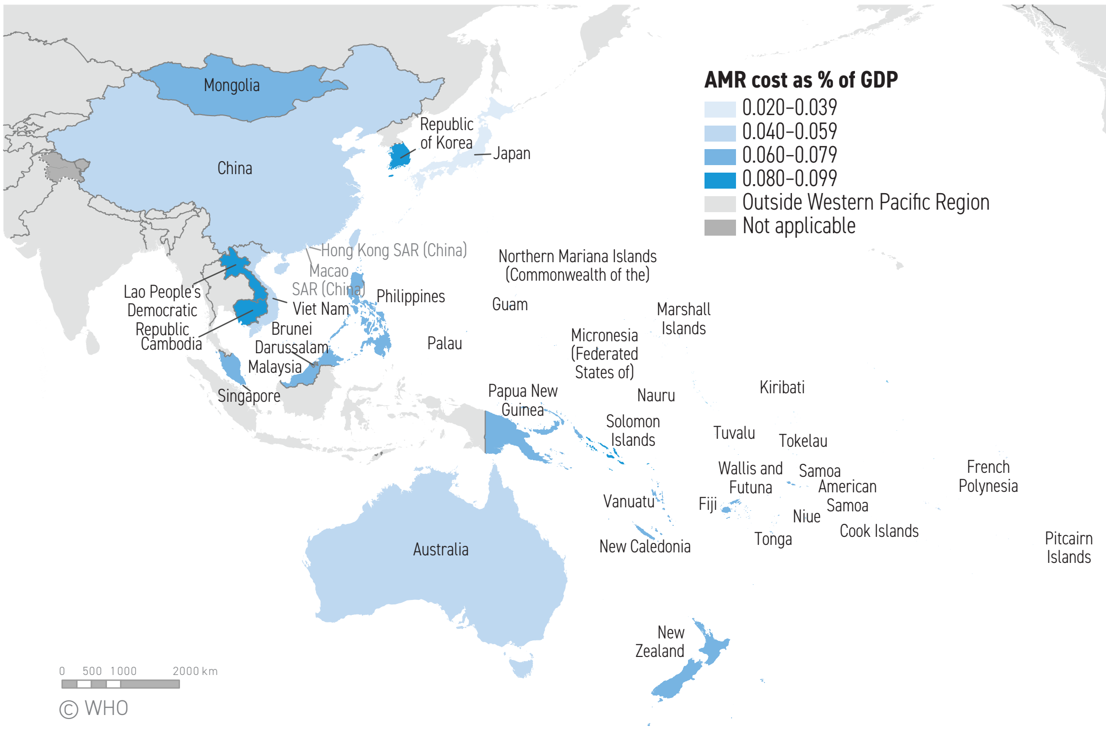
Fig. 5. AMR-related impact by country/area in the Western Pacific Region, 2020–2030

5a. Mortality rate per 100 000 population



Source: Health and Economic Impacts of Antimicrobial Resistance in the Western Pacific Region, 2020–2030.

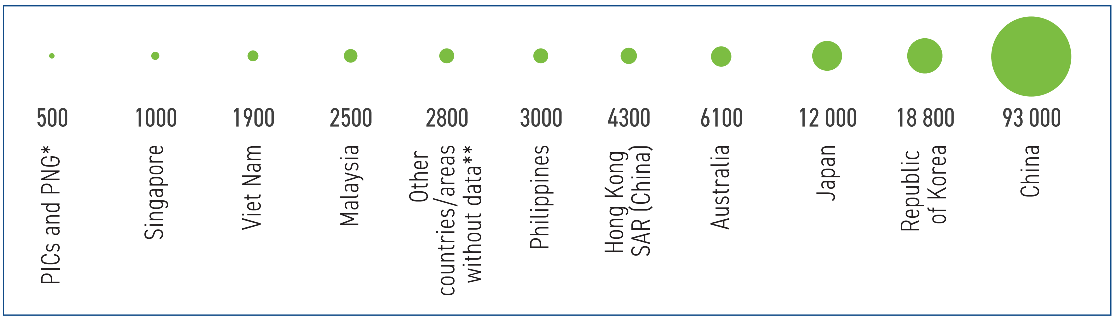
5b. Total economic cost as a percentage of projected country/area GDP



Source: Health and Economic Impacts of Antimicrobial Resistance in the Western Pacific Region, 2020–2030.

AMR infections were estimated to cost US$ 46.3 billion in the 14 high-income countries and areas in the Region, US$ 95.6 billion in the 11 upper middle-income countries/areas, and US$ 5.8 billion in the 12 lower middle-income countries/areas. Absolute costs were highest in China, the Republic of Korea and Japan (Fig. 6 and Table A9).

Fig. 6. AMR-related economic impact in the Western Pacific Region by country/area, 2020–2030 (US$ millions)

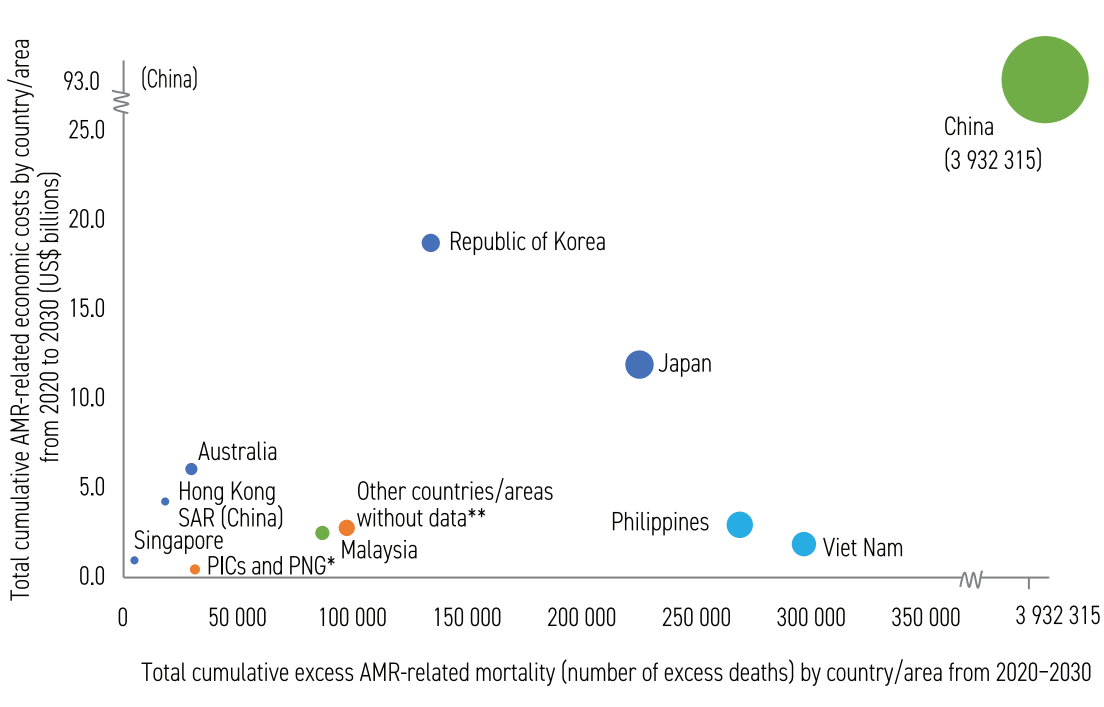


* Pacific island countries and areas and Papua New Guinea
** Brunei Darussalam, Cambodia, the Lao People's Democratic Republic, Macao SAR (China), Mongolia and New Zealand

Source: Health and Economic Impacts of Antimicrobial Resistance in the Western Pacific Region, 2020–2030.

Fig. 7 shows the relationship between AMR-related mortality and total economic cost for countries and areas in the Western Pacific Region. Relative to other countries and areas, AMR-related economic costs are higher in Japan and the Republic of Korea and lower in the Philippines and Viet Nam. The group of six "other" countries and areas comprises Member States with smaller populations and economies. AMR-related mortality and economic costs are affected by country and area population size. In addition, differences in wages and health-care costs probably explain why AMR-related economic costs are higher or lower in some countries and areas relative to others.

Fig. 7. **Relationship between AMR-related mortality and total economic cost by country/area in the Western Pacific Region, 2020–2030**



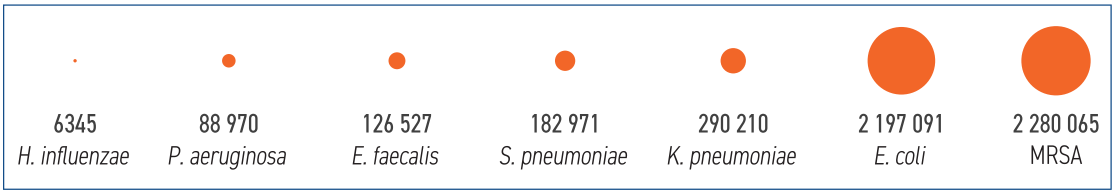
* Pacific island countries and areas and Papua New Guinea
** Brunei Darussalam, Cambodia, the Lao People's Democratic Republic, Macao SAR (China), Mongolia and New Zealand
The size of the bubbles is proportional to the projected country/area population in 2030.

Key: Income classification of countries and areas
- High income
- Upper middle-income
- Lower middle-income
- Mixture of all income groups

Source: Health and Economic Impacts of Antimicrobial Resistance in the Western Pacific Region, 2020–2030.

Among the seven pathogens studied, MRSA and *E. coli* were projected to result in the highest AMR-related health impact over the next decade, each contributing over 2 million deaths (Fig. 8, Table 1 and Annex 7) and more than 70 million additional days in hospital from 2020 to 2030.

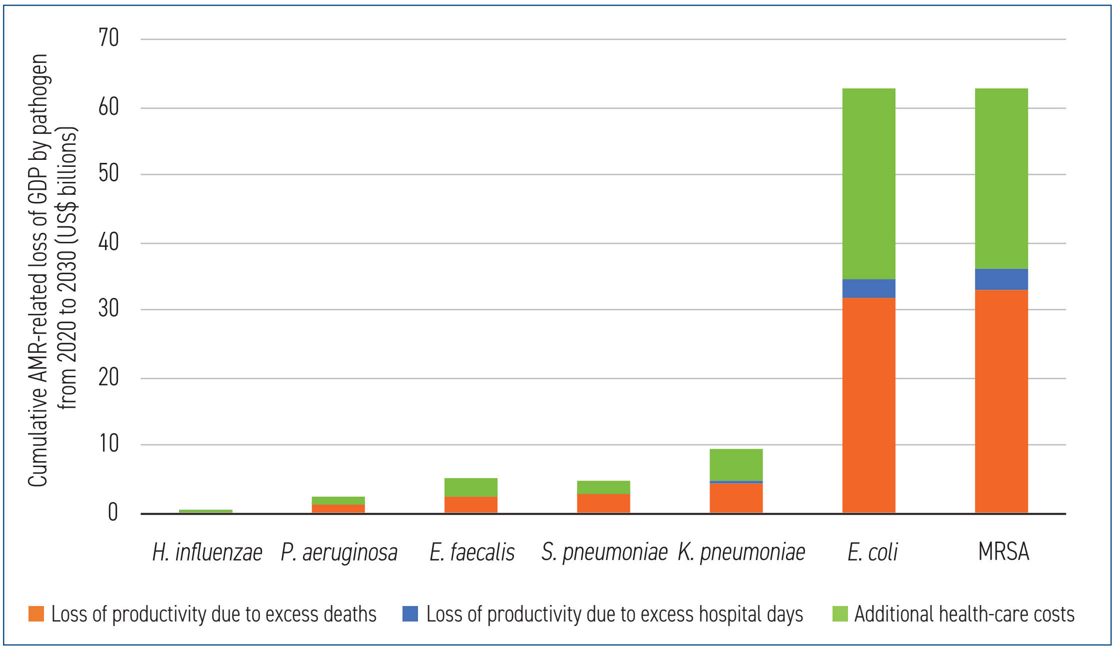
Fig. 8. **AMR-related impact: mortality in the Western Pacific Region by pathogen, 2020–2030 (number of deaths)**



Source: Health and Economic Impacts of Antimicrobial Resistance in the Western Pacific Region, 2020–2030.

Similarly, MRSA and *E. coli* were projected to have the highest AMR-related economic cost, with excess mortality and additional health care, each costing over US$ 30 billion for each pathogen, and additional days spent in hospital resulting in GDP losses of an additional US$ 3 billion for each pathogen (Fig. 9).

Fig. 9. AMR-related impact: cumulative economic costs in the Western Pacific Region by pathogen, 2020–2030 (US$ billions)

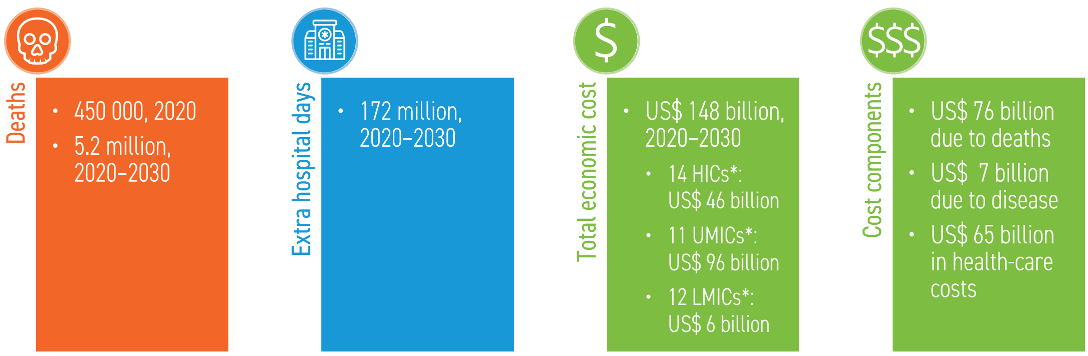


Source: Health and Economic Impacts of Antimicrobial Resistance in the Western Pacific Region, 2020–2030.

Discussion

This study is the first to quantify the health and economic impacts related to AMR infections in the Western Pacific Region. It estimated AMR-related mortality, morbidity and three economic cost components for seven priority bacterial pathogens from 2020 to 2030 (Fig. 10).

Fig. 10. AMR-related health and economic impacts in the Western Pacific Region, 2020–2030



*HIC = high-income country/area, UMIC = upper middle-income country/area, LMIC = lower middle-income country/area

Source: Health and Economic Impacts of Antimicrobial Resistance in the Western Pacific Region, 2020–2030.

The study estimated a regional mortality rate of 23.5 deaths per 100 000 population in 2020. MRSA and *E. coli* accounted for over 80% of the AMR-related impacts among the seven bacteria included in the study.

Health impact

The 450 000 excess AMR-related deaths estimated for the Western Pacific Region in 2020 are similar to the *Global burden of bacterial antimicrobial resistance in 2019: a statistical analysis (2)* estimates of 286 040 (188 060–419 110)[5] deaths attributable to AMR in global burden of disease (GBD) regions that include the Western Pacific Region countries and areas.[6] Put in the context of the 2019 analysis of the global burden of disease by *The Lancet (9)*, bacterial infections would have been the second-leading cause of death[7] globally *(13)*, and AMR the 12th leading cause of death *(2)* ahead of both HIV and malaria.

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5 95% uncertainty interval

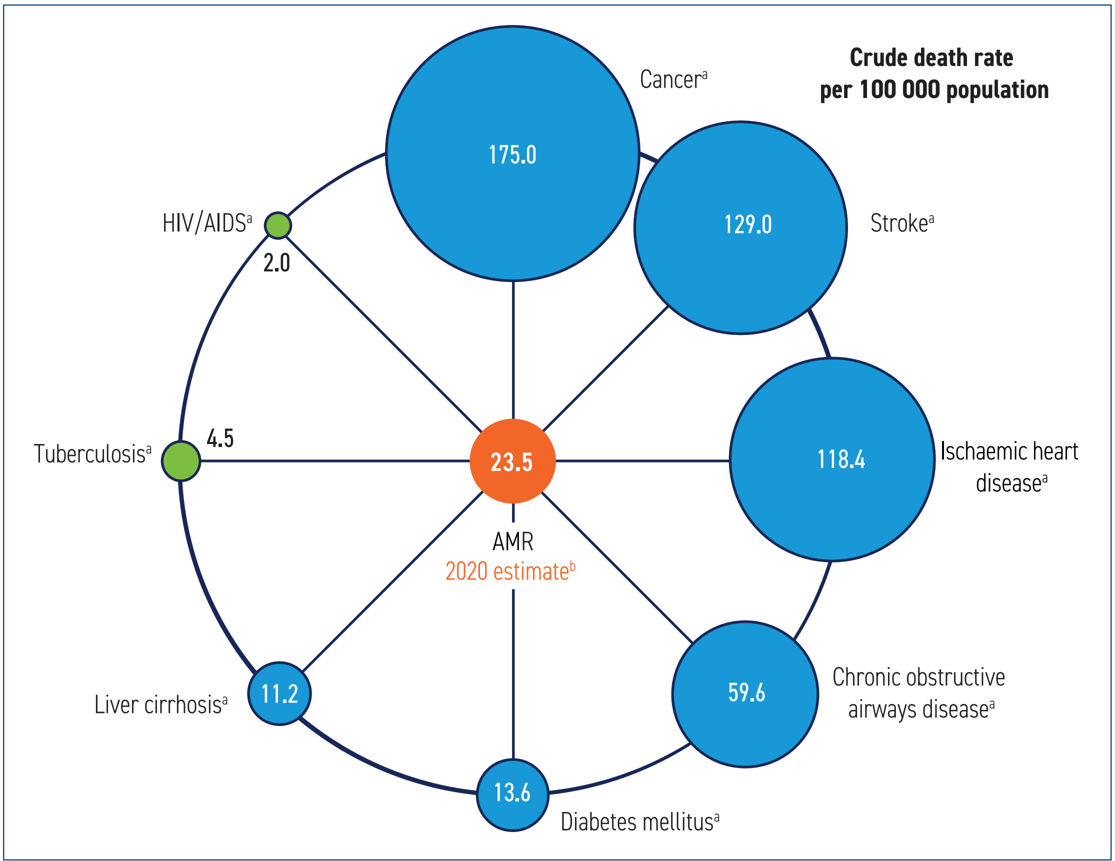
6 Except Mongolia, as well as the Democratic People's Republic of Korea, Indonesia, Maldives, Mauritius, Myanmar, Seychelles, Sri Lanka, Thailand and Timor-Leste.

7 GBD cause hierarchy level 3 – Appendix 1: Methods appendix to *Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019*. Lancet 2020; 396: 1204–22; https://www.thelancet.com/cms/10.1016/S0140-6736(20)30925-9/attachment/7709ecbd-5dbc-4da6-93b2-3fd0bedc16cc/mmc1.pdf. Table S2. pp 1450–1458 *(9).*

Comparisons with other attempts to quantify the burden of AMR are complicated by differences in timescale, geographical coverage, pathogens included[8] and study/model methodologies. All studies are hampered by the complexity of AMR and the lack of reliable data. Nevertheless, despite data and methodological challenges, results consistently indicate that AMR is a major public health issue and poses a serious threat to health systems and economies that is likely to increase in the future.

Fig. 11 shows leading causes of death in the Western Pacific Region in 2019: namely cancer, stroke, ischaemic heart disease and chronic obstructive airways disease *(9)*. The regional AMR-related mortality rate of 23.5 per 100 000 population in 2020 estimated here is comparable to rates for diabetes mellitus and liver cirrhosis as well as kidney diseases and breast cancer (not shown), and it is considerably higher than rates for tuberculosis and HIV/AIDS *(9,10)*. Mortality rates in 2019 estimated by the *Global burden of bacterial antimicrobial resistance in 2019* analysis *(2)* ranged from 6.5 per 100 000 in Australia and New Zealand to 17.0 per 100 000 in the Pacific island countries and areas and Papua New Guinea.

Fig. 11. Comparison of estimated AMR-related mortality rate in 2020 with other causes of death in the Western Pacific Region in 2019



Sources:

[a] Global Health Estimates 2020: Deaths by Cause and by region, 2000–2019. Geneva, World Health Organization; 2020. https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-leading-causes-of-death *(10)*.

[b] Health and Economic Impacts of Antimicrobial Resistance in the Western Pacific Region, 2020–2030.

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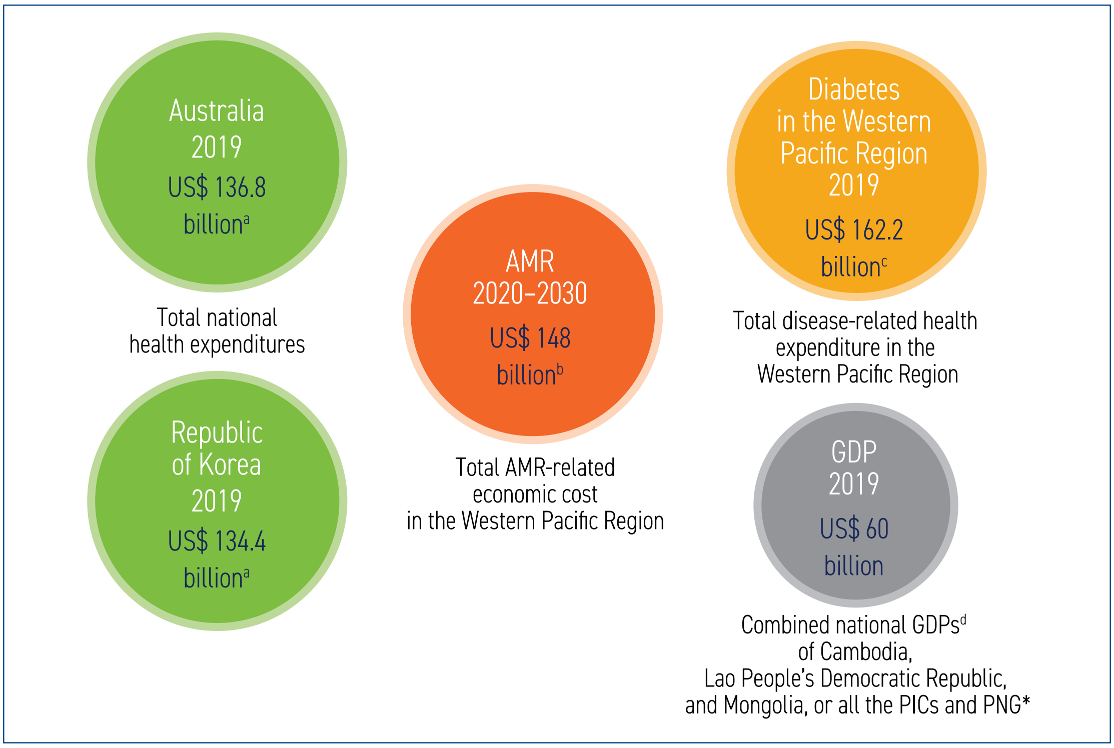
[8] The O'Neill Review included four bacterial pathogens as well as HIV and malaria; the World Bank considered AMR in its broadest sense, covering all resistant pathogens; the Organisation for Economic Co-operation and Development report looked at eight bacteria and a total of 17 antibiotic-pathogen combinations; the *Global burden of bacterial antimicrobial resistance in 2019 analysis* looked at 23 bacterial pathogens including multidrug-resistant tuberculosis and 88 antibiotic-pathogen combinations.

Infections caused by MRSA and *E. coli* are common, and resistance is widespread in the Western Pacific Region with this study predicting resistance rates of 100% for MRSA and nearly 60% for *E. coli* by 2030 (Annex 4). Resistance rates were generally projected to increase between 2020 and 2030, notably of *K. pneumoniae* (by 17%), *S. pneumoniae* (by 17%), *P. aeruginosa* (by 18%) and *H. influenzae* (by 15%) (Annex 7). SDG indicator 3.d.2 showed that among bloodstream infections globally in 2019, 24.9% were due to MRSA and 36.6% to *E. coli* resistant to third-generation cephalosporin *(18)*; MRSA and *E. coli* accounted for about half the AMR mortality in high-income countries/areas in 2019 *(2)*.

Economic impact

The total economic cost of AMR-related infections projected for the Western Pacific Region from 2020 to 2030 of US$ 148 billion is higher than, for example, the total health expenditure in 2019 in Australia (US$ 136.8 billion) and the Republic of Korea (US$ 134.4 billion), and equal to nearly 10% of total health expenditure in the Western Pacific Region in 2019 (US$ 1.68 trillion) *(11)*. It is nearly two and a half times the annual GDPs projected for 2020 for Cambodia, the Lao People's Democratic Republic and Mongolia combined (US$ 60 billion) *(12)* or of all the Pacific island countries and areas Papua New Guinea combined (US$ 59.8 billion). The total cost is similar to the total diabetes-related health expenditure in 2019 in the Western Pacific Region (US$ 162.2 billion, Fig. 12) *(19)*.

Fig. 12. Comparison of total AMR-related economic cost in the Western Pacific Region, 2020–2030, with other economic measures (US$ billions)



* Pacific island countries and areas and Papua New Guinea

Sources: all accessed on 30 March 2023

[a] Global Health Expenditure Database. https://apps.who.int/nha/database/Select/Indicators/en *(11)*.

[b] Health and Economic Impacts of Antimicrobial Resistance in the Western Pacific Region, 2020–2030.

[c] The International Diabetes Federation Diabetes Atlas, 9th edition 2019. https://diabetesatlas.org/.

[d] World Bank. The World Bank - Indicators | Data. https://data.worldbank.org/indicator.

The overriding limitation of this study is the extreme lack of AMR-related data from countries and areas in the Western Pacific Region. Because of this data scarcity, several assumptions had to be made to allow extrapolation to countries and areas without data. The model used linear projections of resistance rates, population, GDP and GDP per capita from 2020 to 2030 (Annex 1). Resistance rates and transmission of infections are affected by a number of elements and are likely to vary significantly in different countries *(15–17,20)*. Population projections are reasonably robust, but economic projections made over an 11-year period clearly contain an element of uncertainty, particularly during times of macro fiscal turbulence.

The different demographics of countries and areas in the Region were not accounted for, but the impact of AMR is likely to be even greater among more vulnerable groups such as young children, older people and people with weakened immune systems. The overall societal costs of AMR will be higher than the economic cost projected in this study as factors – such as the cost of more expensive treatments needed for antibiotic-resistant infections, the greater productivity losses due to longer recovery times and additional indirect costs affecting the informal sector, such as the costs borne by caregivers – were not considered.

In summary, the results presented in this study are an estimate of the potential overall impact of AMR in the Western Pacific Region over the next decade. The estimates are broadly in line with those of other studies and despite inherent uncertainties, indicate that the threats posed by AMR are likely to be substantial and far-reaching. It is also clear that, as a result of considerable variation in epidemiological, demographic and health systems factors, and the risk of natural disasters and public health emergencies, AMR is likely to affect some countries and areas disproportionately.

Future research

The urgent need for more accurate and comprehensive data on AMR is very clear. National surveillance systems and regional networks that include clinical, laboratory and epidemiological data must be rapidly established and strengthened across the Western Pacific Region. In parallel, carefully designed studies are needed to fill knowledge gaps and inform feasible, cost-effective solutions for priority issues. WHO and regional WHO collaborating centres on AMR could lead collaborative research approaches similar to those implemented during the coronavirus disease (COVID-19) pandemic, such as the Recovery, Solidarity and Unity studies, that have demonstrated the value of coordinated multi-country/multicentre studies for generating robust evidence and informing clear-cut recommendations.

Priority research areas on AMR include:

- Population-based incidence rates, resistance rates and clinical outcomes of infectious diseases caused by bacterial and other important pathogens.
- Social science studies of factors underlying antibiotic prescription and consumption to help design interventions to address misuse/inappropriate use of critical medicines.
- Impact investigations and cost-effectiveness studies of interventions to address AMR that provide policy-makers with robust evidence to support decision-making.
- Clinical trials that support the development and testing of new antibiotics and vaccines.

Regional policy implications

This study demonstrates that the health, societal and economic costs of AMR in the Western Pacific Region, now and over the next decade, must not be underestimated. AMR already causes a large number of deaths, comparable to many priority diseases, and it has substantial health-care and economic costs that will increase in the future, unless mitigating actions are implemented. In addition, AMR requires policy and financial attention, proportionate to its impact compared with priority diseases such as diabetes. Money spent now on interventions to control and combat AMR will be an investment for the future, saving on future health-care costs and protecting the workforce and economy.

AMR is a cross-cutting, silent pandemic that is threatening our health security and medical interventions that we take for granted. Maternal, child and reproductive health conditions, infectious diseases, cancer therapy and surgical interventions will all become more dangerous if antibiotics are no longer effective. Stark memories of the COVID-19 pandemic should warn us that if hospital beds are occupied by people with AMR infections, patients with other conditions will suffer. AMR interventions must be integrated within UHC strategies for greater resilience and sustainability, in emergency and pandemic preparedness, prevention and response and in primary care services.

Country-specific and regional data are essential to inform and monitor the impact of interventions to combat AMR. Robust national AMR surveillance, integrated in national health-information systems, that collects case-based clinical, laboratory and epidemiological data on AMR is needed in all countries. Hospital-level surveillance that generates data on local antibiotic susceptibility patterns and monitors antimicrobial consumption and usage must be established to support improved patient care. The Western Pacific Regional Antimicrobial Consumption Surveillance System needs to be expanded to improve its effectiveness as a Region-wide surveillance network that informs policy and clinical practice and strengthens regional early warning capacity.

Strong laboratory infrastructure and cost-effective diagnostics are central to improving clinical management of patients, as well as for detecting infection and antibiotic resistance for surveillance and informing appropriate use of antibiotics. Equitable access to antibiotics and affordable commodities must be ensured, paying attention to research and development, regulation, manufacture, and distribution of medicines and commodities.

Inadequate regulation, overuse and misuse of antibiotics are important drivers of AMR. Regulatory mechanisms must be tightened, banning the availability of antibiotics without prescription over the counter and online, and rooting out falsified medications. Mass-media campaigns and innovative approaches to communication that harness the power of digital platforms and young people acting as champions can be used to manage public expectations and reduce demand for antibiotics.

Education and training must be tailored to different audiences and cadres of health workers, including staff in primary care and laboratories, pharmacists, and young doctors in training as part of their continuous medical education, maximizing the use of e-learning platforms to increase reach. Antimicrobial prescribing habits of more established physicians need to be better understood and innovative approaches to incentivizing antimicrobial stewardship explored to ensure that antibiotics are prescribed wisely, following WHO's Access, Watch and Reserve (AWaRe) classification system *(21,22)*.

Reducing infections reduces the need for antibiotics and slows the emergence of resistance. Prevention of infection must be emphasized, through improved hygiene and sanitation and systematic implementation of strong IPC measures in all health and social-care settings. Vaccines prevent infection and reduce the risk of AMR. Existing vaccines must be rapidly made available to the populations that need them. Innovations and investment in research, development, regulation, marketing, distribution and appropriate use of vaccines should be encouraged.

AMR needs a multisectoral response. The causal factors and impacts of AMR extend beyond the human health sector. AMR does not respect national boundaries, the impacts are not distributed uniformly, and AMR is likely to be an especially serious threat for some of the poorest Member States in the Region. Strong leadership and national and regional multisectoral governance mechanisms that bring together the quadripartite One Health sectors – human and animal health, food, agriculture and environment – to address interconnecting issues including regulation of antimicrobials and cross-border trade, must be established to coordinate surveillance, training, research and interventions on AMR.

Prioritizing AMR requires strong political will and engagement backed up by sufficient investment in financial and human resources to ensure sustainability. The societal cost of ignoring AMR is likely to be disastrous. Health and other policy-makers must recognize the importance and urgency of combatting AMR, based on the magnitude of the threat and the links between the societal and economic costs of AMR and overall development. Evidence suggests that putting resources into mitigating AMR now may be one of the highest-yield investments countries can make *(3)*.

Best-buy interventions include improved IPC and handwashing, antimicrobial stewardship programmes to address over-prescription, and using rapid diagnostic tests to distinguish bacterial from viral infections *(4)*. Decision-makers across the Western Pacific Region face competing priorities for investment and action. We must identify which issues to tackle, as well as how and when. The WHO Regional Office for the Western Pacific is coordinating work to identify and prioritize emerging regional issues on AMR and develop innovative solutions to mitigate their impact.

Conclusions

- AMR is projected to cause substantial morbidity and mortality in the Western Pacific Region over the next decade, at significant economic cost, comparable to priority diseases including cardiovascular disease and diabetes.
- By endangering people's health, AMR poses a threat to health security in the Western Pacific Region and has implications for overall development, particularly in Member States that are more vulnerable to the impacts of AMR.
- The need for targeted actions and cost-effective interventions to combat the threat of AMR is urgent. AMR is a global and a local problem and requires global and regional action as well as national responses tailored to the local context.
- Tackling AMR requires stronger advocacy among policy-makers in all sectors, health professionals and the public to deepen the understanding of the threat of AMR and factors that contribute to that threat, raise awareness of the importance of mitigating measures and urgently galvanize action.
- Political commitment to combatting AMR must be demonstrated through regular revision of national AMR action plans and allocation of sufficient financial and human resources for plans to be implemented.
- There is an overriding need for better quality data to enable more accurate projections on the trajectory of AMR in the Region and reduce uncertainty around its predicted impacts. Actions to establish and strengthen national AMR surveillance systems, integrated in national health-information systems, where possible, must be prioritized.
- WHO will continue to work with Member States, partners, academic institutions and experts to develop and implement national AMR action plans and support AMR surveillance and stewardship, strengthen health systems, conduct research and generate evidence.
- WHO must consolidate its partnership with WOAH, FAO and UNEP to strengthen the AMR quadripartite, focusing on advocacy and awareness-raising, surveillance and monitoring, information-sharing, and emerging and endemic zoonotic diseases to mitigate the impact of AMR now and in the future.

References

1. Review on Antimicrobial Resistance. Antimicrobial Resistance: Tackling a Crisis for the Health and Wealth of Nations. 2014. HM Government Wellcome Trust; 2014 [cited 2022 Jun 1]. Available from: https://amr-review.org/Publications.html.

2. Murray CJ, Ikuta KS, Sharara F, Swetschinski L, Aguilar GR, Gray A, et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. The Lancet. 2022 Feb 12;399(10325):629–55 [cited 2022 Jun 1]. Available from: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02724-0/fulltext.

3. World Bank. Drug-Resistant Infections: A Threat to Our Economic Future. Washington, DC: World Bank; 2017 Mar [cited 2022 Oct 7]. Available from: https://openknowledge.worldbank.org/handle/10986/26707.

4. OECD. Stemming the Superbug Tide: Just A Few Dollars More. Paris: Organisation for Economic Co-operation and Development; 2018 [cited 2022 Oct 7]. Available from: https://www.oecd-ilibrary.org/social-issues-migration-health/stemming-the-superbug-tide_9789264307599-en.

5. World Health Organization. Regional Office for the Western Pacific. For the future: towards the healthiest and safest Region. WHO Regional Office for the Western Pacific; 2020 [cited 2022 Jul 6]. Available from: https://apps.who.int/iris/handle/10665/330703.

6. World Health Organization. Regional Office for the Western Pacific. Framework for accelerating action to fight antimicrobial resistance in the Western Pacific Region. WHO Regional Office for the Western Pacific; 2020 [cited 2022 Jul 6]. ix, 18 p. Available from: https://apps.who.int/iris/handle/10665/340354.

7. World Health Organization. Global action plan on antimicrobial resistance. Geneva: World Health Organization; 2015 [cited 2022 Jun 1]. Available from: https://www.who.int/publications/i/item/9789241509763.

8. World Health Organization. Regional Office for the Western Pacific. Action agenda for antimicrobial resistance in the Western Pacific Region. WHO Regional Office for the Western Pacific; 2015 [cited 2022 Jun 1]. viii, 25 p. Available from: https://apps.who.int/iris/handle/10665/208184.

9. Vos T, Lim SS, Abbafati C, Abbas KM, Abbasi M, Abbasifard M, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet. 2020 Oct 17;396(10258):1204–22 [cited 2022 Jun 1]. Available from: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30925-9/fulltext.

10. World Health Organization. Global Health Estimates 2020: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2019. Geneva: World Health Organization; 2020 [cited 2022 Aug 26]. Available from: https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-leading-causes-of-death.

11. Global Health Expenditure Database [cited 2022 Oct 20]. Available from: https://apps.who.int/nha/database/Select/Indicators/en.

12. World Bank. The World Bank - Indicators | Data [cited 2022 Oct 25]. Available from: https://data.worldbank.org/indicator.

13. Ikuta KS, Swetschinski LR, Aguilar GR, Sharara F, Mestrovic T, Gray AP, et al. Global mortality associated with 33 bacterial pathogens in 2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet. 2022 Nov 21;0(0) [cited 2022 Nov 30]. Available from: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)02185-7/fulltext.

14. Home — SDG Indicators [cited 2022 Aug 14]. Available from: https://unstats.un.org/sdgs/.

15. Burnham JP. Climate change and antibiotic resistance: a deadly combination. Therapeutic Advances in Infection. 2021 Jan 1;8:2049-9361 [cited 2022 Dec 1]. Available from: https://doi.org/10.1177/2049936121991374.

16. Antimicrobial Resistance and the Climate Crisis [cited 2022 Dec 1]. Available from: https://www.amrleaders.org/about-us/why-amr/antimicrobial-resistance-and-the-climate-crisis.

17. Romanello M, Napoli CD, Drummond P, Green C, Kennard H, Lampard P, et al. The 2022 report of the Lancet Countdown on health and climate change: health at the mercy of fossil fuels. The Lancet. 2022 Nov 5;400(10363):1619–54 [cited 2022 Dec 1]. Available from: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)01540-9/fulltext.

18. UNSDG SDG 3.d.2 SH_BLD_MRSA and SH_BLD_ECOLI [cited 2022 Aug 8]. Available from: https://unstats.un.org/sdgs/dataportal/database.

19. International Diabetes Federation. IDF Diabetes Atlas 9th edition. International Diabetes Federation, Brussels, Belgium; 2019 [cited 2022 Oct 14]. Available from: https://diabetesatlas.org.

20. Hashiguchi TCO, Ouakrim DA, Padget M, Cassini A, Cecchini M. Resistance proportions for eight priority antibiotic-bacterium combinations in OECD, EU/EEA and G20 countries 2000 to 2030: a modelling study. Eurosurveillance. 2019 May 16;24(20):1800445 [cited 2022 Oct 7]. Available from: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2019.24.20.1800445.

21. World Health Organization. 2021AWaRe classification. 2021 [cited 2022 Nov 15]. Available from: https://www.who.int/publications-detail-redirect/2021-aware-classification.

22. World Health Organization. WHO releases the 2019 AWaRe Classification Antibiotics [cited 2022 Nov 15]. Available from: https://www.who.int/news/item/01-10-2019-who-releases-the-2019-aware-classification-antibiotics.

Annexes

Annex 1. Model parameters and calculations

- The total economic cost of antimicrobial resistance (AMR) (of antibiotic-resistant compared with antibiotic-susceptible infections) was estimated by combining the loss of GDP accumulated from a permanent loss of work productivity among people who die and reduced productivity because of people spending longer in hospital (indirect costs) and the additional health-care costs resulting from longer hospital stays (direct costs), using the following equation:

$$\textit{Total cost } C = \sum_{i=1}^{k} I_i \times R_i \times \left[M \times P \times D + H \times (P - M) \times \frac{D}{365} + H \times (P - M) \times C_h \right]$$

Parameters

I: incidence of infection for seven pathogens (the most recent pathogen-specific incidence rate data from any country/area was applied across the Region and kept constant from 2020 to 2030).

R: resistance rate (estimates were sought by country/area per pathogen/antibiotic class per year, supplemented with data on antibiotic consumption and extrapolated to countries/areas without data from the country/area with the nearest GDP per capita).

M: AMR-related excess mortality (data were very limited, estimates were pooled for all pathogens and applied across all countries; the maximum value was kept constant from 2020 to 2030 and used to estimate the economic cost).

H: AMR-related increase in length of hospital stay (data were very limited, reported estimates of the excess number of days of hospitalization with infection with any antibiotic-resistant pathogen were pooled and applied across all countries; the maximum value was kept constant from 2020 to 2030 and used to calculate the economic cost).

D: GDP per capita (projected linearly from 2020 to 2030).

P: population size (projected linearly from 2020 to 2030).

C_h: average hospitalization cost per person per day (data were evaluated by country/area where available, projected linearly from 2020 to 2030 and extrapolated to countries/areas without data from the country/area with the nearest GDP per capita).

k: number of pathogens investigated.

Total economic cost, calculated as the sum of indirect and direct costs related to AMR:

- **Indirect costs of AMR**
  - The cost of permanent loss of work productivity (GDP loss due to mortality) calculated as incidence rate x resistance rates x AMR-related excess mortality x population x GDP per capita = *I x R x M x P x D*.
  - The cost of reduced work productivity (GDP loss due to people with AMR infections not being able to work) calculated as incidence rate x resistance rates

x AMR-related excess morbidity x (population – AMR-related excess mortality) x GDP per capita per day = $I \times R \times H \times (P - M) \times D/365$.

- **Direct costs of AMR**
  - The direct cost of hospitalization (additional days spent in hospital by people with AMR infections) calculated as incidence rate x resistance rates x AMR-related excess morbidity x (population – AMR-related excess mortality) x daily hospitalization cost = $I \times R \times H \times (P - M) \times C_h$.
- For an individual pathogen, I and R are constant; for a country/area GDP per capita, population and hospitalization costs were projected linearly; for the Western Pacific Region, the total cost was calculated as the sum of individual country/area costs.
- Pathogen-specific incidence rates and AMR-related excess mortality and morbidity data obtained from the systematic review were kept constant and the resistance rates, GDP per capita, population and daily hospitalization costs were projected linearly from 2020 to 2030.
- For countries and areas without data, the same pathogen-specific incidence rates and AMR-related excess mortality and morbidity data were used and kept constant from 2020 to 2030. The resistance rates and daily hospitalization costs were derived from data for the country/area with the nearest GDP per capita, based on the assumption that countries/areas with a similar GDP per capita would have the same AMR trends and hospitalization costs.

Annex 2. Sensitivity analysis

The sensitivity analysis estimated the total health impact and cost related to AMR in the Western Pacific Region when resistance rates were modelled to increase by 25% (moderate scenario) or 50% (high-impact scenario) from 2020 to 2030 (rates were increased by 50% and 75% for lower middle-income countries – i.e. the Philippines and Viet Nam) (Fig. A1).

Mortality (number of AMR-related deaths):

- 25% increase in AMR resistance: deaths increased from 5.2 million to 5.7 million.
- 50% increase in AMR resistance: deaths increased to 6.1 million.

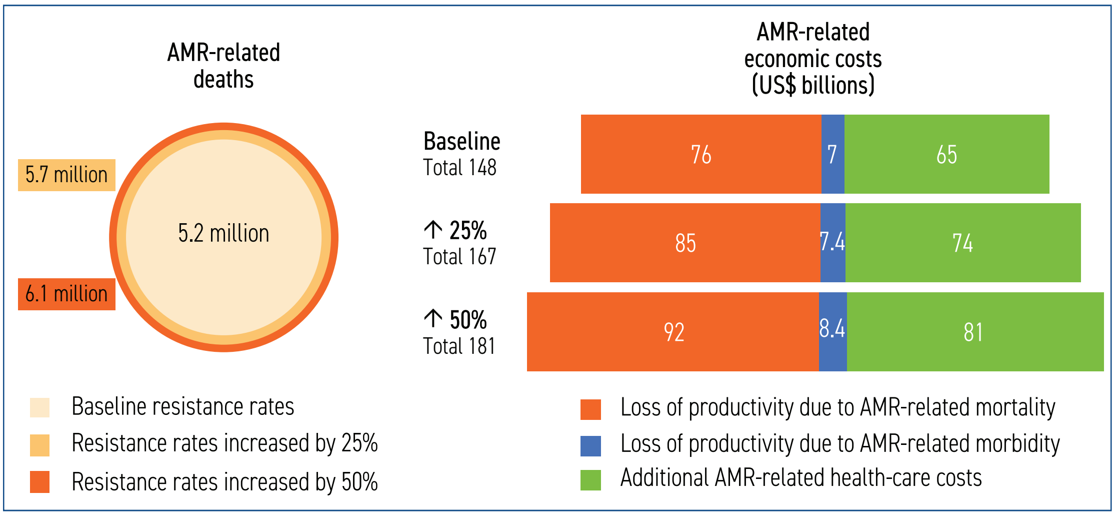
Morbidity (additional hospital days):

- 25% increase in AMR resistance: hospital days increased from 172 million to 190 million.
- 50% increase in AMR resistance: hospital days increased to 204 million.

Economic cost (total economic cost):

- 25% increase in AMR resistance: cost increased from US$ 148 billion to US$ 167 billion.
- 50% increase in AMR resistance: cost increased to US$ 181 billion.

Fig. A1. Sensitivity analysis: AMR-related health and economic impact in the Western Pacific Region, 2020–2030



Source: Health and Economic Impacts of Antimicrobial Resistance in the Western Pacific Region, 2020–2030.

Annex 3. Rationale for pathogen selection

The seven bacterial pathogens preselected for this study are all important in human health due to the diseases they cause and populations they infect. *E. coli, K. pneumoniae* and *P. aeruginosa* are categorized as "critical" in the WHO global priority list of antibiotic-resistant bacteria,[9] due to their ability to escape last-line antibiotics such as carbapenems. *E. coli* can cause several common human infections and is found widely in both animals and the environment. MRSA is listed as "high" and *S. pneumoniae* and *H. influenzae* as "medium" global priority pathogens; MRSA shows high levels of multidrug resistance in hospital environments and although vaccines that can prevent disease caused by *S. pneumoniae* and *H. influenzae* are available, both bacteria still cause a substantial burden of death and disease. *E. faecalis* is not on the global priority list, but its ability to resist multiple classes of antibiotics highlights its potential for AMR and the need for surveillance of this pathogen.

The scope of this study was limited to the bacteria listed above to avoid duplicating work on AMR to HIV, malaria parasites, tuberculosis and other pathogens.

Annex 4. Incidence rates

The systematic review identified very few studies reporting pathogen-specific incidence rates by year for countries/areas in the Western Pacific Region. Canada and New Zealand conduct robust AMR surveillance and have health-care systems comparable to other countries/areas in the Western Pacific Region; incidence rates for *K. pneumoniae, P. aeruginosa* and *E. faecalis* infections were taken from Canadian data and for *E. coli* from New Zealand. Pathogen-specific incidence rates were assumed to be similar across the Region; the most recent reported incidence rate from any country/area for any type of infection was taken for each pathogen, kept constant from 2020 to 2030 and applied to the whole Region (Table A1).

[9] World Health Organization. Prioritization of pathogens to guide discovery, research and development of new antibiotics for drug-resistant bacterial infections, including tuberculosis. Geneva: World Health Organization; 2017. Available from: https://apps.who.int/iris/handle/10665/311820.

Table A1. Incidence rates of infection for the study pathogens

Pathogen	Country/area	Year	Infection	Incidence (per 100 000 population)
MRSA	Japan	2012	-	36.4
Escherichia coli	New Zealand	2005–2011	BSI	60.0
Klebsiella pneumoniae	Canada	2010–2017	BSI	9.1
Pseudomonas aeruginosa	Canada	2000–2006	BSI	3.6
Streptococcus pneumoniae	Australia	2010–2019	IPD	4.4
Enterococcus faecalis	Canada	2011–2018	BSI	6.6
Haemophilus influenzae	Australia	2010–2019	Invasive disease	0.1

BSI: Bloodstream infections; IPD: Invasive pneumococcal disease

Annex 5. Resistance rates

Resistance rates for the seven pathogens against four antibiotic classes, namely fluroquinolones, cephalosporins, penicillins and carbapenems, were reported in 61 population-based studies from the Western Pacific Region from 2010 to 2019. Reported values for individual pathogens varied widely, for example, 0–95.7% reported resistance to penicillin for *S. pneumoniae,* with the highest overall rates reported in China and the Republic of Korea. The highest reported resistance rate in a country/area for a particular year for each pathogen and any antibiotic class was used for predicting trends and estimating the economic cost of AMR (Table A2). Projected resistance rates for 2030 range from 9.1% for *E. faecalis* to 100% for MRSA, *P. aeruginosa* and *H. influenzae*.

If yearly data were not available for a pathogen/country/area combination, antibiotic consumption trends obtained from published studies and national reports were substituted for resistance rates, on the assumption that resistance increases as consumption increases. Reported antimicrobial consumption increased over time in Australia and Hong Kong SAR (China); decreased in China, Japan and Singapore; showed little change in the Republic of Korea; and only a single data point was found for Viet Nam (Table A3).

The same resistance trends were applied to the remaining countries/areas in the Western Pacific Region based on countries/areas with the closest GDP per capita (Table A4), assuming that countries/areas with similar GDP per capita experience similar rates of AMR.

Table A2. Projected resistance rates* by pathogen and World Bank country/area income group, 2020–2030

Pathogen	Year	Lower-middle income (%)	Upper-middle income (%)	High income (%)
MRSA	2020	100.0	93.3	65.5
	2030	100.0	100.0	53.3
E. coli	2020	46.5	61.1	36.7
	2030	56.8	59.3	32.4
K. pneumoniae	2020	34.3	28.3	33.2
	2030	41.9	29.8	53.3
S. pneumoniae	2020	18.5	42.6	31.7
	2030	22.6	43.1	22.4
E. faecalis	2020	35.9	29.1	47.4
	2030	43.9	9.1	59.8
P. aeruginosa	2020	82.1	21.5	24.2
	2030	100.0	21.4	34.3
H. influenzae	2020	72.6	93.0	91.0
	2030	88.8	100.0	92.9

* Average of maximum resistance rates for each pathogen in countries/areas in one income group

Table A3. Antibiotic consumption data for countries/areas in the Western Pacific Region, 2012–2020

Country/area	Year	Data source	Quantity
Australia	2015	Hospitals	848.2#
Australia	2019	Hospitals	883.0#
China	2012	Retail	16.0*
China	2017	Retail	11.4*
Hong Kong SAR (China)	2014	Hospitals	958.7*
Hong Kong SAR (China)	2016	Hospitals	994.5*
Japan	2013	Retail	14.9*
Japan	2020	Retail	10.6*
Republic of Korea	2010	NHI** antibiotic use and prescriptions	25.1*
Republic of Korea	2013	NHI** antibiotic use and prescriptions	24.2*
Singapore	2011	Public hospitals	511*
Singapore	2017	Public hospitals	372*
Viet Nam	2012-2013	Hospitals	918*

Defined daily dose (DDD)/1000 occupied bed days
* DDD/1000 patient days
** National health insurance

Table A4. Countries/areas in the Western Pacific Region by World Bank income group

High income	Upper-middle income	Lower-middle income
Australia	American Samoa	Cambodia
Brunei Darussalam	**China**	Kiribati
French Polynesia	Cook Islands	Lao People's Democratic Republic
Guam	Fiji	Micronesia (Federated States of)
Hong Kong SAR (China)	**Malaysia**	Mongolia
Japan	Marshall Islands	Papua New Guinea
Macao SAR (China)	Niue	Pitcairn Islands
Nauru	Samoa	**Philippines**
New Caledonia	Tonga	Solomon Islands
New Zealand	Tuvalu	Tokelau
Northern Mariana Islands	Wallis and Futuna	Vanuatu
Palau		**Viet Nam**
Republic of Korea		
Singapore		

* Countries/areas in bold type had data available from the systematic review

Annex 6. AMR-related excess mortality and morbidity

The health impact related to AMR infections was estimated as the excess mortality (number of deaths) and morbidity (number of excess hospital days) due to antibiotic-resistant infections compared with antibiotic-sensitive infections. The systematic review yielded seven studies that reported mortality rates and 10 studies that reported the length of hospital stay. The reports covered MRSA (compared to methicillin-susceptible *S. aureus*), extended spectrum beta-lactamase producing *E. coli* and *K. pneumoniae* and carbapenem-resistant *P. aeruginosa, K. pneumoniae and E. coli*. There were no studies reporting on *E. faecalis, S. pneumoniae* or *H. influenzae*.

The excess mortality and morbidity estimates were pooled and used to calculate a maximum economic cost for each country, that was driven by the country/area GDP per capita, population and resistance rates for the different pathogens.

Annex 7. Mortality and morbidity by pathogen

The health impact associated with an individual pathogen is driven by the pathogen-specific resistance rate and the incidence of infection with the same pathogen. For MRSA and *E. coli* both parameters are high and as a result, these two infections account for the highest proportion of projected AMR-related mortality: MRSA 2 280 065 deaths (44%) and *E. coli* 2 197 091 deaths (42%) (Table A5). In contrast, *H. influenzae* is projected to result in 6300 AMR-related deaths (0.1%).

Table A5. AMR-related deaths (mortality) in the Western Pacific Region by pathogen, 2020–2030

Pathogen	2020	2025	2030	10-year change (%)	Cumulative mortality (% among 7 pathogens)
MRSA	195 934	208 496	215 252	9.9	2 280 065 (44%)
E. coli	197 404	199 688	202 210	2.4	2 197 091 (42%)
K. pneumoniae	24 273	26 435	28 362	16.8	290 210 (6%)
S. pneumoniae	15 452	16 583	17 997	16.5	182 971 (4%)
E. faecalis	13 136	11 707	9 374	−28.6	126 527 (2%)
P. aeruginosa	7 256	8 183	8 569	18.1	88 970 (2%)
H. influenzae	524	580	604	15.1	6 345 (0.1%)

Increases in AMR-related excess mortality from 2020 to 2030 are projected to be highest for *P. aeruginosa* (rising by 18.1%, equivalent to about 89 000 cumulative excess deaths over the next decade), *K. pneumoniae* (16.8%, 290 000 excess deaths), *S. pneumoniae* (16.5%, 183 000 excess deaths) and *H. influenzae* (15.1%, 6300 excess deaths), and intermediate for MRSA (9.9%, 2.3 million excess deaths) and *E. coli* (2.4%, 2.2 million excess deaths). Only AMR-related mortality from *E. faecalis* is projected to decrease (falling by 28.6%), with a corresponding decrease in the number of excess deaths from about 13 000 to 9400 from 2020 to 2030.

AMR-related excess hospitalization days are projected to reach over 172 million cumulatively in the Western Pacific Region between 2020 and 2030, also driven mainly by MRSA and *E. coli*, which are estimated to contribute 75 million and 73 million excess hospital days respectively (Table 6). Additional hospitalization days related to *H. influenzae* infection are expected to increase by 15% over the next decade resulting in 211 172 excess hospital days, despite the very low incidence rate of infection with *H. influenzae* applied in this study.

Table A6. AMR-related extra hospital days (morbidity) in the Western Pacific Region by pathogen, 2020–2030

Pathogen	2020	2025	2030	10-year change (%)	Number of hospital days
MRSA	6 521 098	6 939 189	7 164 040	9.9	75 885 394
E. coli	6 570 029	6 646 036	6 729 966	2.4	73 123 829
K. pneumoniae	807 871	879 799	943 945	16.8	9 658 797
S. pneumoniae	514 274	551 904	598 963	16.5	6 089 678
E. faecalis	437 193	389 624	311 991	−28.6	4 211 079
P. aeruginosa	241 505	272 363	285 183	18.1	2 961 122
H. influenzae	17 446	19 309	20 088	15.1	172

Annex 8. Population, GDP and GDP per capita projections

Table A7. Data sources (2010–2020) used for population, GDP and GDP per capita projections for countries/areas in the Western Pacific Region, 2020–2030

Country/area	Data	Source
Australia	Population	Australian Bureau of Statistics
	GDP per capita	World Bank
	GDP	World Bank
China	Population	National Bureau of Statistics
	GDP per capita	World Bank
	GDP	World Bank
Hong Kong SAR (China)	Population	Census and Statistics Department
	GDP per capita	World Bank
	GDP	World Bank
Japan	Population	Statistics Bureau of Japan
	GDP per capita	World Bank
	GDP	World Bank
Malaysia	Population	Department of Statistics, Malaysia
	GDP per capita	World Bank
	GDP	World Bank
Philippines	Population	World Bank
	GDP per capita	World Bank
	GDP	World Bank
Republic of Korea	Population	Statistics Korea
	GDP per capita	World Bank
	GDP	World Bank
Singapore	Population	Singapore Department of Statistics
	GDP per capita	World Bank
	GDP	World Bank
Viet Nam	Population	World Bank
	GDP per capita	World Bank
	GDP	World Bank

Sources: all accessed on 30 March 2023

World Bank - https://data.worldbank.org/indicator (GDP (current US$) and GDP per capita (current US$)

Australia - https://www.abs.gov.au/statistics/people/population/national-state-and-territory-population/sep-2020#data-downloads-data-cubes

China - http://www.stats.gov.cn/english/Statisticaldata/AnnualData/

Hong Kong SAR (China) - https://www.censtatd.gov.hk/en/web_table.html?id=1A#

Japan - https://www.stat.go.jp/english/data/nenkan/69nenkan/index.html

Malaysia - https://www.dosm.gov.my/v1/index.php?r=column3/accordion&menu_id=amZNeW9vTXRydTFwTXAxSmdDL1J4dz09

Republic of Korea - http://kostat.go.kr/portal/eng/pressReleases/8/7/index.board

Singapore - https://www.singstat.gov.sg/find-data/search-by-theme/population/population-and-population-structure/latest-data

Annex 9. Study limitations

The study assumed constant incidence rates of infection and death rates across the Western Pacific Region and over time, but it did not account for differences in population age structure. Available data mostly referred to bloodstream infections in hospitalized patients, with little information available on community-acquired infections. Resistance rates as a proportion of isolates are affected by the availability and practice of sampling and testing. A study of resistance rates in OECD, European Union and G20 countries projected only marginal increases in resistance rates from 2000 to 2030 but noted significant heterogeneity in resistance proportions across countries and antibiotic-bacterium combinations *(20)*. Mortality rates may lack external and internal validity.

The *Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis* study found that the geographical distribution of infections was not uniform and that AMR all-age death rates were highest in some lower middle-income countries. This may be because of higher resistance rates and more frequent serious infections coupled with limited laboratory infrastructure, poorer access to second- and third-line antibiotics, less stringent antimicrobial stewardship, and greater risk of natural disasters and public health emergencies, and suggests that AMR may be an especially serious threat for some of the poorest countries/areas in the Western Pacific Region.

Mortality generally increased in countries/areas across the Region over the period 2020 to 2030, but as the incidence of infection and excess mortality related to antibiotic-resistant infections were kept constant, the temporal trend of AMR-related excess mortality in a country/area was driven only by changes in resistance rates, population size and GDP per capita. Where adequate data were not available, trends in resistance rates were substituted by antibiotic consumption trends, a relationship the *Global Burden of Disease Study 2019* noted to be strong, though these data were also scarce. The sensitivity analysis showed that if resistance rates were increased by 25% and 50%, total cumulative mortality from 2020 to 2030 would increase from 5.2 million deaths to 5.7 million and 6.1 million deaths, respectively.

Annex 10. AMR-related mortality and economic cost by country/area

Table A8. AMR-related deaths by country/area in the Western Pacific Region, 2020–2030

Country/area	Cumulative excess AMR-related deaths	25% increase in resistance rates	50% increase in resistance rates
AMR resistance rates reported			
Australia	29 703	38 027	42 666
China	3 932 315	4 329 914	4 639 194
Hong Kong SAR (China)	18 433	18 767	19 897
Japan	225 215	287 109	303 365
Malaysia	86 852	96 686	103 277
Philippines	268 744	282 048	296 173
Republic of Korea	134 330	156 858	175 573
Singapore	4 702	7 263	8 145
Viet Nam	296 581	315 750	335 349
No AMR resistance rates reported			
American Samoa	136	151	161
Brunei Darussalam	1 167	1 365	1 529
Cambodia	52 104	55 495	58 958
Cook Islands	23	26	28
Fiji	2 490	2 741	2 937
French Polynesia	551	610	683
Guam	434	507	568
Kiribati	369	393	418
Lao People's Democratic Republic	22 601	24 071	25 573
Macao SAR (China)	765	980	1 100
Marshall Islands	165	182	195
Micronesia (Federated States of)	278	292	307
Mongolia	8 146	8 551	8 981
Nauru	31	34	36
New Caledonia	740	865	969
New Zealand	12 861	13 098	13 897
Niue	4	4	5
Northern Mariana Islands	116	128	143
Palau	35	39	43
Papua New Guinea	22 279	23 388	24 565
Pitcairn Islands	0	0	1
Samoa	467	489	514
Solomon Islands	2 227	2 374	2 523
Tokelau	5	5	6
Tonga	283	311	333
Tuvalu	34	37	40
Vanuatu	784	823	865
Wallis and Futuna	31	35	37

Table A9. AMR-related total economic cost by country/area in the Western Pacific Region, 2020–2030 (US$ thousands)

Country/area	Cumulative AMR-related total economic cost	25% increase in resistance	50% increase in resistance
Countries/areas with data on AMR (at least one report)			
Australia	6 071 918	7 804 266	8 798 978
China	92 955 113	102 810 528	110 612 534
Hong Kong SAR (China)	4 256 725	4 340 528	4 616 131
Japan	12 000 342	15 182 533	16 014 919
Malaysia	2 536 517	2 830 704	3 029 991
Philippines	3 038 543	3 191 900	3 354 262
Republic of Korea	18 810 052	22 063 681	24 759 861
Singapore	965 379	1 526 503	1 720 569
Viet Nam	1 867 907	1 996 634	2 127 229
Countries/areas without data on AMR			
American Samoa	5 216	5 803	6 194
Brunei Darussalam	90 689	106 071	118 837
Cambodia	336 961	360 329	384 018
Cook Islands	2 338	2 590	2 898
Fiji	53 129	58 636	62 960
French Polynesia	33 087	36 565	40 831
Guam	57 501	67 472	75 732
Kiribati	1 818	1 935	2 055
Lao People's Democratic Republic	247 068	264 169	281 508
Macao SAR (China)	223 783	287 072	322 889
Marshall Islands	2 387	2 636	2 831
Micronesia (Federated States of)	3 381	3 553	3 735
Mongolia	101 676	106 723	112 078
Nauru	1 332	1 472	1 582
New Caledonia	76 630	89 341	99 911
New Zealand	1 773 782	1 807 052	1 918 325
Niue	278	310	332
Northern Mariana Islands	12 114	13 546	15 258
Palau	2 226	2 479	2 784
Papua New Guinea	195 590	205 394	215 783
Pitcairn Islands	3	4	4
Samoa	6 405	6 721	7 058
Solomon Islands	17 764	18 958	20 172
Tokelau	112	124	133
Tonga	4 526	4 989	5 350
Tuvalu	445	491	527
Vanuatu	7 064	7 416	7 790
Wallis and Futuna	931	1 034	1 102

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