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Global Economic Impacts of Antimicrobial Resistance

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Abstract

Antimicrobial resistance (AMR) is a growing global health threat that led to 1.27 million deaths in 2019. Given the widespread use of antimicrobials in healthcare, agriculture, and industrial applications and a range of factors affecting AMR, including demographic trends and physical climate risks, an economy-wide approach is essential to understand and assess the economic consequences of AMR. We model the global economic impacts of AMR under six alternative scenarios. These scenarios are designed to incorporate assumptions about changes in AMR-related disease incidence, the impact of a central scenario about future demographic change on AMR over time, and explore the sensitivity of assumptions about the effects of AMR on agriculture productivity. We also examine the additional impacts of changing climate risks on the evolution of AMR (focusing on one climate scenario), the consequences of changes in country risk premia due to the differential impacts of the evolution of AMR on countries, and the global economic impacts of changes in government expenditure in response to AMR. Our results find a significant global economic burden of worsening AMR due to demographic change and climate change risks, as well as significant economic benefits of taking action to address AMR. We emphasize that a "one-health" approach to managing AMR will have substantial economic benefits over the coming decades.

Keywords

antimicrobial resistance, antibiotic resistance, infectious diseases, macroeconomic modelling

JEL Classification

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ABSTRACT

Antimicrobial resistance (AMR) is a growing global health threat that led to 1.27 million deaths in 2019. Given the widespread use of antimicrobials in healthcare, agriculture, and industrial applications and a range of factors affecting AMR, including demographic trends and physical climate risks, an economy-wide approach is essential to understand and assess the economic consequences of AMR. We model the global economic impacts of AMR under six alternative scenarios. These scenarios are designed to incorporate assumptions about changes in AMR-related disease incidence, the impact of a central scenario about future demographic change on AMR over time, and explore the sensitivity of assumptions about the effects of AMR on agriculture productivity. We also examine the additional impacts of changing climate risks on the evolution of AMR (focusing on one climate scenario), the consequences of changes in country risk premia due to the differential impacts of the evolution of AMR on countries, and the global economic impacts of changes in government expenditure in response to AMR. Our results find a significant global economic burden of worsening AMR due to demographic change and climate change risks, as well as significant economic benefits of taking action to address AMR. We emphasize that a "one-health" approach to managing AMR will have substantial economic benefits over the coming decades.

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1 INTRODUCTION

Before the discovery of antimicrobial medicine in the early twentieth century, the preventative and therapeutic options for diseases were limited. While the preventative options were almost non-existent, the therapeutic options included using herbal substances and chemicals, surgical procedures, and supportive care, with low effectiveness. Without therapeutic interventions, infections, including pneumonia, tuberculosis, and skin and soft tissue infections, were significant causes of death. A minor wound could lead to sepsis. The effectiveness of surgical procedures was uncertain without treatment options for postoperative infections. Outbreaks, such as cholera, typhoid, and diarrhea, were unpreventable.

The discovery of penicillin by Alexander Fleming in 1928 and sulphonamides for chemotherapy by Gerhard Domagh in 1932 revolutionized the field of medicine. The discoveries resulted in a "golden age" of developing antimicrobial therapy. The mass production of antimicrobial drugs and their widespread use ensured that minor infections were no longer life-threatening and were more quickly curable. Surgical procedures like cesarean sections and organ transplants were much safer and more effective. Rapid treatment of infected individuals prevented contagion and epidemics. The antimicrobials could also be extended to agriculture, primarily for livestock, to prevent and treat diseases and promote growth. Accordingly, antimicrobials collectively reduced mortality and morbidity from diseases, improved quality of life, and enhanced labor and agriculture productivity.

However, as Davies and Davies (2010) illustrate, by 1970, medical researchers were already studying mechanisms via which microorganisms developed resistance to antimicrobials. Antimicrobial resistance (AMR) is a natural phenomenon. However, as mass production of antimicrobials increased their accessibility at affordable prices, an assortment of reasons, including lack of oversight, suboptimal prescriptions, and suboptimal consumption, also led to overuse, misuse, and underuse of antimicrobials in healthcare settings. Mass consumption in agriculture (primarily livestock) for disease prevention and treatment and growth promotion also rose. The widespread consumption of antimicrobials increased the selective pressure for microorganisms, promoting the survival of resistant strains. Although researchers could outperform resistant strains by further developing antimicrobials for a few more decades, pathogens (those microorganisms that are harmful to humans and animals) adapted, and their pace of developing resistance has subsequently exceeded the speed of the new medicine development.

Consequently, the world is threatened by the reduced effectiveness of antimicrobial medicine and chemicals used in various industrial applications. The threat has not slowed down as microbes have been developing multi-drug resistant forms and surviving and evolving even stronger. These "superbugs" have reduced the therapeutic power of antimicrobial medicine in treating infections caused by them, resulting in extended recovery periods and increasing deaths. In 2019, 1.27 million deaths were attributable to the failure of existing medicine to treat diseases due to AMR (Murray et al. 2022). Ineffective drugs have also threatened medical procedures, such as chemotherapy for cancer patients and surgical procedures for cesarean sections and organ transplants.

O'Neill et al. (2016) postulate that if the current rise in resistance is not contained, AMR could cause at least 10 million deaths a year by 2050. Furthermore, as the livestock sector is the major non-medicinal antimicrobial consumer, the ineffectiveness of existing antimicrobials used for animals could reduce livestock productivity and threaten food safety and security (Food and Agriculture Organization [FAO] 2021). Quite strikingly, the ability to further improve antimicrobials has been reduced, and few new antimicrobials are in the development pipeline to replace the ineffective antimicrobials. AMR poses a significant socioeconomic threat to the world.

Although AMR is a natural process, the underlying cause for heightened AMR, since the initial discovery of antimicrobials less than a century ago, lies in the underuse, overuse, and misuse of antimicrobials for humans and animals. An absence of or an inability to obtain sufficient information when using antimicrobials has led to suboptimal consumption, which promotes AMR. The resulting distortion in their supply and demand leads to prices that do not reflect the actual social costs of using antimicrobials. This mispricing further aggravates the negative externalities beyond geographical boundaries due to the widespread use of antimicrobials worldwide. Thus, according to Woolhouse et al. (2015), AMR is a classic market failure that requires global coordination and support. However, initiatives towards achieving this coordination have been limited.

Despite the need to respond proactively to AMR, the world is still not sufficiently committed. According to Smith and Coast (2013), this lack of action is due to framing AMR as a problem of concern only for the health sector in the absence of economic studies demonstrating the economy-wide impacts of AMR. The high uncertainty about the AMR impact transition pathways and difficulty obtaining data have been the main reasons for the insufficiency of economic studies. As Fernando and McKibbin (2022) argue, the existing studies present room for conceptual and methodological improvements when analyzing AMR. In response to this research gap, this paper evaluates the global economic impacts of AMR. Due to the collective economic and political significance, we focus on the countries that are members of the Group of 20 (G20).

This paper applies the approach of Fernando and McKibbin (2022), which proposed a comprehensive framework for modeling the economic impacts of AMR. Section 2 outlines the economic importance of microorganisms, the origins and evolution of AMR, and factors affecting AMR. It also assesses the current understanding of AMR implications and evaluates the existing modeling approaches and their strengths and limitations. Section 3 introduces the methodology, including a conceptual framework for AMR economic impact pathways, the details of the G-Cubed model used for evaluating the economic impacts of AMR, and shock formulation to replicate the economic impact pathways of AMR. The simulation results from the G-Cubed model illustrating the economic effects of AMR are discussed in Section 4. Section 5 distills the policy implications arising from the paper. Section 6 concludes with a summary and proposes future directions for extending the research. The results from various analyses and modeling in the paper and additional details are also provided via an online interactive dashboard.

2 ANTIMICROBIAL RESISTANCE: A BACKGROUND

2.1 Economic Importance of Microorganisms

Microorganisms, including bacteria, fungi, viruses, algae, and protozoa, have played a vital role in the survival and evolution of humans, animals, and plants. One of the most important functions of microorganisms is recycling organic and inorganic matter through their interactions in the carbon, nitrogen, and sulphur cycles, which contribute to maintaining the stability of the biosphere. Microorganisms are also the initial source of nutrients in many food chains. The chemical reactions of microorganisms on organic and inorganic matter are applied in various agricultural (e.g., production of fertilizers) and industrial applications (e.g., fermentation and synthesis of proteins and enzymes). However, microorganisms also have a range of undesirable effects on the survival of humans, animals, and plants, including microbial diseases. Historical plagues such as the "Black Death" and the COVID-19 pandemic exemplify the negative implications of microorganisms on humans.

With the advancement of science and technology, methodologies have been developed to harness the positive impacts and reduce the negative impacts of microorganisms. The discovery and mass production of antimicrobial medicines and chemicals have been an effective response to control the undesirable effects of microorganisms. The discovery of antimicrobial drugs, such as penicillin and sulfonamides, in the early 1900s revolutionized the treatment of microbial infections and has been vital to medical procedures, such as cesarean sections, chemotherapy, organ transplants, and other surgeries. Currently, antimicrobials are used in agriculture and aquaculture for therapeutic, metaphylaxis, and prophylaxis purposes and growth promotion. In industrial applications, antimicrobials control microbial activity where physical processes (such as irradiation or heat) are ineffective or impractical.[1] Antimicrobial paints, coatings, additives, and preservatives are widely used in the manufacture of wood, paper, textiles and cosmetics, plastic and metal, energy production, construction, transportation, utilities, and healthcare.

However, harmful microorganisms, or the pathogens that cause infections among humans and animals, have developed resistance to antimicrobials (World Health Organization [WHO] 2021a). In general, the increase in resistance in microorganisms against antimicrobials is called antimicrobial resistance (AMR), and AMR threatens the effective use of antimicrobials.

2.2 Origins and Evolution of Antimicrobial Resistance

Adapting to challenging and changing environments or circumstances is a fundamental driver of the evolution of all living beings, which is also applicable to microorganisms. Accordingly, developing resistance to antimicrobials is an element of the natural evolution of microorganisms. While some microorganisms

[1] The spectrum of industrial applications of antimicrobials includes static (preventing growth of a microorganism), antiseptic (preventing infection), sanitizer (reducing the number of harmful microorganisms to a safe level), cidal (eliminating microorganisms of a particular type), disinfectant (eliminating all infectious bacteria), sporicidal (eliminating spores), and sterilant (completely eliminating all living microorganisms) (McEntee 2000).

are intrinsically resistant to antimicrobials, there are two main ways a non-intrinsically resistant microorganism acquires resistance: (1) genetic mutations within the cell to its chromosomal DNA, and (2) acquisition of genetic material from a resistant cell via transformation, transduction, or conjugation. Antimicrobials often destroy a microorganism or prevent its growth via several mechanisms: (1) disrupting the cell membrane; (2) inhibiting cell wall synthesis; (3) inhibiting protein synthesis; (4) inhibiting nucleic acid (DNA or RNA) synthesis, and (5) inhibiting metabolism (Rani et al. 2021). While intrinsically resistant microorganisms would either have an impermeable cell membrane or lack the target of antimicrobials, acquired resistance could lead to producing enzymes that deactivate antimicrobials, pumping antimicrobials out of the cells, or modifying the target of antimicrobials.[2] When antimicrobials are used to eliminate the susceptible and non-resistant strains to the antimicrobials, the survival advantage for the resistant strains increases. Overuse, misuse, and underuse of antimicrobials for various applications, including therapeutic uses, and continuous exposure of antimicrobials in the environment (such as in healthcare settings, wastewater treatment facilities, and the built environment) further increase the selective pressure and accelerate the resistant acquisition rates among microorganisms. With exposure to a broader array of antimicrobials, some microorganisms have developed resistance not only to a single antimicrobial targeting them but to multiple antimicrobials. These microorganisms are called "superbugs" (Davies & Davies 2010).

2.3 Factors Driving Antimicrobial Resistance

Suboptimal consumption of antimicrobials and selective pressure exerted by such consumption is the uncontested and immediate factor driving AMR. A vast body of literature explores how antimicrobial consumption in different sectors, particularly healthcare and agriculture (including crops, livestock, and aquaculture), has aggravated AMR.[3] In the healthcare sector, a wide range of literature analyzes the suboptimal antimicrobial consumption among individuals (self-prescription or not following the prescription by a healthcare practitioner[4]), within primary care settings (via suboptimal diagnosis and prescription by general practitioners[5]), and within hospital settings (via mismanagement and suboptimal consumption of antimicrobials[6]). The literature also often focuses on different infections and/or antimicrobial-pathogen combinations and illustrates possible interventions to reduce suboptimal diagnosis, prescription, and consumption.

The widely cited framework for the epidemiology of AMR by Linton (1977) illustrates the role of antimicrobials in human consumption, agriculture (crops, livestock, and aquaculture), and industrial applications.

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[2] See Reygaert (2018), Kapoor et al. (2017), and Munita & Arias (2016) for an extensive review of AMR acquisition pathways and mechanisms.

[3] See Bell et al. (2014) for a systematic review and meta-analysis of the effect of antibiotic consumption on antibiotic resistance during the previous 50 years and van Boeckel et al. (2015), Rushton et al. (2014), and Acar et al. (2012) for a review of antimicrobial use in food animals.

[4] See El Zowalaty et al. (2016) and Grosso et al. (2012) for country case studies and Morgan et al. (2011) for a global review of non-prescription antimicrobial use.

[5] See Calbo et al. (2013) for a review of factors influencing antimicrobial prescriptions.

[6] See Schuts et al. (2016) for a review of the role of antimicrobial stewardship in hospitals in AMR and Stein et al. (2018), Ashraf & Cook (2016), Fridkin et al. (2014), and Hecker et al. (2003) for country case studies.

It also outlines how antimicrobial consumption in households, agriculture, and industries could interact with environmental ecosystems and contaminate the environment. Fernando and McKibbin (2022) extend this framework to highlight industrial applications of antimicrobials that are amenable to economic modeling. Figure 1 presents the modified framework. The framework illustrates the interactions of the economic sectors with soil, freshwater, and marine ecosystems. It does not explicitly show the interactions with the atmosphere due to the assumption that the economic sectors or the other ecosystems could interact with it anywhere within the framework. Unless explicitly added, antimicrobials are always assumed to reach the ecosystems through an economic sector.

Agriculture consists of crops, aquaculture and fisheries, livestock and companion animals, and forestry and wildlife. Antimicrobials (such as Streptomycin, Oxytetracycline, Gentamicin, etc.) are used to prevent diseases in crops (mainly rice, wheat, cereals, vegetables, and fruits) and as an additive to fertilizers.[7] Animal feed and aquaculture use antimicrobials for therapeutic, metaphylaxis, and prophylaxis purposes and growth promotion.[8] The main industrial applications of antimicrobials are food production and packaging, textile manufacturing, sanitizers, paints, coatings, additives, preservatives, and petroleum recovery (in the energy sector). The paints, coatings, additives, and preservatives are then used in secondary applications in manufacturing (such as wood, paper, textiles and cosmetics, plastics, and metal), energy, and services (such as construction, transportation, and utility) sectors, demonstrating the economy-wide consumption of antimicrobials.[9]

Antimicrobial residues from agriculture, industries, and services contaminate ecosystems mainly through solid waste and effluents. The exposure of antimicrobials to the atmosphere via their industrial applications also increases the selective pressure. Interactions among forestry and wildlife with soil and water bodies facilitate resistance gene transfer and the discovery of new hosts. Human interactions with the ecosystems and wildlife, mainly via recreational activities and agricultural and industrial applications, also enable resistance gene transfer.

As Llor and Bjerrum (2014) suggest, health standards and practices, sociocultural characteristics (such as attitudes, beliefs, perceptions, etc.), and socioeconomic background (such as the healthcare financing structure, economic incentives provided by the pharmaceutical industry, and income distribution) of various countries influence the behavior of patients and healthcare practitioners when consuming antimicrobials. The WHO (2015) recommends using the Knowledge-Attitude-Practice (KAP) framework to understand the underlying factors driving antimicrobial consumption in the healthcare sector. Many regional, national, and sub-national studies explore the role of sociocultural and socioeconomic factors above in driving antimicrobial diagnosis, prescription, and consumption practices in various parts of the world.

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[7] See McManus et al. (2002) for a review of antimicrobial use in crops and the implications on human and animal health.
[8] See Sibergeld et al. (2008) for a review of antimicrobials used in animal feed production.
[9] See McEntee (2000) for a compendium of antimicrobials used in industrial applications.

Demography is another crucial factor often highlighted in KAP studies when explaining the variation of antimicrobial consumption across countries. There is also a wide range of studies assessing the demographic characteristics of patients suffering from various infections affected by AMR and the role of demographic factors in the consumption of antimicrobials (e.g., Di et al. 2022; Nugent et al. 2022; Alnasser et al. 2021; Jimah & Ogunseitan 2020; Chen et al. 2019; Schroder et al. 2016). Some common demographic factors considered in these studies are age, gender, marital status, educational level, income, occupation, and place of residence. Although limited, existing time-series studies have also explored the implications of broader demographic trends on AMR. The demographic trends include changes in population growth and density (e.g., Michael et al. 2014; Bruinsma et al. 2003), population aging (e.g., McKee et al. 2021; Yoshikawa 2002), and migration (e.g., Elisabeth et al. 2021; Peters et al. 2020; Abbas et al. 2018; Nellums et al. 2018). Fernando (2023b) reviews the impacts of critical demographic trends on AMR, including the growth changes in population, population aging, population density, and urbanization.

Notably, the studies on population aging point out a two-way relationship with AMR. As the susceptibility to infections increases with age and multimorbidity (the co-occurrence of multiple chronic conditions), the elderly populations require more antimicrobial medicine. Consuming more antimicrobials by the elderly population increases the selective pressure for microorganisms and aggravates AMR. Polypharmacy, or the reliance on multiple antimicrobials to treat various diseases and conditions among older people, enables resistance acquisition among various microorganisms and gives rise to superbugs. Aggravating AMR, in turn, reduces the effectiveness of existing medicine and disproportionately affects the aging population.

An ecological perspective of AMR recognizes the interactions among pathogens and commensal microorganisms and how such interactions would strengthen the acquisition, retention, and increase of AMR (Gonzalez-Zorn & Escuredo 2012; Marshall et al. 2009; Summers 2002). Palecchi et al. (2008) summarize the presence of AMR genes in humans and animals, especially in remote areas of the world, even without sustained exposure to antimicrobials. They emphasize the role of environmental contamination and environmental ecosystems (such as rivers) in transmitting AMR genes. Preventing both the natural (such as the atmosphere, soil, and waterways) and built environment (such as sanitation infrastructure) from becoming reservoirs of antimicrobial genes is thus crucial to preventing the spread of AMR (World Economic Forum 2020; Bengtsson-Palme et al. 2017; Prestinaci et al. 2015).

Environmental pollution also affects AMR. The United Nations Environment Programme (UNEP) (2017) discusses the role of antimicrobial medicine and other antimicrobial chemicals, such as biocides, in promoting AMR. An emerging body of evidence demonstrates how plastic pollution, particularly microplastics in marine ecosystems, increases the surface area for the growth of pathogens, thereby aggravating AMR (Bank 2022; Pham et al. 2021; Moore et al. 2020). A similar strand of studies discusses the role of soil pollution induced by heavy metals (particularly mercury, cadmium, copper, and zinc) in co-selection to aggravate AMR (Seiler & Berendonk 2012; Knapp et al. 2011). UNEP (2022) highlights the importance of effectively managing effluent and waste from pharmaceutical industries, healthcare facilities, crops, livestock, fish processing industries, and other industries extensively using antimicrobials.

With the prevalence of antimicrobial genes in the environment, the movement of humans and live animals, especially across borders, enables the global spread of AMR. In a recent review, Bokhary et al. (2021) found that out of 30,060 resistant isolates evaluated, the most common origin of resistant genes was Asia, accounting for 36 percent of the total isolated genes. Globally, high-income countries are more likely to be recipients of AMR genes. Plaza-Rodriguez et al. (2021) present evidence for AMR genes in migrant birds, and Arnold et al. (2016) emphasize the role of aquatic and terrestrial wildlife trade and transfer in the spread of AMR genes. Collignon et al. (2018) also observe the role of governance in explaining the diversity of AMR across countries. These findings highlight the importance of empowering health systems and policies worldwide and how AMR has become a 'global wicked problem' requiring collective action.

Climate variability is another critical mechanism affecting AMR. Existing studies have found evidence of rising AMR amidst increasing average temperatures (e.g., Kaba et al. 2020 and McGough et al. 2020 in Europe; MacFadden et al. 2018 in the US). Rodriguez-Verdugo et al. (2020) illustrate that the increasing temperature could affect the response of pathogens to antimicrobials at three primary levels: physiological, genetic, and community levels. Gudipati et al. (2020) argue that some factors contributing to climate change, such as land-use changes via deforestation and intensive agricultural practices, have aggravated AMR from disruptions to animal habitats. In addition to the direct implications on AMR, physical climate risks could also indirectly affect AMR through its impacts on the incidence of infections and the resulting demand for antimicrobial consumption. Cavicchioli et al. (2019) explain how host-pathogen interactions change amidst climate variability, prompting water, air, food, and vector-borne diseases to spread faster. Addressing climate change is also likely to be crucial for taming AMR. The existing studies, however, overlook the contribution of extreme climate risks to aggravate AMR. Fernando (2023c) addresses this gap by incorporating a host of indicators representative of both chronic and extreme climate risks to assess the impacts of climate variability on AMR. The chronic climate risks cover gradual changes in temperature, precipitation, and relative humidity, and the extreme climate indicators are illustrative of hot and cold conditions, prolonged extremely dry and wet conditions, and extreme wind speeds.

The extended framework for the epidemiology of AMR in Figure 1 assumes antimicrobial consumption to be the sole driver of AMR. While it is the dominant driver, other factors, such as socioeconomic, sociocultural, demographic, and environmental factors, either directly affect AMR or indirectly affect AMR via antimicrobial consumption. Figure 2, from Fernando and McKibbin (2022), frames all these factors contributing to AMR and antimicrobial consumption. Figure 2 reinforces that in addition to antimicrobial consumption in healthcare, agriculture, and industries, contamination of ecosystems with antimicrobials and other AMR promoters, global and national demographic trends, governance, health system resilience to internal and external health threats, physical climate risks, and openness to travel are essential factors that influence AMR.

2.4 Implications of Antimicrobial Resistance

Most existing studies have emphasized the implications of AMR on human, animal, and environmental (mostly plant) health. The existence of AMR among pathogens was known even before the discovery of antimicrobial medicine, and the development of resistance was expected even during the early stages of antimicrobial medicine development (Davies & Davies 2010). Since the 1950s, when most of today's antimicrobial drugs were developed, the pharmaceutical industry has continued to learn about biochemical reactions and resistance mechanisms of pathogens and improved the medicine to withstand them. However, with the increase in resistance, the antimicrobial drug administration regulations require the use of new antimicrobial medicine sparingly to reduce the exposure of the antimicrobial medicine to pathogens or microorganisms in general. These regulations constrain the pharmaceutical industry from recovering the underlying significant investment costs in antimicrobial medicine by selling the medicine widely and for a more extended period. This has meant that no new classes of antimicrobial medicine have been discovered since the 1980s (Wellcome Trust 2020; Ventola 2015). About 43 traditional antimicrobial drugs are currently in clinical development, and 292 are in pre-clinical development. Of these, only 26 and 60, respectively, focus on the priority pathogens[10] (some of which are multidrug-resistant) (WHO 2022).

WHO (2021a) recognizes AMR as one of the top ten global public health threats. The declining efficacy of antimicrobial drugs is leading to numerous challenges:

- Infections are taking longer to heal and are costlier to treat,
- Some infections cannot be treated with existing antimicrobial medicine,
- Susceptibility to infections and the risk of death from infections are increasing,
- Infections once eradicated in one part of the world are re-emerging or emerging in a different part,
- New infections are emerging, and
- The effectiveness of medical procedures is reduced.

Increasing mortality and morbidity from infections is the main pathway AMR affects humans. In 2014, KPMG and RAND Europe estimated that 700,000 deaths from HIV, Malaria, Tuberculosis, and three priority pathogens (*Staphylococcus aureus, Escherichia coli, and Klebsiella pneumoniae*) were attributable to AMR and that the deaths could reach 10 million per annum by 2050 (O'Neill 2016). Cecchini et al. (2015) illustrated that the likelihood of dying from an infection could increase three-fold in G7 countries if the infection does not respond to antimicrobial medicine. The Centre for Disease Control (2019) estimated that two million infections in 2017 were attributable to AMR in the US alone, leading to at least 23,000 deaths. The European Centre for Diseases (ECDC) (2009) estimated 25,000 AMR-attributable deaths annually in Europe. The latest global estimate on AMR-attributable deaths is in the *Global Burden of Bacterial Antimicrobial Resistance* study (hereafter referred to as the GRAM study) for 2019, released in 2022. According to the

[10] See Tacconelli et al. (2018) for the list of WHO-priority antibiotic-resistant bacteria.

study, 1.27 million lives lost in 2019 are attributable to 23 pathogens resistant to existing antimicrobial medicine (Murray et al. 2022).

A one-health framework recognizes human, animal, and plant (environmental) health as interconnected components when achieving optimal planetary health. Within a one-health framework, as Morel et al. (2020) point out, direct and indirect costs of AMR could be identified. The direct costs of AMR encompass out-of-pocket expenditures (from patients or farmers), treatment costs borne by the health services, treatment costs for patients for long-term complications, costs of environmental decontamination, AMR surveillance, training for healthcare and other relevant professionals, and legal and insurance costs. The indirect costs include opportunity costs of morbidity and mortality among the labor force, public healthcare expenditure, healthcare resources, research and development costs, loss of livestock productivity, and additional burden to consumers from reduced production. Recognizing the direct and indirect costs of AMR within a one-health framework demonstrates the relevance of an economy-wide response to AMR and how implications on one component of the triad could spill over to the other components.

Alternatively, the burden of AMR could also be evaluated at multiple tiers: patient, healthcare system, and the economy or society (Dadgostar 2019; Wozniak et al. 2019; Shrestha et al. 2018). Health economic approaches have been widely utilized to assess the burden of AMR at the first two levels. The costs considered include hospital occupancy, use of medicine, laboratory services and medical procedures, and human resource utilization. The focus has been on the loss of productivity and healthcare expenditure at the societal or economic level.

Several studies have estimated the economic burden of AMR. KPMG (2014) and RAND Europe (2014) project that the cumulative economic burden of AMR could reach $US100 trillion by 2050. The studies consider HIV, Malaria, Tuberculosis, and three priority pathogens (*Staphylococcus aureus, Escherichia coli, and Klebsiella pneumoniae*), as well as their effects on morbidity and mortality among employees and government expenditure on healthcare. Using a similar methodology, Ahmed et al. (2017) estimate the burden of AMR to reach $US85 trillion between 2015 and 2050. The Organization for Economic Co-operation and Development (OECD) (2018) estimates that in 33 European countries alone, the direct annual healthcare cost associated with AMR could be as high as $US3.5 billion. The World Bank (2017), considering implications on livestock in addition to mortality and morbidity among humans due to AMR, estimates that under a low-AMR scenario, global annual GDP losses could exceed $US1 trillion after 2030 and reach $US2 trillion by 2050. Under a high-AMR scenario, the yearly GDP losses could reach $US3.4 trillion by 2030 and $US6.1 trillion by 2050. WHO (2021b) also demonstrates the disproportionate burden of AMR on developing countries and how an additional 28.3 million people could be pushed into poverty in these countries. Progress toward achieving at least seven Sustainable Development Goals (SDGs) is directly affected, and about six additional SDGs could be indirectly affected by AMR. Therefore, containing AMR is central to both sustainable economic growth and development.

2.5 Modeling the Economics of Antimicrobial Resistance

The methodologies assessing the economic burden of AMR have evolved. Early studies assessing the economic impacts of AMR extended the fundamental health economic approaches, such as cost minimization, cost-effectiveness, cost-benefit, or cost-utility analyses, to evaluate the additional burden of infections affected by AMR (Coast et al. 1996; Holmberg et al. 1987; and Liss & Batchelor 1987). With the growing appreciation of the significance of AMR as a problem beyond infections, three main strands of recent literature assessing the economic impacts of AMR can be identified. The first strand considers the burden of patients due to mortality and morbidity from AMR-related infections. The second strand assesses the burden on the healthcare system due to secondary AMR-related infections in patients and extended hospital care induced by infections affected by AMR. These studies mainly utilize regression analysis and significance tests (Naylor et al. 2016). The third strand assesses the economy-wide impacts of AMR. These studies mostly use partial or computable generable equilibrium models.

One of the earliest modeling attempts focused on assessing the implications of Methicillin-Resistant *Staphylococcus aureus* (MRSA) in Britain (Smith et al. 2005). The closed-economy Computable General Equilibrium (CGE) Model featured ten sectors, a representative firm in each sector, a representative consumer, a bank, and a government. AMR was introduced as a shock on labor supply, sectoral productivity, and healthcare delivery costs. The simulations demonstrated the implications of AMR on macroeconomic aggregates, such as GDP, investment, savings, consumption, employment, and welfare. The application of the GLOBE model by Keogh-Brown et al. (2009) extended closed-economy CGE modeling to the global economy. The approach involved evolving antibiotic resistance as a function of prescription and calculating morbidity and mortality estimates due to pathogens developing antibiotic resistance. The study explored the impacts on savings, trade, and exchange rates and evaluated the potential of interventions to reduce antibiotic consumption and optimize antibiotic prescriptions.

Several other studies have also used economic modeling to estimate the economic burden of AMR. The first systematic review of the economic implications arising from the priority pathogens and infections acquiring resistance to existing antimicrobials against them was commissioned in 2014 by the Prime Minister of the UK. The review, chaired by Jim O'Neill and completed in 2016, included two economic studies conducted by KPMG and RAND Europe in 2014. KPMG (2014) utilized a partial general equilibrium model where total factor productivity (TFP) was modeled as a function of five factors: macroeconomic stability, the openness of the economy, the quality of infrastructure, the strength of public institutions, and human capital. The impacts on TFP were combined with the effects modeled on the labor force due to augmented mortality and morbidity related to AMR and capital-income ratio to derive the implications on the global economy. The study was also supplemented with an analysis of financial impacts at the regional level emanating from public health expenditure spent on combating AMR. The CGE model used by RAND Europe (2014) had shocks on population growth and labor efficiency due to the mortality and morbidity impacts of AMR.

Ahmed et al. (2017) used the GLOBE-Dyn model, the recursive dynamic version of the GLOBE model, to assess the global macroeconomic impacts of AMR due to the same priority pathogens and infections covered in the AMR Review by O'Neill et al. (2016). Extending the KPMG (2014) and RAND Europe (2014) studies, the reduction in livestock production and global restrictions on livestock trade were considered. The World Bank (2017) also estimated the AMR implications on the labor force and livestock under two AMR evolution scenarios. The OECD (2018) used its Strategic Public Health Planning for AMR (SPHeP-AMR) model, a health economic model with an extensive focus on the evolution of AMR and the epidemiology of the infections affected by AMR. The study also covered eight pathogens and considered the implications of AMR on medical procedures and infections.

2.6 Challenges for Modeling the Economics of Antimicrobial Resistance

The existing studies provide potential estimates of the economic burden of AMR. However, Hillock et al. (2022) outline several limitations that future studies should address. Firstly, designing reliable future AMR evolution scenarios is fundamental to modeling. Such efforts should consider the transmission dynamics of AMR within a one-health framework. Secondly, the factors affecting AMR via antimicrobial consumption must be better understood. The existing studies do not demonstrate the role of behavioral and social factors, such as patient compliance with infection prevention and antimicrobial treatment measures. Thirdly, they also emphasize obtaining country-specific estimates to capture the heterogeneity across various parts of the world and increase transparency when reporting modeling methodologies and results.

As Fernando and McKibbin (2022) point out, another major challenge in assessing the economic implications of AMR lies in the lack of antimicrobial consumption and resistance data. There is no comprehensive accounting of the economy-wide production of antimicrobials, particularly antimicrobial medicines. Even the best available data on antimicrobial medicine consumption, which comes from the *Global Antibiotic Consumption and Usage in Humans* study by the Institute for Health Metrics and Evaluation (IHME) (Browne et al. 2021), is likely to underestimate actual antimicrobial medicine consumption because of the prevalence of informal antimicrobial production, especially in developing countries. Although proprietary higher-quality data on antimicrobial sales are available from pharmaceutical companies and private entities that collect such data, the data are not affordable for most researchers. Although the trade data from the United Nations Comtrade Database could help identify pharmaceutical sales across countries, disaggregating the data for antimicrobial classes remains challenging. The availability of global granular data on the use of antimicrobial chemicals in agriculture and industries is even rarer.

Global surveillance of AMR is essential to overcoming the data challenges pertaining to AMR. WHO launched the Global Antimicrobial Resistance and Use Surveillance System (GLASS) in 2015. GLASS provides a standardized approach to collecting, analyzing, interpreting, and sharing data on AMR. Before that, only a handful of high-income countries (including Europe and the US) had extensive national or regional surveillance mechanisms. Although the data on AMR rates related to agriculture and the environment is even more limited than in healthcare, GLASS is expected to gradually incorporate those sectors into surveillance. Currently, the GRAM study (Murray et al. 2022) is the most reliable source for AMR data. It provides the regional AMR rates for 88 drug-pathogen combinations covering 23 pathogens and 12 infection groups in 2019. The study also provides a consistent framework to map the consumption of antimicrobial medicine to infections, which was a challenge until the study was published.

3 METHODOLOGY

3.1 Economics of Antimicrobial Resistance within a Stylized Economy Interacting with the Natural Environment

Figure 3[11] illustrates the interactions among economic agents within a stylized economy that interacts with the broader environment.[12] The environment mainly consists of four ecosystems: the atmosphere, marine ecosystems, freshwater ecosystems, and soil. Plants, animals, and microorganisms in the environment interact with households and firms in the economy. In addition to interacting with ecosystems and living beings, firms rely on the environment for energy. The activities of households and firms generate solid waste, effluents, and emissions, which are passed on to the environment.

The domestic economy has four main agents: households, firms, the government, and asset markets. The domestic economy interacts with foreign economies via an external sector. Households provide labor to the firms and receive wages in return. Households rely on firms for consumption and pay for goods and services using their income and assets, both physical and financial. Households also pay taxes to the government and receive subsidies and public goods from the government. The excess income is accrued into assets via savings. When constrained for liquidity, households could borrow from the asset markets.

Firms utilize household labor, capital (debt and equity) from asset markets, and imports from the external sector when producing goods and services for households, the government, and exports. Firms pay wages to households, capital rents to asset markets, and taxes to the government. Firms could also receive investments from the external sector as foreign direct investments and invest in the asset markets or conduct foreign direct investments.

The government provides public goods and transfers and subsidies to households and firms. It also purchases goods and services from firms. Government expenditure is financed with taxes from households and firms, public bonds issued to asset markets, and foreign aid from the external sector.

The asset markets combine savings from households, investments from firms and the government, and foreign portfolio investments from the external sector. The asset markets could lend to households and the government and invest in or lend to firms.

[11] Developed by the authors with reference to WHO (2009) and Woolhouse et al. (2015).
[12] The economic and environmental interactions are much more complex than illustrated. Thus, the illustration is not exhaustive of all plausible interactions. Even the interactions of households, microorganisms, animals, and plants with the atmosphere, soil, and water are avoided to reduce the complexity of the illustration.

The economy is assumed to interact with the ecosystems only through households and firms. The sectors illustrated in Figure 1 are the main channels of antimicrobial consumption by households and firms. Households interact with microorganisms, animals, and plants when consuming goods and services firms provide. Microorganisms, animals, and plants also interact among themselves and with the ecosystems (although not explicitly illustrated in Figure 3 for simplicity). Firms interact with the ecosystems via resource extractions, emissions, and disposal of solid waste and effluents. The ecosystems also interact among themselves.

3.2 The G-Cubed Model

The framework in Figure 3 is applied to a global intertemporal general equilibrium model with heterogeneous agents called the G-Cubed model to assess the global economic impacts of AMR. This model is a hybrid of Dynamic Stochastic General Equilibrium (DSGE) models and Computable General Equilibrium (CGE) models developed by Warwick McKibbin and Peter Wilcoxen (2013, 1999). The 6G version of the G-Cubed model used in this paper focuses on the G20 members and is detailed in McKibbin and Triggs (2018). The 6G version features six sectors and 24 countries and regions.[13] Table 1 presents all the regions and sectors in the model. Some data inputs include the input-output tables from the Global Trade Analysis Project (GTAP) Database (Aguiar et al. 2019), which enables differentiating sectors by country of production within a DSGE framework. Firms in each sector in each country produce goods using the primary factor inputs of capital (K) and labor (L) as well as the intermediate inputs of energy (E) and materials (M). These linkages exist both within and across countries. Several key features of the standard G-Cubed model are highlighted below.

First, the model accounts for stocks and flows of physical and financial assets. For example, budget deficits accumulate into government debt, and current account deficits accumulate into foreign debt. The model imposes an intertemporal budget constraint on all households, firms, governments, and countries. Thus, a long-run stock equilibrium is obtained through the adjustment of asset prices, such as the interest rate for government fiscal positions or real exchange rates for the balance of payments. However, the adjustment towards the long-run equilibrium of each economy can be slow, occurring over much of a century.

Second, firms and households in the model must use money issued by central banks for all transactions. Thus, central banks in the model set short-term nominal interest rates to target macroeconomic outcomes (such as inflation, unemployment, exchange rates, etc.) based on Henderson-McKibbin-Taylor monetary rules (Henderson & McKibbin 1993; Taylor 1993). These rules are designed to approximate actual monetary regimes in each country or region in the model. These monetary rules tie down the long-run inflation rates in each country and allow short-term policy adjustments to even out fluctuations in the real economy.

Third, nominal wages are sticky and adjust over time based on country-specific labor contracting assumptions. Firms hire labor in each sector up to the point that the marginal product of labor equals the real wage defined in terms of the output price level of that sector. Any excess labor enters the unemployed pool of

[13] Supplementary Annexures 1 and 2 present the mapping of GTAP regions and sectors to the G-Cubed model, respectively.

workers. Unemployment or excess demand for labor causes the nominal wage to adjust to clear the labor market in the long run. In the short run, unemployment can arise due to structural supply shocks or changes in aggregate demand in the economy.

Fourth, rigidities prevent the economy from moving quickly from one equilibrium to another. These rigidities include nominal stickiness caused by wage rigidities and investment adjustment costs by firms with physical capital being sector-specific in the short run. The adjustment path is also affected by a lack of complete foresight in expectation formation by monetary and fiscal authorities following particular monetary and fiscal rules. Short-run adjustment to economic shocks can differ significantly from long-run equilibrium outcomes. Focusing on short-run rigidities is essential for assessing the impact over the first decades of a major shock.

Fifth, the model features heterogeneous households and firms. Firms are modeled separately within each sector. There are two types of consumers in the economy and two types of firms within each sector in each country/region. One group of consumers and firms base their decisions on forward-looking expectations using the solution of the model in future periods to form those expectations. The other group follows simple rules of thumb, which are optimal in the long run but do not update information period by period.

Table 1: Regions in the G-Cubed Model (GGG6G_v176)

	Region Code	Description
1	ARG	Argentina
2	AUS	Australia
3	BRA	Brazil
4	CAN	Canada
5	CHN	China
6	DEU	Germany
7	EUZ	Rest of Eurozone
8	FRA	France
9	GBR	United Kingdom
10	IDN	Indonesia
11	IND	India
12	ITA	Italy
13	JPN	Japan
14	KOR	Korea
15	MEX	Mexico
16	OAS	Rest of Asia
17	OEC	Rest of the OECD Countries
18	OPC	Other Oil-Exporting Developing Countries
19	ROW	Rest of the World
20	RUS	Russia
21	SAU	Saudi Arabia
22	TUR	Turkey
23	USA	United States
24	ZAF	South Africa

Source: The G-Cubed Model (GGG6G_v176).

3.3 Baseline

Given the historical experiences and assumptions about future drivers of economic growth, the G-Cubed model baseline projects how the economies would grow without AMR. The AMR scenarios are assessed against this baseline. The baseline starts in 2018 and is projected out to 2100. The year 2018 corresponds to the latest year for which a comprehensive data collection is available to calibrate the model. The region-specific sectoral production growth rates are a function of labor force growth and sectoral labor productivity growth, as well as endogenous capital accumulation in each sector in the respective countries. These factors drive the overall baseline economic growth.

The potential labor force growth rates are derived from the working-age population projections from the United Nations Population Prospects study (UN 2022). The sectoral labor productivity growth rates (labor-augmenting technological progress) are determined using a Barro-style catch-up model, which assumes that an individual sector's average annual catch-up rate to the worldwide frontier would close the gap by two percent per year. The initial sectoral productivity data are obtained from the Groningen Growth and Development database (Timmer et al. 2015), and the corresponding sectors in the US are assumed to form the frontier. The baseline also varies the catch-up rates of different economies, given the most recent growth experiences.

Given the above approach to baseline construction, we assume that the impacts of AMR are not in the baseline. Also, the baseline does not include the interaction between demographic change and AMR evolution (as estimated in Fernando 2023b) and AMR and climate change (as estimated in Fernando 2023c). The shocks under the AMR scenarios are, hence, introduced as unanticipated disturbances to the G-Cubed model baseline, and the simulation results indicate the current effects of AMR on economic activity and how these effects adjust relative to the baseline over time, given the shocks imposed. For example, the results for 2020 in each scenario will show the effects of AMR in 2020 from AMR in 2020, as well as the impact of expectations of the future impacts of AMR under each alternative scenario.

3.4 AMR Scenarios and Shocks

Fernando and McKibbin (2022) illustrate six possible shocks or pathways via which AMR could impact the stylized economy, discussed in Section 3.1. These pathways include (1) labor productivity changes due to morbidity and mortality from AMR-related diseases, (2) agriculture productivity changes and their spillovers into other sectors, (3) changes in consumption patterns, (4) changes in household wealth, (5) changes in country and sector risk premia and (6) changes in government expenditure to treat and prevent additional disease incidence from AMR. Except for country risk premium changes, the shocks could be evaluated in both DSGE and CGE models. Substantial characterization of financial markets is necessary to assess the fifth shock and is thus amenable only to DSGE models. This paper incorporates four shocks (1,2, 5, and

6)[14] and endogenizes the responses of 3 and 4 within the model. The following subsections explain how the existing data is used to construct these shocks to be evaluated within the G-Cubed model.

We design six scenarios varying the assumptions about the evolution of the shocks. The scenarios are summarized in Table 2. When designing the labor productivity variations under the scenarios, the AMR interactions with other existing broader socioeconomic challenges, such as climate change (Fernando 2023c) and demographic trends (Fernando 2023b), are considered. When formulating mortality and morbidity shocks, we project the variation in diseases as a function of population growth projections and the variation in AMR rates as a function of demographic trends and physical climate risks. For demographic trends, the Medium Variant Scenario of the World Population Projections (MVPP) (UN 2022) is used, and for climate risks, the Shared Socioeconomic Pathways (SSP) 2-4.5 is used.

The shocks to agriculture productivity are formulated only as a gradual rise of the initial rates in 2020 to reach 20 and 40 percent increases by 2100, which are introduced in Scenarios 1 and 3, respectively. Scenario 2 has the same agriculture productivity shocks as Scenario 1, and Scenarios 4, 5, and 6 have the same agriculture productivity shocks as Scenario 3. Changes in financial risks are introduced in Scenario 5, and a plausible change in government spending is introduced in Scenario 6.

Table 2: Design Assumptions for AMR Scenarios

Scenario	Assumptions
1	**Labor Productivity:** Diseases evolve as a function of MVPP, and resistance rates remain constant at 2019 rates*. **Agriculture Productivity:** Initial change in 2020** increases by 20 percent by 2100.
2	**Labor Productivity:** Diseases evolve as a function of MVPP, and resistance rates evolve as a function of MVPP from 2020*. **Agriculture Productivity:** Initial change in 2020** increases by 20 percent by 2100.
3	**Labor Productivity:** Diseases evolve as a function of MVPP, and resistance rates evolve as a function of MVPP from 2020. **Agriculture Productivity:** Initial change in 2020** increases by 40 percent by 2100.
4	**Same as Scenario 3 with Climate Risks.** Diseases evolve as a function of MVPP, and resistance rates evolve as a function of MVPP and SSP 2-4.5*** from 2020.
5	**Same as Scenario 4 with Financial Risks**. The initial changes in Country Risk Premia in 2020 (approximated using 10 percent of those due to COVID-19 for 2020 from Fernando and McKibbin [2021]) rise by 20 percent annually until 2100.
6	**Same as Scenario 5 with Government Expenditure Response:** The initial changes in Government Expenditure in 2020 (approximated using 10 percent of COVID-19-related Government Expenditure Rate for 2020 from Fernando and McKibbin [2021]) rise by 20 percent by 2100.

*MVPP is the Medium Variant Population Projections. The resistance rates for 2019 are from Murray et al. (2022). **Agriculture Productivity Impact for 2000 is from Laxminarayan et al. (2015).
Source: Constructed by the Authors.

[14] Currently, empirical estimates on how AMR could exogenously change consumption preferences within the healthcare, agriculture, and other industrial sectors are absent. Similarly, empirical research is absent on how AMR could exogenously affect intertemporal risk preferences (which change the subjective discount rate at which households discount their future income streams). Thus, this study does not incorporate the fourth and fifth impact pathways. Future modeling studies could incorporate these pathways as new research emerges.

3.4.1 Shocks to Labor Productivity

A reduction in labor productivity due to morbidity and mortality from AMR-related diseases is a dominant pathway via which AMR affects the economy. Amidst a reduction in the effectiveness of antimicrobial medicine and medical procedures relying on antimicrobial drugs, the susceptibility to diseases rises, the diseases take longer to heal, and the probability of death from the diseases increases. Consequently, the quantity and quality of existing and potential labor force available for productive economic activities are reduced. The burden of the dependent population groups (such as children and retired workers) suffering from AMR-related diseases further diminishes the productivity of the working-age population group. Various economic sectors would be differently affected depending on the role of labor inputs in their production processes.

This paper considers the economic shocks on labor productivity due to 20 AMR-related diseases from the *Global Burden of Diseases* study (hereafter referred to as the GBD study) (IHME 2020b). We map these diseases onto 12 infection groups from the GRAM study (Murray et al. 2022), as Supplementary Annexure 3 shows. The AMR rates affecting these infection groups due to the interactions between 23 bacterial pathogens and 18 antimicrobial drugs (leading to 88 pathogen-drug combinations) are available from the GRAM study. Supplementary Annexures 4 and 5 present the pathogens and the antimicrobial drugs covered in the GRAM study. Supplementary Annexure 6 summarizes the 88 drug-pathogen combinations.

We employ a three-tier approach in this paper to obtain the morbidity and mortality outcomes of AMR-related diseases, which involves (1) modeling the evolution of AMR as a function of demographic trends and physical climate risks, (2) modeling the evolution of AMR-related diseases, and (3) obtaining the AMR-related changes in morbidity and mortality.

1. Modeling the Evolution of AMR

We incorporate the estimates from two accompanying studies (Fernando 2023b, c) to model the AMR evolution as a function of antimicrobial consumption, GDP per capita growth, demographic trends[15], and physical climate risks.[16] As Section 2.3 discusses, this approach places AMR within the context of broader global natural and socioeconomic challenges and the widely spoken driver of AMR: antimicrobial consumption.

The estimates from Fernando (2023b, c) for the responsiveness of AMR to demographic trends and physical climate risks, alongside antimicrobial consumption and GDP per capita growth, are presented in Supplementary Annexures 7A to 7P.[17] Due to the lack of global time-series data on antimicrobial resistance

[15] The demographic trends are the growth in population, population aging, population density, and urbanization.
[16] The physical climate risks account for both chronic and extreme risks. The chronic risks include gradual changes in temperature, precipitation, and relative humidity. The extreme risks include extremely warm and cold conditions during the day and night, extremely dry and wet conditions, and extremely windy conditions.
[17] Fernando (2023b) discusses the demographic indicators, presents a framework for understanding the impacts of demographic trends on AMR, and discusses their historical and projected variations under alternative demographic scenarios, and the historical and projected variation of AMR. Fernando (2023c) discusses the physical climate risk

and consumption, the estimates have been obtained from a sample of seven pathogens[18] from 34 countries.[19] As AMR is a global phenomenon that could rapidly spread worldwide, we assume that the estimates from the above sample apply to the whole world when using them in this paper. For those pathogens and drugs not covered in the above sample, we use the average of the estimates or those of the virologically closest pathogen-drug combination.

We then project the growth in population and population aging following Fernando (2023b) under the Medium Variant Scenario of the World Population Projections (UN 2022) and the physical climate risks following Fernando (2023a, c) under SSP 2-4.5, which is one of the climate scenarios used by the Intergovernmental Panel on Climate Change (IPCC).

This paper, however, does not use empirical estimates for antimicrobial consumption and GDP per capita growth rates when modeling the evolution of AMR for two main reasons. Firstly, the lack of comprehensive data on global antimicrobial prescription and consumption patterns for AMR-related diseases prevents us from independently projecting antimicrobial consumption. Secondly, the growth assumptions in the G-Cubed model baseline apply to all the scenarios. Hence, the effect of GDP per capita growth on AMR rates does not change across the scenarios compared to the baseline.

We project the AMR evolution as a function of the growth in population, population aging, and physical climate risks for 15 UN regions. The projected growth rates of population, population aging, physical climate risks, and AMR rates across the UN regions are presented in the online dashboard. The projected AMR rates are for the Years of Life Lost due to Premature Mortality (YLLs) and Disability (YLDs)[20] under the 12 GRAM infection groups.

2. Modeling the Evolution of AMR-related Diseases

We estimate the evolution of AMR-related diseases as a function of the growth in population, GDP, and the Sociodemographic Index.[21] The Sociodemographic Index (IHME 2020a) is a representative indicator of the socioeconomic development of a country as it combines information on the economy, education,

indicators, how they affect AMR, their historical and projected variations, and the historical variation of AMR under Shared Socioeconomic Pathways.

[18] The seven pathogens are *Acinetobacter spp., Enterococcus faecalis, Enterococcus faecium, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, and Streptococcus pneumoniae* (ECDC 2022).

[19] The 34 countries under the purview of ECDC are Austria, Belgium, Bulgaria, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the UK (ECDC 2022).

[20] DALYs for a specific cause are calculated as the sum of the years of life lost due to premature mortality (YLLs) from that cause and the years of healthy life lost due to disability (YLDs) for people living in states of less than good health resulting from the specific cause (WHO 2023).

[21] This estimation strategy abstracts from the conventional approach to epidemiological modeling (widely known as SIR [Susceptible-Infected-Recovered] models), as the information on the Susceptible, Infected, and Recovered portions of the populations is unavailable. Such exercises, however, have been conducted at more granular levels, such as at the hospital/community level, and could also incorporate AMR rates to identify the impact of AMR on the epidemiology of the diseases (see Niewiadomska et al. 2019 and Birkegard et al. 2018 for reviews of mathematical modeling with AMR.). Lack of time-series data on global AMR rates and a more granular breakdown of diseases (for subcategories and by the pathogens causing the diseases) constrain our ability to incorporate AMR rates into the epidemiological regressions.

and fertility of the country. We estimate the responsiveness of YLDs and YLLs to the growth in population, GDP, and the Sociodemographic Index, using the GBD data (IHME 2020b) for 204 countries from 1990 to 2019 for the 20 AMR-related diseases in Supplementary Annexure 3. Supplementary Annexures 8A and 8B summarize the estimates. We then project the evolution of diseases under the Medium Variant Scenario for the 204 countries spread across the 15 UN regions for the 20 AMR-related diseases. The online dashboard presents the historical and projected total YLDs and YLLs from AMR-related diseases in the 15 UN regions.

3. Obtaining the AMR-related Changes in Morbidity and Mortality

We apply the AMR growth rates to the 2019 AMR rates from the GRAM study to obtain the projected AMR rates across the scenarios following the assumptions in Table 2. In Scenario 4, where the demographic trends interact with physical climate risks, the arithmetic summation of the AMR growth rates is used, assuming complete independence between the two phenomena. We apply the AMR rates for a given scenario to the disease projections to estimate the AMR-attributable YLDs and YLLs for the 204 countries. We obtain the total AMR-attributable morbidity and mortality outcomes as a proportion of the working population for the 24 regions in the G-Cubed model in Table 1. The online dashboard summarizes the labor productivity shocks across the regions under the scenarios.

3.4.2 Shocks to Agriculture Productivity

The impacts on sectoral productivity and spillovers into other sectors relying on them are critical AMR impact pathways. When the effectiveness of antimicrobials used in agriculture and industrial applications declines, the productivity of those sectors reduces. The sectors that rely on those sectors will also subsequently be affected due to production linkages within the G-Cubed model. Figure 1 illustrates antimicrobial consumption in different economic sectors. Although subnational and national studies exploring antimicrobial consumption in different sectors exist, global antimicrobial consumption statistics/studies in different sectors are limited. As livestock substantially consumes antimicrobials, antimicrobial consumption patterns in livestock and their impact on livestock productivity are better understood.

This paper relies on estimates from Laxminarayan et al. (2015), who estimated the impact of antimicrobials on livestock productivity for 1980 and 2000. They specifically estimate the annual meat production loss for 194 countries if antimicrobials were to be withdrawn from the livestock sector. We use their estimates for 2000 as the initial reduction in productivity in 2020. In Scenarios 1 and 2, the initial estimates gradually decrease by 20 percent by 2100. In Scenarios 3, 4, 5, and 6, the initial estimates gradually decrease by 40 percent by 2100. The online dashboard summarizes the livestock productivity reductions due to livestock exposure to AMR across the regions in the G-Cubed model under the scenarios.

3.4.3 Shocks to Country Risk Premia

Asset markets, particularly financial markets, respond to changes in relative systematic risks among countries and unsystematic risks among the sectors. When faced with a global threat that affects different countries and sectors differently, investor preferences change. These changes would be reflected in financial markets by rebalancing investment portfolios. COVID-19 exemplifies such changes in financial markets (Jabeen et al. 2022; Bradley & Stumpner 2021). As AMR affects specific sectors directly due to their reliance on antimicrobials (such as agriculture), labor (such as services), and other sectors indirectly through production linkages with affected sectors, investor preferences for sectors could change. As the systematic risk of AMR differs across countries depending on the differential exposure of countries to factors driving AMR (discussed in Section 2.3), investor preferences for countries could also change. General equilibrium models with an illustration of financial markets could demonstrate the economic consequences of AMR due to changes in country and sector risk premia.[22]

This paper illustrates the economic consequences of country risk premia changes due to investors pricing in AMR risks to their investment evaluations. The country risk premium change due to COVID-19 in the US, as estimated by Fernando and McKibbin (2021), is used to approximate the initial country risk premium change in 2020. In Scenario 5, the initial estimates in 2020 gradually increase to reach a 20 percent increase by 2100. We use the AMR Preparedness Index compiled by the Global Coalition on Aging (2021) to derive the initial relative changes in risk premia across the other regions in the G-Cubed model due to exposure to AMR risks.

The AMR Preparedness Index scores 11 countries[23], which are within the regions in the G-Cubed model as standalone countries, across seven dimensions: (1) prevalence of a national AMR strategy and policy commitment; (2) government support for innovation, (3) appropriate and responsible use of antimicrobials; (4) collaborative environment; (5) awareness and prevention; (6) access to both older and novel antimicrobials, and (7) lifecycle management of antimicrobials. We use the aggregated score for 2021 relative to the US to determine the relative vulnerability of each country to AMR. We use those of our closest regional peers for regions without scores. The online dashboard summarizes the risk premia changes in Scenario 5 across the regions.

3.4.4 Shocks to Government Expenditure

The fiscal burden of managing AMR risks is another significant source of the economic impacts of AMR. The fiscal burden of AMR would far exceed the incremental cost of treating additional diseases affected by AMR. WHO (2015) guidance on national action plans for AMR suggests strategies such as strengthening national AMR surveillance, strengthening infection prevention and control, and improving awareness of the development of AMR and rational use of antimicrobials. However, national action plans are still being developed in most countries, and specific estimates of the fiscal expenditure allocated for managing AMR are absent.

[22] See McKibbin and Fernando (2023, 2021, 2020) for applying changes in country and sector risk premia when modeling the macroeconomic consequences of COVID-19.
[23] Specifically, Brazil, Canada, China, France, Germany, India, Italy, Japan, South Korea, the UK, and the US.

This paper uses the estimates from the International Monetary Fund (IMF) (2020) for the government health expenditure to manage the COVID-19 pandemic in 2020 to approximate the fiscal burden of AMR, i.e., the additional government spending required to deal with the evolution of AMR. We adjust these figures in 2020 to be 10 percent of the government spending under COVID-19. While arbitrary, this figure is a plausible proxy for the cost of dealing with AMR. Following the procedure in Fernando and McKibbin (2021), we summarize the estimates for the regions in the G-Cubed model. These estimates also account for the pandemic potential of AMR in addition to incremental fiscal expenditure for AMR-related disease management. In Scenario 6, the initial estimates in 2020 gradually increase to reach a 20 percent increase by 2100. The spending is assumed to be financed by increasing the fiscal deficit in each economy and, thus, by issuing government debt. A lump sum tax equal to the incremental interest costs of the additional debt is imposed to ensure long-run fiscal sustainability. The online dashboard summarizes the government expenditure changes in Scenario 6 across the regions in the G-Cubed model.

4 RESULTS

Section 4 discusses the global economic consequences of AMR. While the G-Cubed model produces results for a wide range of both real and nominal economic variables and sector results for key variables, Section 4 focuses on a few selected real variables, which include real GDP (Section 4.1), consumption and investment (Section 4.2), exports and imports (Section 4.3), and sectoral output (Section 4.4). Figures 4 to 14 present the short-, medium--, and long-term macroeconomic and sectoral results for the first four scenarios. The online dashboard presents the dynamic macroeconomic and sectoral results for all the scenarios and decomposition of the real GDP for its constituents, the sectoral decomposition of consumption, investment, exports, and imports, and results for real interest rates, current account balance, real exchange rate, trade balance, inflation, and employment.

The results are initially driven by the supply-side effects of AMR on labor and livestock productivity. These ultimate effects are also determined by the reactions of economic agents, particularly forward-looking households and firms, and monetary and fiscal authorities. General equilibrium effects, mainly arising from the income and price effects (whereby regions dominant in certain sectors could influence the global prices and subsequent changes in terms of trade and consumption patterns across the world), due to changes in production patterns across the sectors in the world, also affect the results. These results are intended to be illustrative and are conditional on the model used and how the shocks have been designed.

The results are discussed relative to a baseline. As mentioned in Section 3.3, the G-Cubed model baseline does not assume any AMR shocks. Therefore, the results should be interpreted as the economic consequences of unanticipated AMR shocks under the alternative AMR scenarios.

4.1 Changes in Real GDP

When assessing the global economic impacts of AMR, given the sectoral disaggregation in the G-Cubed model, productivity shocks are introduced at the sectoral level. Given the ability to introduce sectoral shocks from the supply side of each economy, the ultimate real GDP changes are the cumulative effect of the sectoral production changes. From the demand side of the economy, the ultimate real GDP changes are the cumulative effect of the changes in consumption, investment, government expenditure, and expenditure on net exports.

The differences in the results across countries have several sources. The differences can be traced to the different sizes of shocks and the economic structures through which the shocks are transmitted within the model. The size of shocks is driven by several factors, including the different reliance on agriculture in each economy, the demographic structure of the population in each economy, and the differential impact of climate shocks on productivity, risk, and the response of governments, which are varied under each scenario. The economic structure of each economy is determined by the economic linkages across sectors within economies and the different international trade linkages across economies.

For example, Japan stands out as experiencing larger economic losses in each scenario compared to other advanced economies. This difference is notable when the climate shocks are considered in Scenario 4. This result might be surprising given that agriculture is a small part of the Japanese economy and the initial shocks to Japan are smaller than in many countries. The main difference is that Japan is a major producer and exporter of durable manufacturing goods (both in size and relative to the scale of other economic sectors). These durable goods are a key sector that feeds into physical investment in many sectors in many economies. To the extent that private investment falls in a scenario, the demand for durable goods tends to fall, reducing the demand for Japanese durable goods that would have fed into future investment growth. There is a substantial decline in private investment (relative to baseline) in the climate shocks we explore. Thus, the spillovers to the durable goods sector globally are a key channel for the transmission of the shocks from AMR, although AMR only has a small direct effect on that sector.

Table 3 summarizes the cumulative losses the regions experience across the scenarios from 2021 to 2050 in $US billions. These figures are estimated as cumulative losses over 30 years. For example, the outcome of a cumulative GDP loss for Australia of $US293 billion under Scenario 1 would be approximately $US10 billion on average per year from 2021.

China, India, Japan, Other Oil-Exporting Developing Countries, the Rest of the World, and the US experience the highest cumulative losses across the first four scenarios. These illustrate how highly populated regions could be disproportionately vulnerable to the health risks of AMR. The results for Scenario 1 are consistent with those in earlier studies surveyed in Section 2.4. Globally, the losses increase as the gravity of AMR risks increases, and allowing for the interaction of demographic factors and climate change further increases the estimated costs of AMR. The losses could exceed $US32, 89, 90, and 268 trillion over 30 years under Scenarios 1, 2, 3, and 4, respectively.

The global losses are further aggravated if the financial markets price in AMR risks, as illustrated by the results for Scenario 5. Interestingly, the change in relative risks across countries can reduce the GDP losses for countries with better health standards than the rest of the regions. France, the Euro Zone, Germany, the UK, and the US attract financial capital and experience lower GDP losses (compared to Scenario 4) from the global flight of capital from severely affected countries, mainly in the developing world. Globally, the world loses an additional $US10 trillion solely due to the expected investment rebalancing in the financial markets. The losses further increase in Scenario 6 if the governments have to scale up healthcare spending to address AMR-related diseases. The increase in losses across the regions is different depending on the healthcare standards and the responsiveness of the governments to the global threat.

Table 3: Regional Cumulative GDP Change up to 2050 under AMR Scenarios (2018 $US billion)

Region	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5	Scenario 6
ARG	-279	-499	-514	-1,697	-2,195	-2,260
AUS	-293	-952	-971	-2,692	-2,793	-2,968
BRA	-1,073	-2,216	-2,258	-8,962	-11,350	-11,627
CAN	-234	-754	-767	-3,562	-3,854	-4,043
CHN	-3,456	-7,159	-7,382	-18,139	-27,930	-29,224
DEU	-724	-1,677	-1,688	-6,045	-4,194	-4,441
EUZ	-592	-1,944	-1,963	-8,461	-6,068	-6,433
FRA	-544	-1,038	-1,046	-3,555	-2,077	-2,263
GBR	-209	-656	-660	-6,859	-4,260	-4,467
IDN	-228	-517	-527	-1,630	-2,921	-3,123
IND	-2,357	-3,346	-3,404	-7,548	-9,083	-9,222
ITA	-183	-1,090	-1,097	-4,808	-5,638	-5,841
JPN	-1,283	-6,954	-6,976	-22,371	-22,982	-23,605
KOR	-154	-1,029	-1,038	-3,292	-3,611	-3,755
MEX	-290	-641	-656	-2,630	-4,201	-4,415
OAS	-464	-1,174	-1,189	-3,912	-5,005	-5,118
OEC	-230	-656	-669	-4,104	-3,251	-3,445
OPC	-1,979	-6,939	-6,988	-14,919	-11,979	-12,491
ROW	-12,545	-34,482	-34,840	-79,893	-94,923	-96,549
RUS	-959	-2,222	-2,257	-6,729	-7,221	-7,499
SAU	-207	-398	-401	-957	-134	-365
TUR	-273	-559	-571	-1,180	-1,299	-1,397
USA	-2,760	-9,641	-9,717	-46,548	-33,134	-33,737
ZAF	-436	-2,856	-2,864	-7,584	-7,404	-7,455
Total	-31,753	-89,399	-90,443	-268,077	-277,508	-285,744

Source: Results from the G-Cubed Model (GGG6G_v176) Simulations.

Figure 4 presents the short-, medium-, and long-term changes in real GDP under the first four scenarios, compared to the baseline. The short-, medium-, and long-term results shown in each panel are for 2030, 2040, and 2050, respectively. All the regions experience higher GDP losses compared to the baseline under all the scenarios. The losses increase for all the regions from Scenario 1 to 2 as AMR interacts with demographic trends, notably for Japan, Other Oil-Exporting Developing Countries, South Africa, Russia, and the Rest of the World. The increase in agriculture productivity losses from Scenario 2 to 3 does not substantially affect the GDP outcomes. Some regions may experience lower increments in losses when AMR interacts with physical climate risks (Scenario 4) if global warming reduces pathogenic activity and the spread of AMR-related diseases in those regions. Other Oil-Exporting Developing Countries, Russia, South Africa, and the Rest of the World experience the highest percentage losses throughout. Notably, Japan also experiences higher GDP losses in the long term when AMR interacts both with demographic trends and physical climate risks (Scenario 4). This difference reflects the different demographic structure and reliance on durable manufacturing goods production in Japan when shocks impact global investment.

4.2 Changes in Consumption and Investment

Figure 5 presents the short-, medium-, and long-term consumption changes under the first four scenarios. The consumption patterns closely follow real GDP changes, indicating the effects of income on consumption. The breakdown of real GDP changes for its constituents also illustrates that the highest impact on real GDP arises from consumption changes. Across the scenarios, in the short term, Other Oil-Exporting Developing Countries, Russia, South Africa, and the Rest of the World experience the most significant consumption adjustments. The sectoral decomposition of consumption changes reveals that households noticeably reduce their expenditure on services. The observation is consistent across all the above regions. Consumption of non-durable manufacturing goods reduces next. Several countries, such as China, India, Indonesia, Other Oil-Exporting Developing Countries, and the Rest of the World, also experience notable reductions in agriculture consumption, indicating AMR effects on subsistence consumption.

The short-, medium-, and long-term investment change patterns are mainly analogous to consumption. However, the investment changes in the G-Cubed model are much larger than consumption and real GDP changes because investment responds to changes in the returns to capital in different sectors. There is a distinction between physical capital in a production function, which is sector and country-specific, and financial capital. In response to an economic shock or a series of economic shocks expected in the future for a given sector, the financial markets swiftly respond. As a result, the financial capital in a relatively more vulnerable sector could immediately get relocated to markets with sectors experiencing lower risks. Furthermore, the costs of readjusting physical investment discourage investors from reinvesting in the sectors and countries more vulnerable to AMR risks. Also, the global decline in investment across countries will reduce the demand for capital goods from countries that export durable goods, which are the primary source of goods entering the physical capital stock of sectors.

As Figure 6 presents, the change in investment in most countries follows patterns similar to real GDP changes. However, the changes are larger than those for real GDP and consumption, and the distribution of the changes is diverse across time and regions. For example, Other Oil-Exporting Developing Countries experience larger short-term investment adjustments. In contrast, other regions experience increasing investment reductions over time. When AMR interacts with demographic trends (Scenario 2), China, India, Japan, South Africa, and some European countries experience the highest investment reductions from the baseline in the long term. When both demographic trends and physical climate risks interact with AMR (Scenario 4), Brazil, Japan, Other Oil-Exporting Developing Countries, Russia, and South Africa experience substantial investment reductions from the baseline in the long term. The real GDP decomposition illustrates that investment reductions are the second largest contributor to real GDP changes across most regions.

4.3 Changes in Exports and Imports

In the G-Cubed model, the change in the trade balance depends on the change in savings relative to investment. The composition of the trade balance reflected in the changes in exports and imports is affected by the AMR impacts on productivity and the income and price effects in the trade response of each sector. Figure 7 presents the changes in exports under the first four scenarios in the short, medium, and long term compared to the baseline. Exports are affected by sectoral productivity changes, income effects on trade partners, and price effects via changes in exchange rates driven by the response of capital flows reflecting saving and investment dynamics. Under Scenario 1, where the AMR growth rates remain constant, the percentage reduction in exports is higher in the short term and lower in the long term, reflecting the initial movement of financial capital followed by the repatriation of returns on investments. However, the exports reduce over time under Scenarios 2, 3, and 4. Under all scenarios, Japan and the Euro Zone experience the most significant decline in the long term. Japan, the Euro Zone, Other Oil-Exporting Developing Countries, and South Africa experience the highest export reductions under Scenario 4. A sectoral decomposition of export changes illustrates that durable goods in developing and developed countries contribute a higher proportion of changes. Agricultural and non-durable goods also contribute to some changes, especially in developing countries.

Figure 8 presents the changes in imports under the first four scenarios in the short, medium, and long term compared to the baseline. Similar to exports, the changes in imports are affected by both the income and price effects via feedback. Also similar to exports, the changes in imports are evened out when the AMR growth rates are constant under Scenario 1 and increase over time under other scenarios. Under Scenarios 1-3, all regions experience minimal adjustments across the scenarios in the short to medium term. South Africa undergoes a substantial contraction in imports in the long term. In the long term, Australia, Canada, Germany, Japan, and the Euro Zone also experience notable percentage reductions in imports.

The real GDP decomposition illustrates that the import adjustments have the least impact on the real GDP changes. The sectoral decomposition of imports indicates that most import reductions are contributed by durable goods, followed by non-durable goods. These patterns contrast with the sectoral decomposition of consumption reductions, where services dominate. Different from consumption, energy imports also reduce following durable and non-durable imports.

4.4 Changes in Sectoral Output

The sectoral output changes, presented in Figures 9 to 14, are directly driven by the labor and livestock productivity shocks. In the G-Cubed model, the general equilibrium effects could also moderate the impacts of the shocks, as highlighted in this discussion.

Agriculture: Being labor-intensive, agriculture is disproportionately vulnerable to increased AMR impacts on the population via AMR-related diseases. Agriculture is also vulnerable to sectoral productivity changes due to the increased exposure of livestock to AMR risks with its heavy antimicrobial consumption. Figure

9 illustrates the short-, medium-, and long-term changes in agriculture output under the first four scenarios. In the short term, under all scenarios, Argentina, Australia, Brazil, Canada, Japan, Other Oil-Exporting Developing Countries, Russia, South Africa, and the Rest of the World experience the highest losses, which exceed one percent from the baseline. In the long term, Argentina, Australia, Japan, Other Oil-Exporting Developing Countries, Russia, South Africa, and the Rest of the World experience the highest losses, exceeding two percent under Scenario 4. Notably, the incremental losses from Scenario 2 to 3, when agriculture productivity losses increase, are minimal up to 2050.

Mining: Mining is mainly exposed to AMR risks only through its effects on labor productivity. The sectoral linkages and other general equilibrium effects of macroeconomic changes could also affect mining output. Figure 10 shows the short-, medium-, and long-term changes in mining output under the first four scenarios. When AMR interacts with demographic trends (Scenario 2), Other Oil-Exporting Developing Countries and South Africa experience significant mining output losses compared to the other regions. When AMR interacts with both demographic trends and physical climate risks (Scenario 4), the percentage losses compared to the baseline exceed three and seven percent in the medium and long term, respectively, for some regions.

Energy: Similar to mining, energy is also exposed to AMR risks mainly through its effects on labor productivity. Figure 11 demonstrates the short-, medium-, and long-term changes in energy output under the first four scenarios. The risks notably increase when AMR interacts with demographic trends and physical climate risks. In the short term, Other Oil-Exporting Developing Countries, South Africa, and the Rest of the World experience the highest losses. In the medium to long term, especially under Scenario 4, where AMR interacts with both demographic trends and physical climate risks, more regions experience increasing losses. The output contractions exceed one percent from the baseline in the long term for most regions.

Manufacturing: The G-Cubed model distinguishes between durable and non-durable manufacturing. The durable manufacturing sector produces capital goods that feed into the sectoral capital stock via investment, while the non-durable manufacturing sector primarily produces consumables.

Being capital-intensive and the sector that provides goods for investment purposes across all sectors, the durable manufacturing sector is mainly exposed to AMR risks through investment reductions. Figure 12 shows the short-, medium-, and long-term changes in durable manufacturing output under the first four scenarios. While the durable manufacturing output reduction patterns are similar to investment, the magnitude of the changes is lower on average compared to investment. The durable manufacturing sector in Japan, Other Oil-Exporting Developing Countries, Russia, South Korea, and South Africa is relatively more vulnerable when AMR interacts with both demographic trends and physical climate risks (Scenario 4) in the long term. The losses generally exceed one percent from the baseline in the medium to long term. The impact on Japan is particularly due to the decline in the production of durable manufacturing goods for both domestic and foreign consumption amidst the reduced global investment.

The non-durable manufacturing sector is affected by AMR risks due to its close reliance on agriculture to produce consumables and its relatively higher labor intensity. Figure 13 shows the short-, medium-, and long-term changes in non-durable manufacturing output under the first four scenarios. In the short term, Argentina, Other Oil-Exporting Developing Countries, South Africa, and the Rest of the World experience the highest losses under all the scenarios. In the medium to long term, Japan and Russia also experience relatively higher losses, exceeding 1.5 percent from the baseline.

Services: Services are directly affected by labor exposure to AMR-related diseases and their linkages to the agriculture sector. It is also affected by the general equilibrium effects of macroeconomic changes, such as income and price changes. Figure 14 presents the short-, medium-, and long-term changes in service sector output under the first four scenarios. The patterns of changes in production are quite similar to those of other sectors. However, the contractions are the lowest in the service sector compared to the other sectors, with most regions experiencing losses below one percent under most scenarios. Japan, Other Oil-Exporting Developing Countries, Russia, South Africa, and the Rest of the World generally experience the highest adjustments.

5 POLICY PRIORITIES AND RECOMMENDATIONS

The first notable recognition of AMR in the policy arena was the Global AMR Strategy published by WHO in 2001. The reports emphasized the importance of AMR surveillance, infection prevention and control, prudent use of antimicrobials, and fostering research and development of new antimicrobials and alternative treatments (WHO 2001). The development of the Global Action Plan on AMR in 2015 (WHO 2015) focused on increasing the awareness of AMR and actioning the other strategic areas recognized in the Global AMR Strategy. The political declaration by the UN member nations in 2016 acknowledging the severity of AMR and committing to the development of National Action Plans was another significant milestone in global AMR policymaking. Tripartite collaboration between the FAO, the WHO, and the World Organization for Animal Health (OIE) strengthened the multisectoral approach to addressing AMR. The tripartite was extended to a quadripartite when the UNEP joined in 2022. The collaboration between these bodies aims to take a holistic view of managing AMR, considering human, animal, plant, and environmental interfaces (FAO, UNEP, WHO & OIE 2023).

Within the above broader policy context of AMR, this paper recognizes four main policy priorities:

1. A global multisectoral one-health approach to AMR
2. Global cooperation for AMR
3. Preserving and expanding the existing stock of antimicrobials and preventing the emergence and contagion of new diseases
4. Alleviating uncertainties for policymakers.

5.1 A Global Multisectoral One-health Approach to AMR

AMR should be recognized as a global problem with complex interactions between the natural environment, socioeconomic systems, and economic sectors. This paper provides two main arguments to support this position.

1. Importance of a one-health approach with environmental and socioeconomic interactions: As illustrated in Figures 1 and 2 and discussed in Section 2.3, AMR is at the intersection of the environment and the socioeconomic systems, and AMR is affected both by socioeconomic (such as demographic trends, governance, and cross-border mobility) and environmental factors (such as climate risks and the quality of the natural and built environment), beyond overuse, underuse, and misuse of antimicrobials. Hence, adopting a one-health approach, which recognizes the interactions between the socioeconomic and environmental systems, when assessing the economic consequences of AMR is essential. Similar to integrated assessments of climate change, the environmental aspects of AMR could be factored into its economic modeling. This paper modeled AMR as a function of other broader socioeconomic and environmental risks and incorporated those insights into economic modeling. Under the various scenarios, Section 4 illustrated how the economic consequences of AMR change when different risk factors interact with AMR.

2. Importance of a global multisectoral economic approach: Within an economic framework, AMR is a global multisectoral problem with important implications for global growth, development, and welfare. Firstly, as illustrated in Figure 3, almost all sectors rely on antimicrobials directly or indirectly via linkages to those sectors directly depending on antimicrobials. Secondly, as discussed in Section 4, no country/region is immune to AMR risks. Almost all the countries/regions are directly affected by AMR impacts on labor and agriculture and indirectly affected via global supply and investment linkages, especially as illustrated in Scenario 5. Thirdly, the general equilibrium effects and the existing economic structure and policies of a given country/region are crucial qualifiers of AMR impacts. They could amplify or dampen the ultimate economic consequences in ways very different from direct economic impacts. Hence, AMR should no longer be perceived as a challenge to the health or agriculture sector alone but rather as a global economy-wide problem.

5.2 Global Cooperation for AMR

AMR is a global phenomenon requiring global solutions built on global cooperation for two main reasons.

1. The transboundary nature of AMR: As argued in Section 1, AMR is a global transboundary wicked problem with the actions of one sector/country affecting the other sectors/countries. Section 2.3 discussed factors affecting AMR that are beyond the control of an individual country/region. Therefore, one country/region alone cannot resolve AMR and reduce its vulnerability to AMR.

2. The disparity in economic consequences of AMR: As illustrated in Section 4, on the one hand, from both health and economic perspectives, developing countries are disproportionately affected by AMR. They experience substantial economic and welfare contractions due to direct and indirect AMR effects. On the other hand, they are further likely to aggravate AMR, given their already existing suboptimal consumption patterns (e.g., informal pharmaceutical markets), already existing vulnerabilities to diseases demanding further antimicrobial consumption, and their development needs (e.g., to maintain and extend agriculture being at early stages of development).

Therefore, global cooperation is essential to address AMR collectively. The developed nations should support developing nations via technical and financial capacity building to strengthen their antimicrobial supply chains and improve consumption patterns, as well as technological and development aid to improve healthcare systems and agriculture. The historical and ongoing lessons from global actions towards transboundary problems, such as ozone depletion, marine plastic pollution, and climate change, could provide valuable insights to initiate and sustain global cooperation toward AMR.

The quadripartite cooperation between the WHO, FAO, OIE, and UNEP promotes and facilitates global cooperation in the work on AMR. Given the AMR interactions with economic growth and development, as illustrated in this paper, it is necessary to involve the economic/development organizations when driving global cooperation on AMR. The lack of an economic perspective on solutions may reduce policy effectiveness, and garnering political support for solutions may become challenging. The explicit focus on the economic aspects of AMR and its interactions with growth and development is critically missing from the current quadripartite initiative. International development organizations, such as the World Bank and/or the UN Development Program (UNDP), should also partner in the initiative. The global response should also be a more comprehensive network of organizations (similar to the Network for Greening the Financial System [NGFS] in the climate space) involving a wide range of global and national policy institutions.

5.3 Preserving and Expanding the Existing Stock of Antimicrobials and Preventing the Emergence and Contagion of New Diseases

Preserving and expanding the existing stock of antimicrobials is critical to preventing the emergence and contagion of new infections. Additional short-term and long-term measures need to be implemented.

1. Short-term measures: The development of new antimicrobials is inhibited by numerous challenges; thus, preserving the existing stock of antimicrobials is essential. Firstly, all the elements of the antimicrobial supply chain should be regulated. This includes production, evaluation and market authorization, procurement and supply, consumption, and disposal (FAO, OIE, and WHO 2020). Secondly, the informal production of antimicrobials should be disincentivized, and further expansion of informal markets, especially in developing countries, should be prevented. Experienced nations should support developing nations with financial and technical aid to improve their capacities in these aspects. Thirdly, global awareness of prudent antimicrobial consumption among firms and households should be promoted to enhance diagnosis and prescription standards (particularly in the healthcare sector), and antimicrobial disposal should be regulated.

2. Long-term measures: Incentivizing research and development and innovations to sustain the efficacy of existing antimicrobials and to explore alternatives to antimicrobials[24] are critical long-term measures. Furthermore, preventing the emergence of new infections and controlling contagion at early stages via preventative measures (such as vaccinations) is also crucial. Moreover, cooperating with the pharmaceutical sector and other antimicrobial producers and regulating where necessary in research, development, sales, and distribution is essential. Lessons could be drawn from the global collective initiative to respond to COVID-19.

5.4 Alleviating Uncertainties for Policymakers

Evaluating the economic consequences of AMR involves at least three primary sources of uncertainties: (1) Lack of understanding of AMR evolution, (2) Lack of data and access, and (3) Methodological uncertainties.

1. Lack of understanding of AMR evolution: As illustrated in Section 2.3, enormous uncertainty exists regarding the factors driving AMR. From a microbiological perspective, most resistance mechanisms are well understood. Yet, the external stressors or factors that incentivize those mechanisms have not been comprehensively studied. Most of the studies attribute the rise in AMR to antimicrobial consumption. However, little is known about factors beyond antimicrobial consumption. This paper utilized two main external factors: demographic trends and physical climate risks. In Fernando (2023b, c), where the impacts of those factors on AMR are measured, the more substantial role of those factors than antimicrobial consumption (in the case of certain drug-pathogen combinations) is illustrated. Therefore, further research into AMR evolution and how AMR affects humans, animals, plants, and the environment will improve the understanding of the economic costs and benefits of addressing AMR.

2. Lack of data and access: A constraint preventing the exploration and quantification of factors affecting AMR is the lack of global data on resistance rates and antimicrobial consumption. There is also a lack of access to existing data, especially regarding antimicrobial consumption. Furthermore, the AMR rates for various antimicrobial drug-pathogen combinations are yet to be discovered. The GRAM study (Murray et al. 2022) was the first systematic attempt to provide the regional resistance rates for antimicrobial drug-pathogen combinations for 2019. Scaling up AMR surveillance, making national surveillance data widely available after quality assurances, and enabling open-source access to antimicrobial consumption and sales data are vital to producing research evidence for policymaking. The possibility of harnessing recent innovations, such as distributed ledger technologies, for crowdsourcing such data could also be explored.

3. Methodological uncertainties: The methodologies used to assess AMR effects are naturally constrained by their assumptions and historical data used for calibration. Transparency about the strengths and limitations of different perspectives on modeling AMR and the use of different scenarios in different models will help policymakers better understand the extent of uncertainty surrounding AMR.

[24] See Ghosh et al. (2019) for a review of alternatives to antibiotics and Davies and Oxlade (2021) for a detailed discussion on how to prioritize investments in alternative therapies for AMR.

6 CONCLUSION

AMR is a natural phenomenon where microorganisms acquire resistance to antimicrobials as part of their evolution. However, overuse, misuse, and underuse of antimicrobials in healthcare, agriculture (crops, livestock, and aquaculture), and industrial applications have aggravated AMR. In addition to antimicrobial consumption, socioeconomic, sociocultural, demographic, and environmental factors contribute to AMR. These include climate change, demographic trends (such as the growth in population, population aging, population density, urbanization, and migration), and plastic and metal pollution. Given the widespread consumption of antimicrobials in healthcare, agriculture, and industry, worsening AMR threatens global economic stability, growth, and development. Thus, addressing AMR collectively is vital to preventing global economic disruptions from AMR.

This paper explores and attempts to quantify the economic impacts of AMR under six scenarios where four main impact pathways are varied. The impact pathways account for (1) labor productivity changes from morbidity and mortality due to AMR-related diseases, (2) agriculture productivity changes due to AMR effects on livestock, (3) risk premia changes in financial markets due to the differential exposure to AMR risks, and (4) fiscal expenditure changes to manage AMR risks. We account for the AMR interactions with demographic trends (growth in population and population aging) and physical climate risks when projecting the changes in AMR-related diseases. We evaluate the shocks within the G-Cubed model, which is a global multisectoral intertemporal general equilibrium model, and estimate the economic consequences of AMR.

The economic losses under alternative scenarios increase as new risk factors interact with AMR. The highest increment in losses is experienced when physical climate risks are introduced. Under Scenarios 1 to 4, most regions experience larger GDP reductions compared to the baseline. However, emerging and developing countries, especially those with higher populations, are disproportionately affected by AMR. The results suggest substantial consumption and investment adjustments affecting exports and imports. The results reveal that the agriculture and manufacturing sectors are the most vulnerable. Comparing the shocks with ultimate results, we also illustrate the role of general equilibrium effects in moderating the economic consequences.

Despite efforts to reduce the uncertainties associated with data and methodologies, the results in this paper are subject to a great deal of uncertainty. The sources of uncertainty include the economic model being used and the empirical relationships estimated using historical data in Fernando (2023b, c). Many more scenarios are possible than the six scenarios explored in this paper.

We recognize four main policy priorities. We reiterate the importance of an economy-wide approach to modeling AMR within a one-health framework that recognizes socioeconomic and environmental interactions. Given the transboundary nature of AMR and the disparity of economic consequences, global cooperation is essential to address AMR collectively. We highlight the importance of preserving and expanding the existing stock of antimicrobials and preventing the emergence and contagion of evolving and new diseases. Finally, we emphasize the importance of alleviating the uncertainties surrounding AMR and better quantifying the costs of inaction globally. An estimate of the cost of inaction should better inform policy-makers of the scale of investment that can be justified in dealing with AMR.

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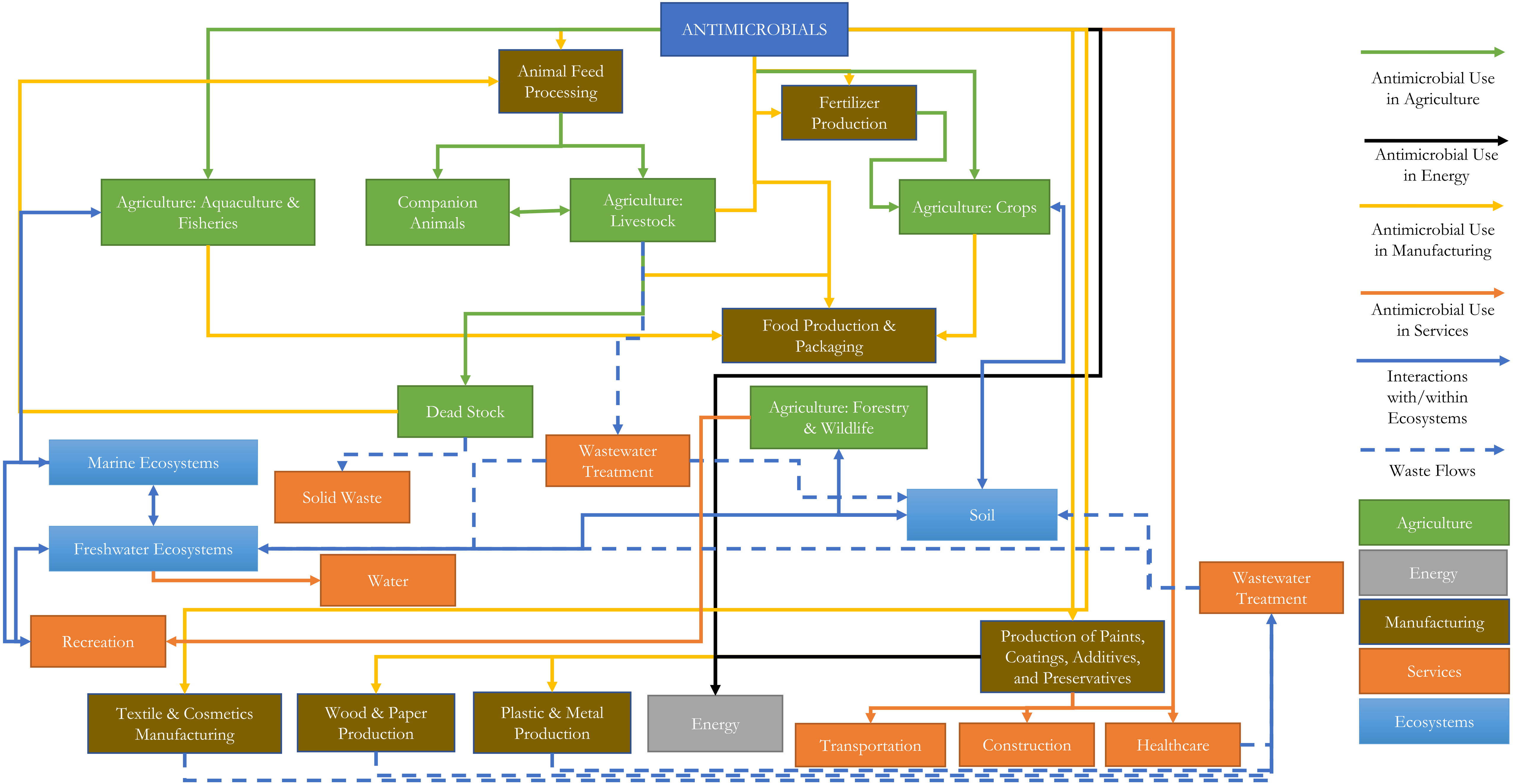
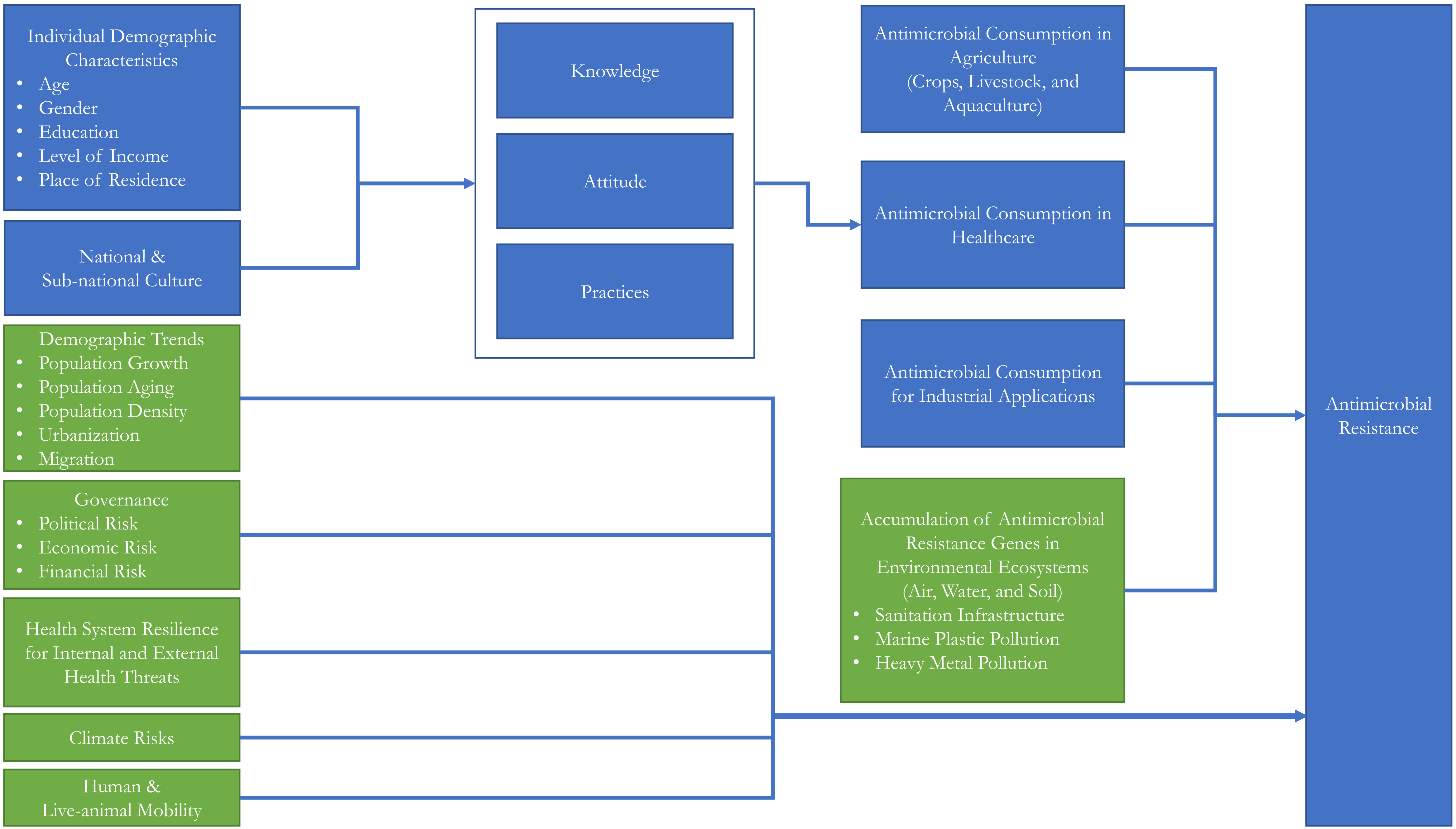
Figure 1: Economywide Antimicrobial Consumption



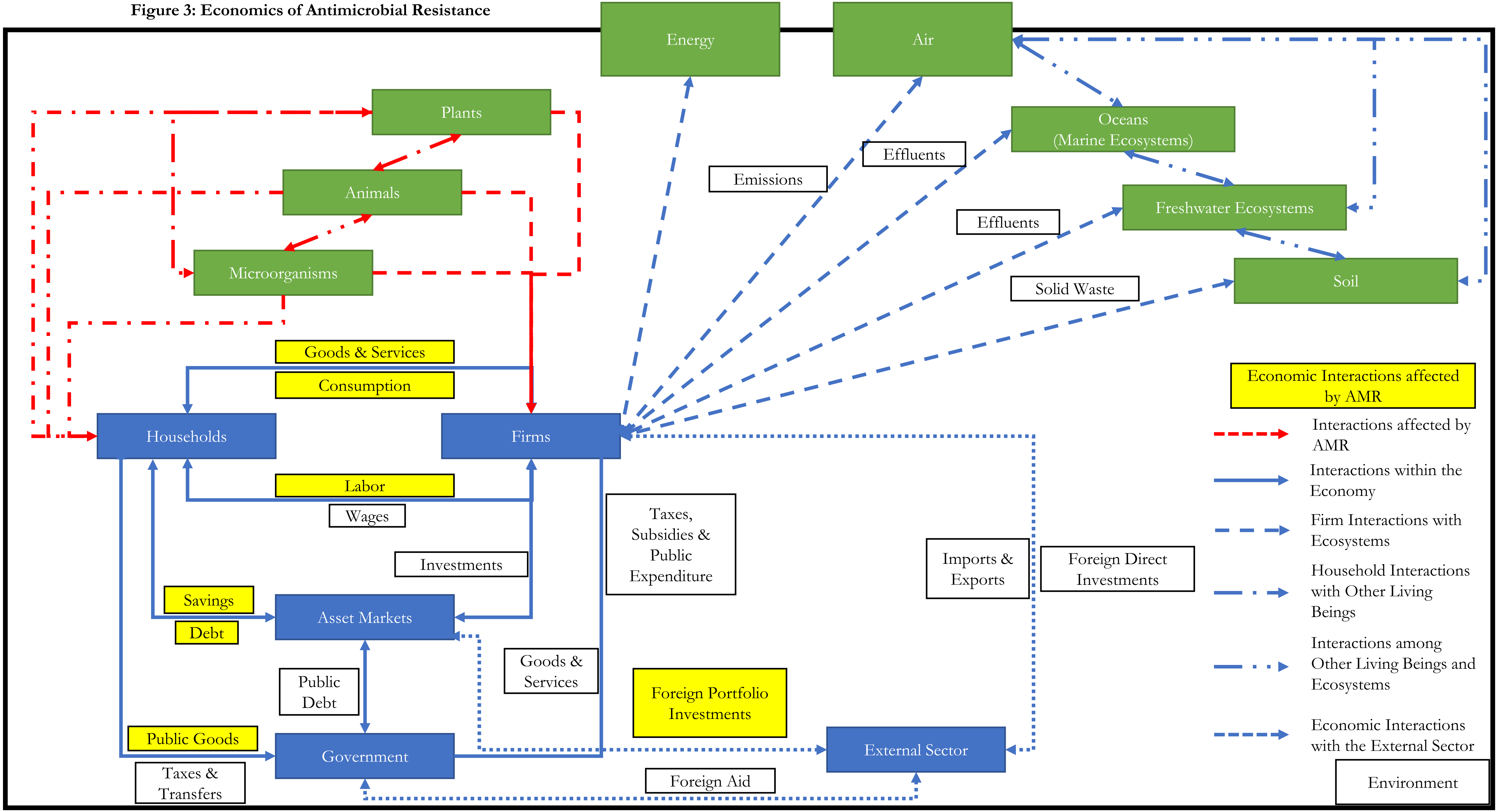
Source: Fernando & McKibbin (2022).

Figure 2: Factors Affecting Antimicrobial Resistance



Source: Fernando & McKibbin (2022).

Figure 3: Economics of Antimicrobial Resistance

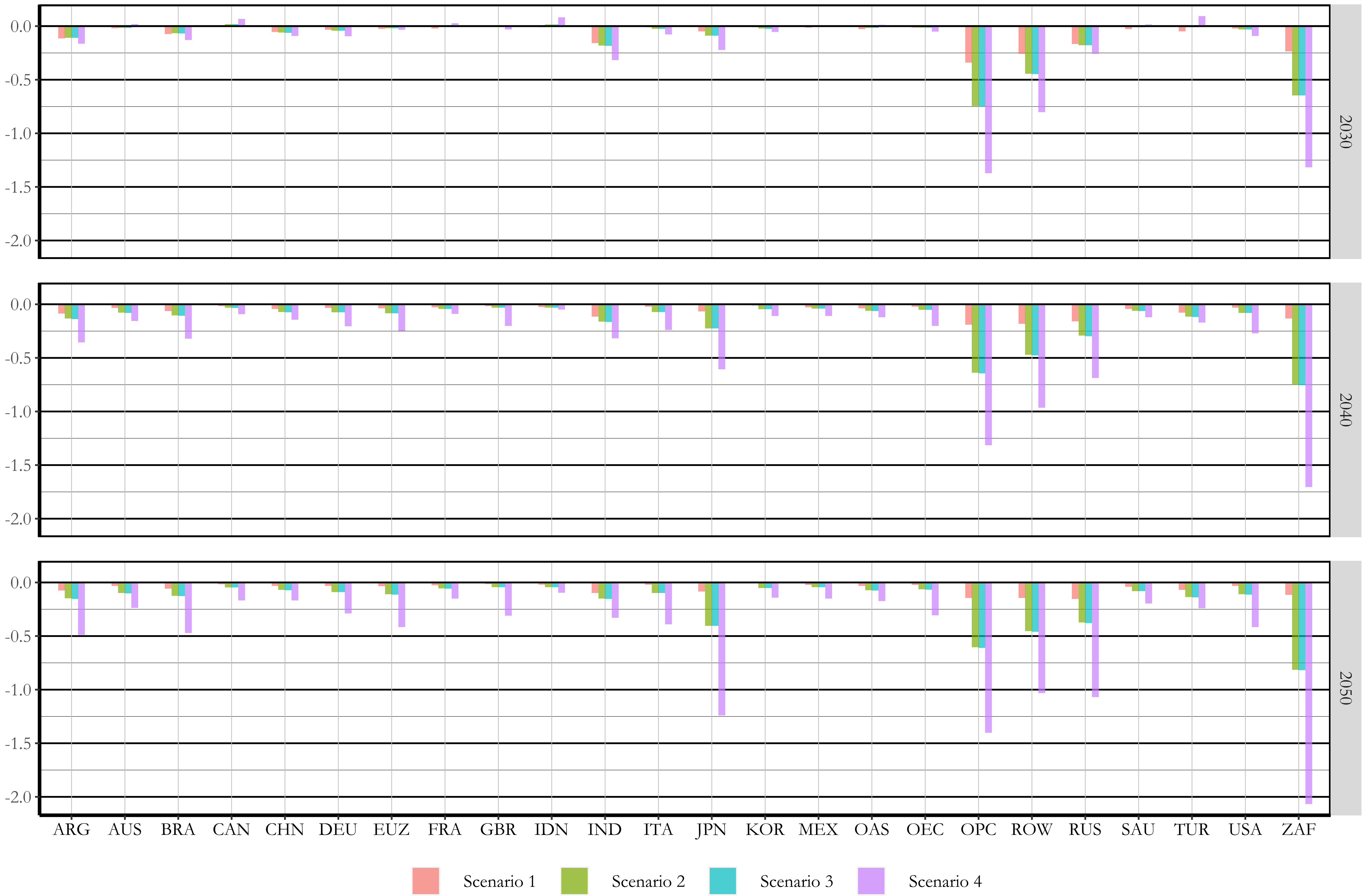


Source: Fernando & McKibbin (2022).

Figure 4: Percentage Change in Real GDP from the Baseline

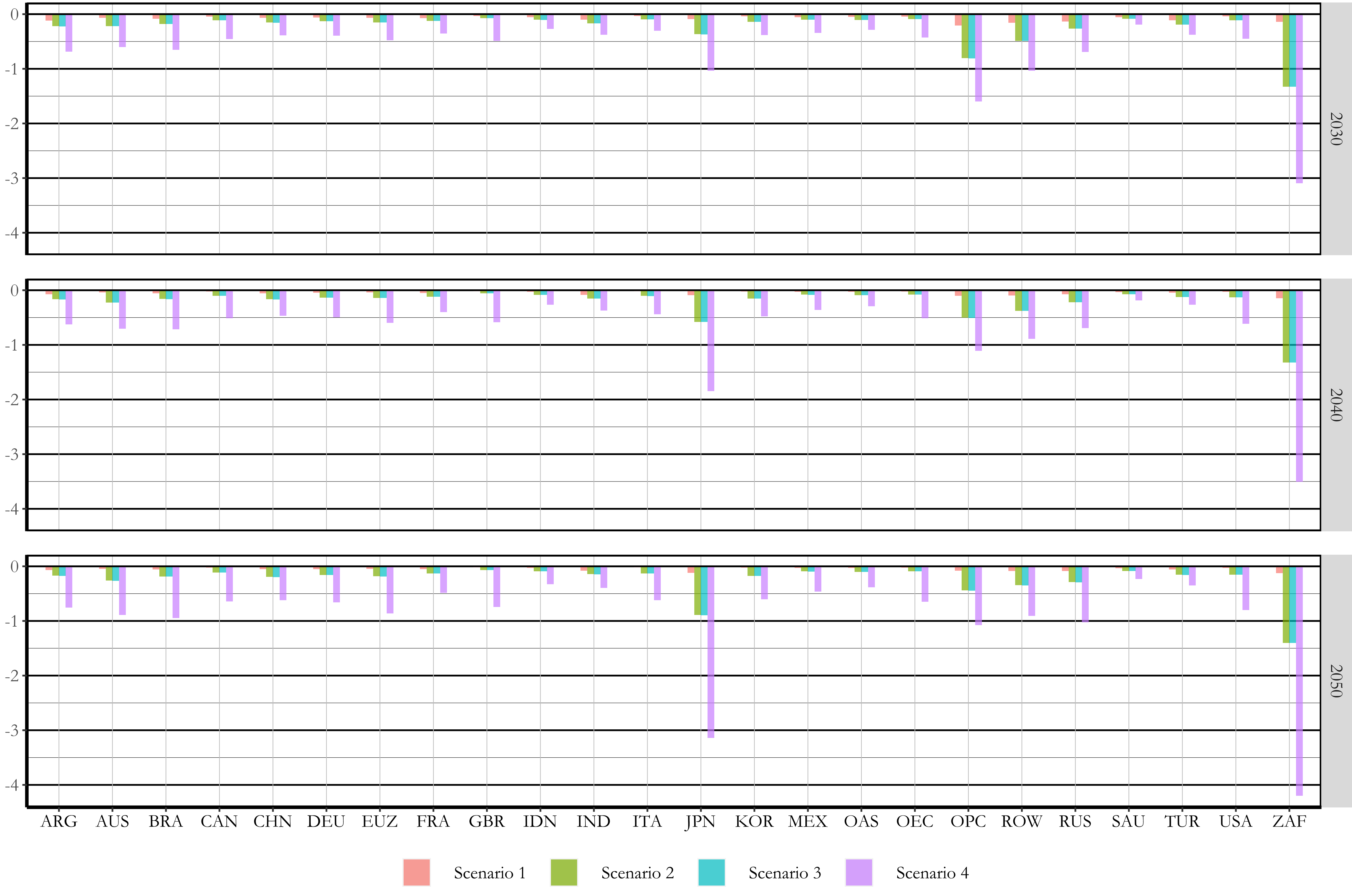
Source: Results from the G-Cubed Model (GGG6G_v176) Simulations.

Figure 5: Percentage Change in Consumption from the Baseline



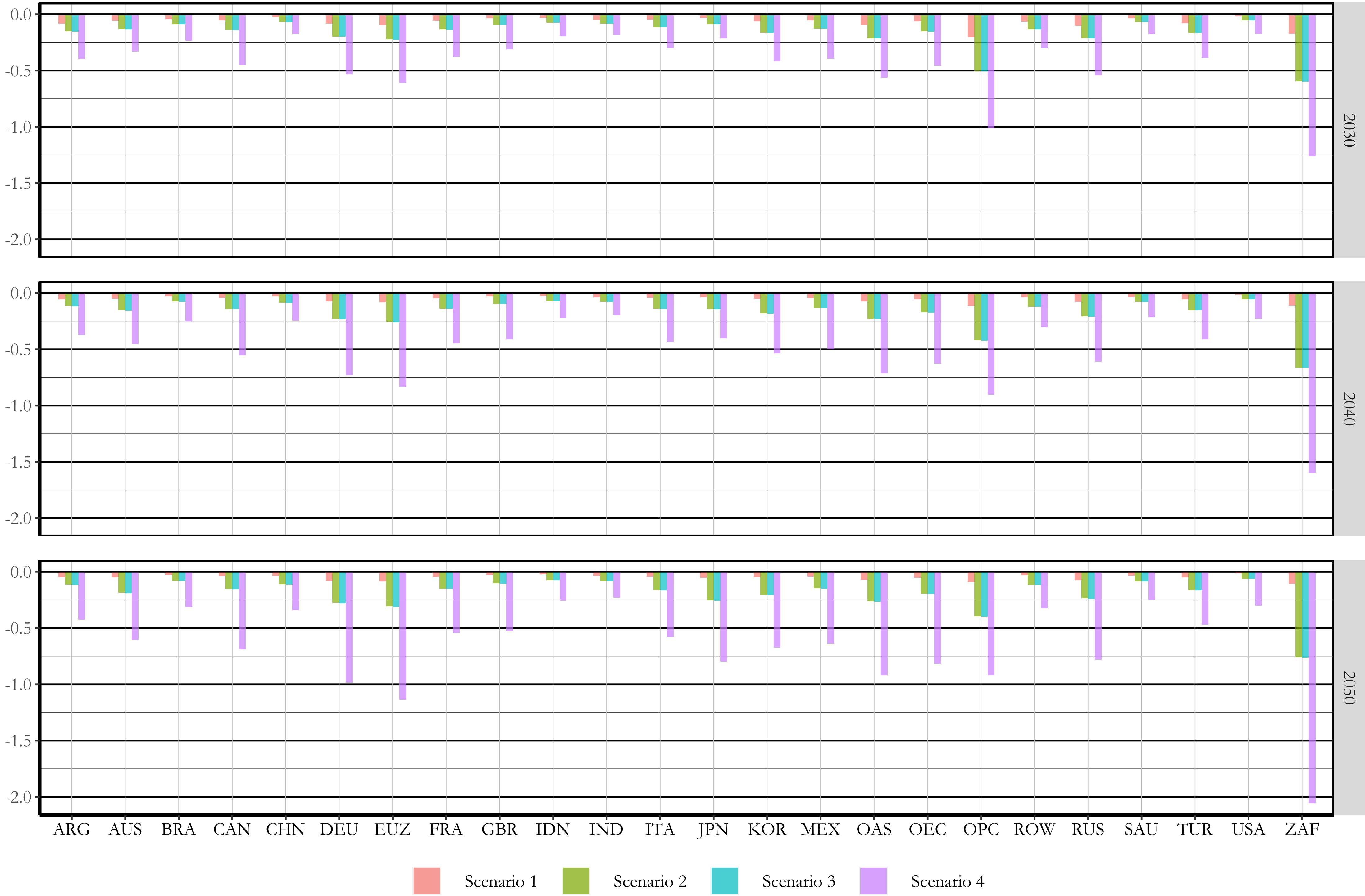
Source: Results from the G-Cubed Model (GGG6G_v176) Simulations.

Figure 6: Percentage Change in Investment from the Baseline



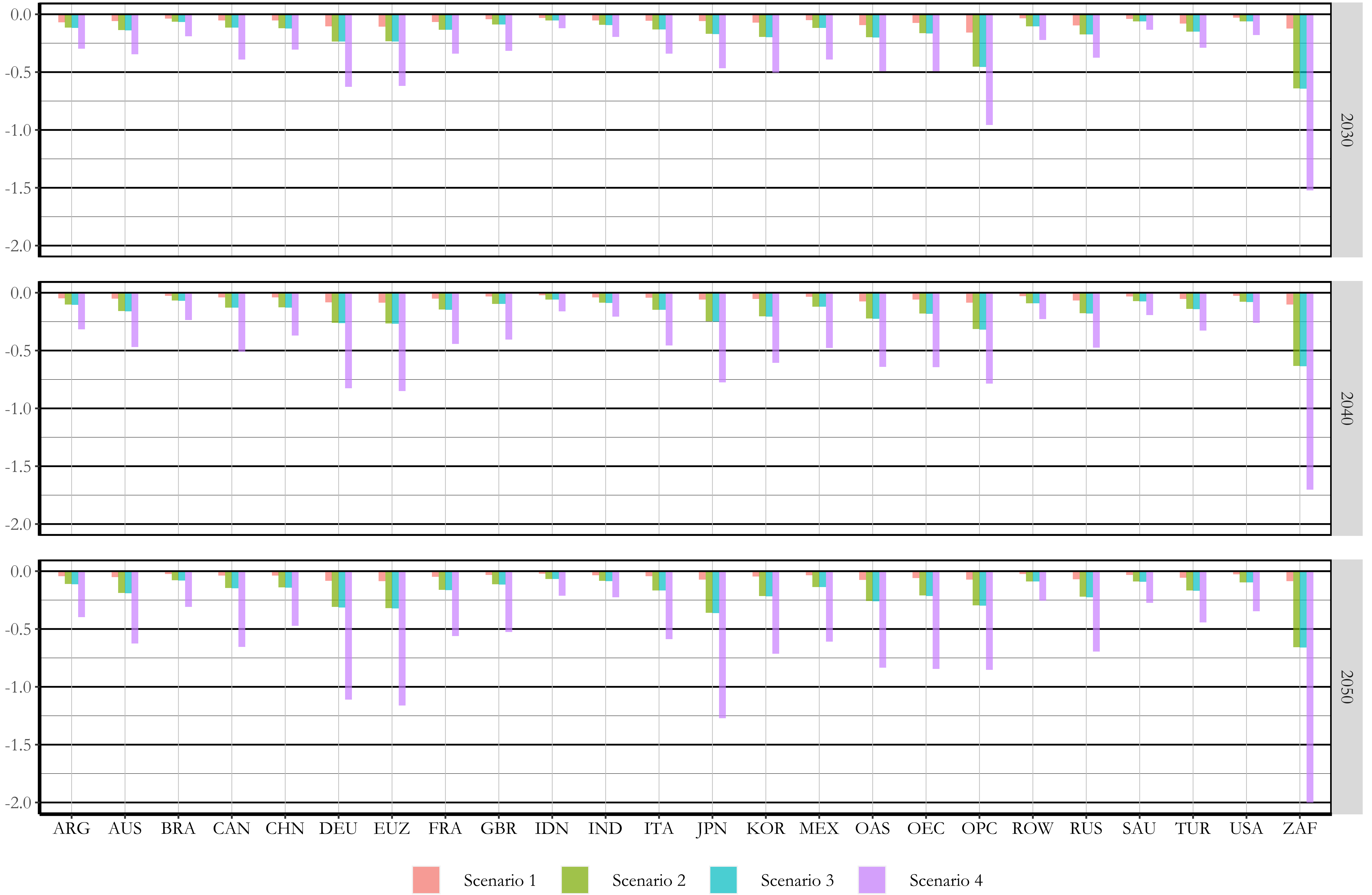
Source: Results from the G-Cubed Model (GGG6G_v176) Simulations.

Figure 7: Percentage Change in Exports from the Baseline



Source: Results from the G-Cubed Model (GGG6G_v176) Simulations.

Figure 8: Percentage Change in Imports from the Baseline

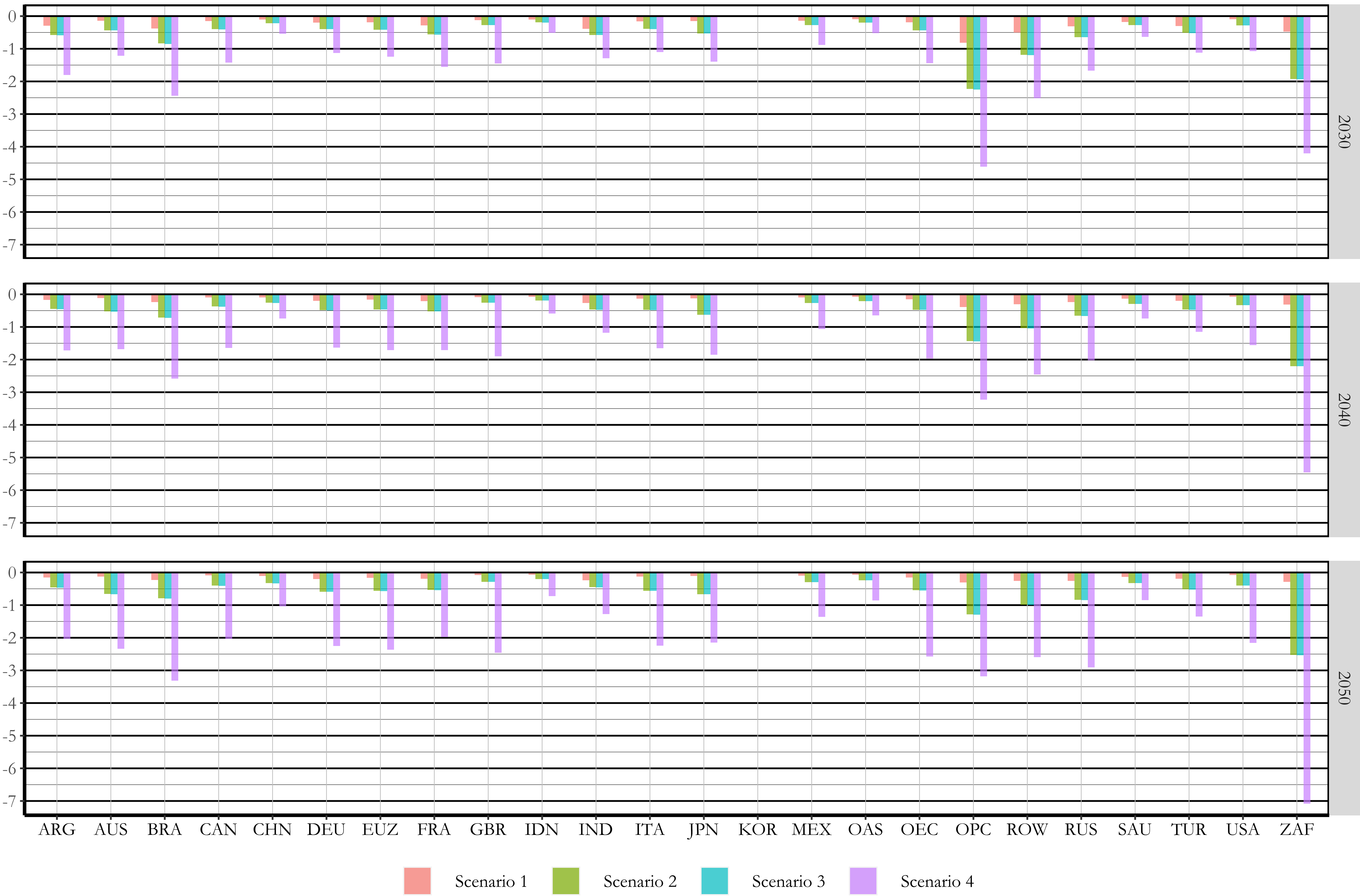


Source: Results from the G-Cubed Model (GGG6G_v176) Simulations.

Figure 9: Percentage Change in Output from the Baseline: Agriculture

Source: Results from the G-Cubed Model (GGG6G_v176) Simulations.

Figure 10: Percentage Change in Output from the Baseline: Mining

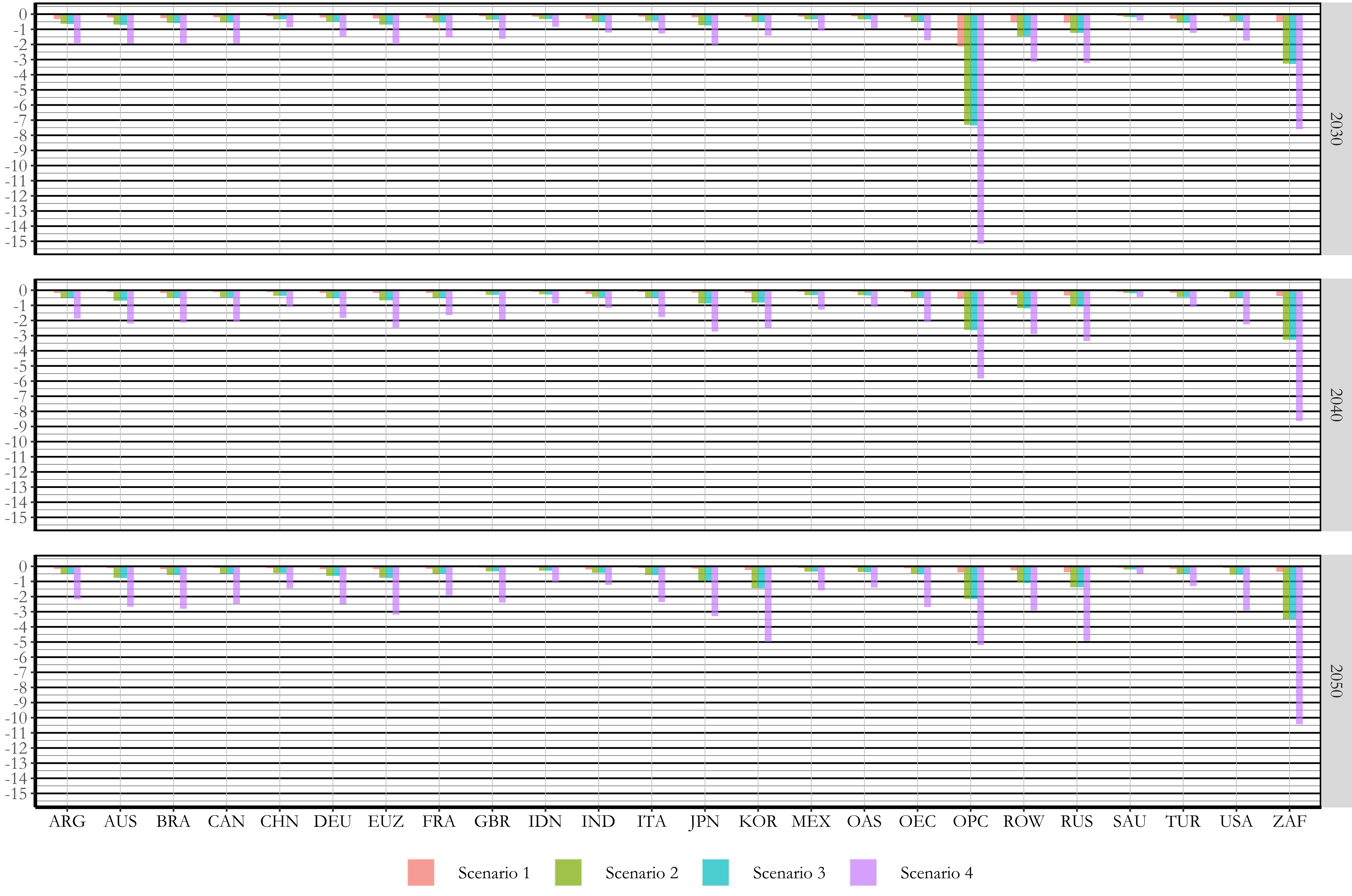


Source: Results from the G-Cubed Model (GGG6G_v176) Simulations.

Figure 11: Percentage Change in Output from the Baseline: Energy

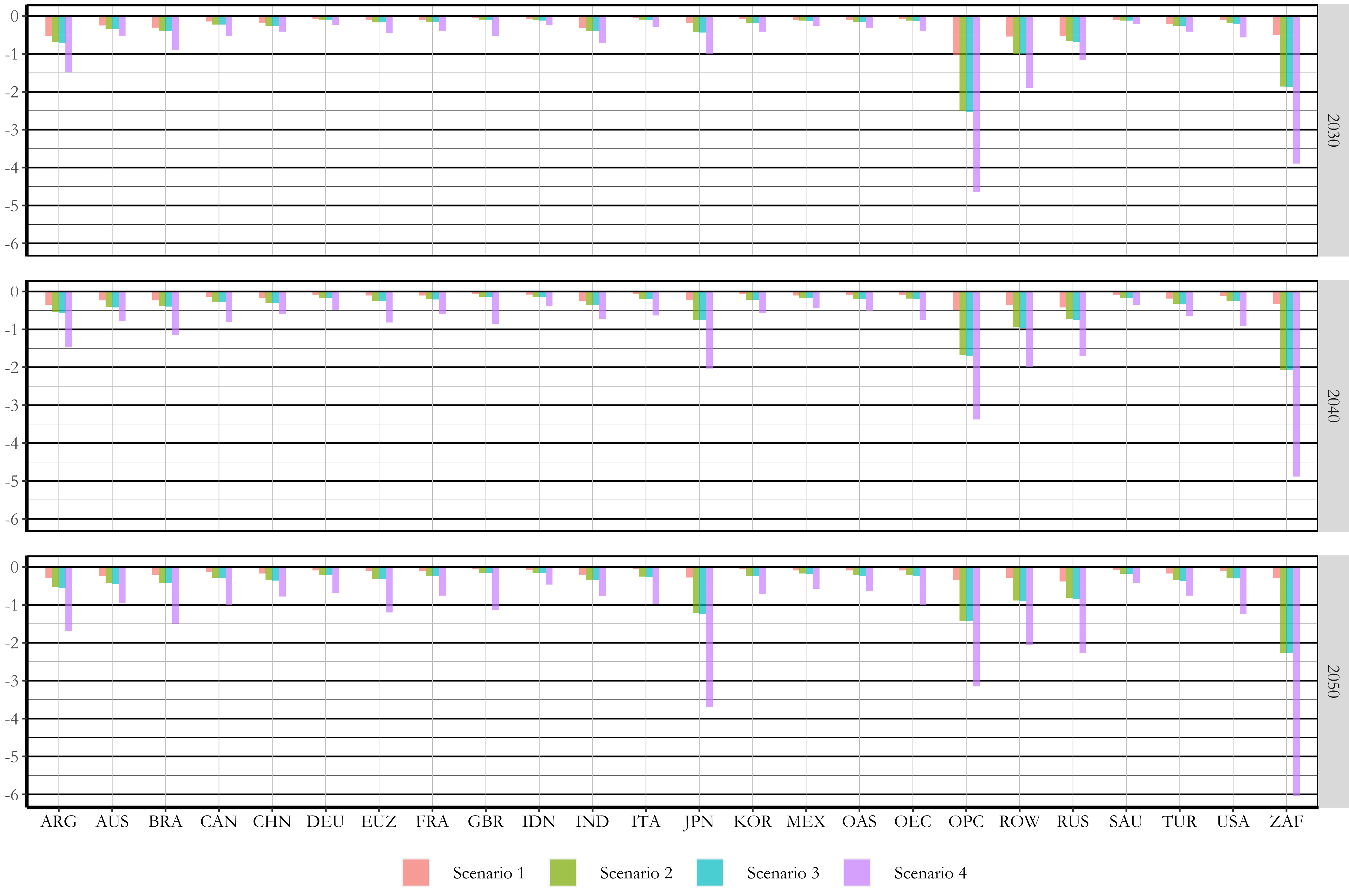
Source: Results from the G-Cubed Model (GGG6G_v176) Simulations.

Figure 12: Percentage Change in Output from the Baseline: Durable Manufacturing



Source: Results from the G-Cubed Model (GGG6G_v176) Simulations.

Figure 13: Percentage Change in Output from the Baseline: Non-Durable Manufacturing



Source: Results from the G-Cubed Model (GGG6G_v176) Simulations.

Figure 14: Percentage Change in Output from the Baseline: Services

Source: Results from the G-Cubed Model (GGG6G_v176) Simulations.

GLOBAL ECONOMIC IMPACTS OF ANTIMICROBIAL RESISTANCE

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SUPPLEMENTARY ANNEXURES

Supplementary Annexure 1: Concordance between GTAP and G-Cubed Regions

GTAP	G-Cubed	GTAP	G-Cubed
AUS	AUS	MLT	EUZ
NZL	OEC	NLD	EUZ
XOC	ROW	POL	ROW
CHN	CHN	PRT	EUZ
HKG	OAS	ROU	ROW
JPN	JPN	SVK	EUZ
KOR	KOR	SVN	EUZ
MNG	ROW	ESP	EUZ
TWN	OAS	SWE	OEC
XEA	ROW	GBR	GBR
BRN	ROW	CHE	OEC
KHM	ROW	NOR	OEC
IDN	IDN	XEF	OEC
LAO	ROW	ALB	ROW
MYS	OAS	BLR	ROW
PHL	OAS	RUS	RUS
SGP	OAS	UKR	ROW
THA	OAS	XEE	ROW
VNM	OAS	XER	ROW
XSE	ROW	KAZ	ROW
BGD	ROW	KGZ	ROW
IND	IND	TJK	ROW
NPL	ROW	XSU	ROW
PAK	ROW	ARM	ROW
LKA	ROW	AZE	ROW
XSA	ROW	GEO	ROW
CAN	CAN	BHR	OPC
USA	USA	IRN	OPC
MEX	MEX	ISR	OPC
XNA	ROW	JOR	OPC
ARG	ARG	KWT	OPC
BOL	ROW	OMN	OPC
BRA	BRA	QAT	OPC
CHL	ROW	SAU	SAU
COL	ROW	TUR	TUR
ECU	ROW	ARE	OPC
PRY	ROW	XWS	OPC
PER	ROW	EGY	ROW
URY	ROW	MAR	ROW
VEN	OPC	TUN	ROW
XSM	ROW	XNF	OPC
CRI	ROW	BEN	ROW
GTM	ROW	BFA	ROW
HND	ROW	CMR	ROW
NIC	ROW	CIV	ROW
PAN	ROW	GHA	ROW
SLV	ROW	GIN	ROW
XCA	ROW	NGA	OPC
DOM	ROW	SEN	ROW
JAM	ROW	TGO	ROW
PRI	ROW	XWF	ROW
TTO	ROW	XCF	ROW
XCB	ROW	XAC	OPC
AUT	EUZ	ETH	ROW
BEL	EUZ	KEN	ROW
BGR	ROW	MDG	ROW
HRV	ROW	MWI	ROW
CYP	EUZ	MUS	ROW
CZE	ROW	MOZ	ROW
DNK	OEC	RWA	ROW
EST	EUZ	TZA	ROW
FIN	EUZ	UGA	ROW
FRA	FRA	ZMB	ROW
DEU	DEU	ZWE	ROW
GRC	EUZ	XEC	ROW
HUN	ROW	BWA	ROW
IRL	EUZ	NAM	ROW
ITA	ITA	ZAF	ZAF
LVA	ROW	XSC	ROW
LTU	ROW	XTW	ROW
LUX	EUZ		

Source: The G-Cubed Model (GGG6G_v176).

Supplementary Annexure 2: Concordance between GTAP and G-Cubed Sectors

	Code	Description	G-Cubed Sector
1	PDR	Paddy Rice	Agriculture
2	WHT	Wheat	Agriculture
3	GRO	Other Cereal Grains	Agriculture
4	V_F	Vegetables, Fruit, Nuts	Agriculture
5	OSD	Oil Seeds	Agriculture
6	C_B	Sugar Cane, Sugar Beet	Agriculture
7	PFB	Plant-based Fibers	Agriculture
8	OCR	Other Crops	Agriculture
9	CTL	Bovine Cattle, Sheep, Goats, and Horses	Agriculture
10	OAP	Other Animal Products	Agriculture
11	RMK	Raw Milk	Agriculture
12	WOL	Wool, and Silk-worm Cocoons	Agriculture
13	FRS	Forestry	Agriculture
14	FSH	Fishing	Agriculture
15	COA	Coal	Mining
16	OIL	Oil	Energy
17	GAS	Gas	Energy
18	OXT	Extraction of Other Minerals	Mining
19	CMT	Bovine Meat Products	Non-Durable Manufacturing
20	OMT	Other Meat Products	Non-Durable Manufacturing
21	VOL	Vegetable Oils and Fats	Non-Durable Manufacturing
22	MIL	Dairy Products	Non-Durable Manufacturing
23	PCR	Processed Rice	Non-Durable Manufacturing
24	SGR	Sugar	Non-Durable Manufacturing
25	OFD	Other Food Products	Non-Durable Manufacturing
26	B_T	Beverages and Tobacco Products	Non-Durable Manufacturing
27	TEX	Textiles	Non-Durable Manufacturing
28	WAP	Wearing apparel	Non-Durable Manufacturing
29	LEA	Leather Products	Non-Durable Manufacturing
30	LUM	Wood Products	Agriculture
31	PPP	Paper Products, and Publishing	Non-Durable Manufacturing
32	P_C	Petroleum, and Coal Products	Energy
33	CHM	Chemical Products	Non-Durable Manufacturing
34	BPH	Basic Pharmaceutical Products	Non-Durable Manufacturing
35	RPP	Rubber and Plastic Products	Non-Durable Manufacturing
36	NMM	Other Mineral Products	Durable Manufacturing
37	I_S	Ferrous Metals	Durable Manufacturing
38	NFM	Other Metals	Durable Manufacturing
39	FMP	Metal Products	Durable Manufacturing
40	ELE	Computer, Electronic, and Optical Products	Durable Manufacturing
41	EEQ	Electrical Equipment	Durable Manufacturing
42	OME	Other Machinery and Equipment	Durable Manufacturing
43	MVH	Motor Vehicles and Parts	Durable Manufacturing
44	OTN	Other Transport Equipment	Durable Manufacturing
45	OMF	Other Manufactures	Durable Manufacturing
46	ELY	Electricity	Energy
47	GDT	Gas Manufacture and Distribution	Energy
48	WTR	Water	Services
49	CNS	Construction	Services
50	TRD	Trade	Services
51	AFS	Accommodation, Food, and Service Activities	Services
52	OTP	Other Transport	Services
53	WTP	Water Transport	Services
54	ATP	Air Transport	Services
55	WHS	Warehousing and Support Activities	Services
56	CMN	Communication	Services
57	OFI	Other Financial Services	Services
58	INS	Insurance	Services
59	RSA	Real Estate Activities	Services
60	OBS	Other Business Services	Services
61	ROS	Recreational and Other Services	Services
62	OSG	Public Administration and Defense	Services
63	EDU	Education	Services
64	HHT	Human Health and Social Work Activities	Services
65	DWE	Dwellings	Services

Source: The G-Cubed Model (GGG6G_v176).

Supplementary Annexure 3: AMR-related Diseases and Corresponding Disease Groups

	Disease Group in the GRAM Study	AMR-related Disease Group from GBD Studies
1	Bacterial infections of the skin and subcutaneous systems	Bacterial skin diseases
2		Decubitus ulcer
3	Bloodstream infections	HIV/AIDS
4		Acute hepatitis
5		Maternal sepsis and other maternal infections
6		Neonatal sepsis and other neonatal infections
7	Diarrhoea	Diarrheal diseases
8	Endocarditis and other cardiac infections	Endocarditis
9	Gonorrhoea and chlamydia	Gonococcal infection
10		Chlamydial infection
11	Infections of bones, joints, and related organs	Musculoskeletal disorders
12	Lower respiratory infections and all related infections in the thorax	Lower respiratory infections
13		Upper respiratory infections
14	Meningitis and other bacterial central nervous system infections	Meningitis
15		Encephalitis
16	Peritoneal and intra-abdominal infections	Appendicitis
17	Tuberculosis	Tuberculosis
18	Typhoid fever, paratyphoid fever, and invasive non-typhoidal Salmonella	Typhoid and paratyphoid
19		Invasive Non-typhoidal Salmonella (iNTS)
20	Urinary tract infections and pyelonephritis	Urinary tract infections and interstitial nephritis

Source: Constructed by the Authors.

Supplementary Annexure 4: Pathogens Covered in the GRAM Study

	Pathogen
1	*Acinetobacter baumannii*
2	*Citrobacter spp.*
3	*Enterobacter spp.*
4	*Enterococcus faecalis*
5	*Enterococcus faecium*
6	*Escherichia coli*
7	*Group A Streptococcus*
8	*Group B Streptococcus*
9	*Haemophilus influenzae*
10	*Klebsiella pneumoniae*
11	*Morganella spp.*
12	*Mycobacterium tuberculosis*
13	*Neisseria gonorrhoeae*
14	*Non-typhoidal Salmonella*
15	*Other enterococci*
16	*Proteus spp.*
17	*Pseudomonas aeruginosa*
18	*Salmonella Paratyphi*
19	*Salmonella Typhi*
20	*Serratia spp.*
21	*Shigella spp.*
22	*Staphylococcus aureus*
23	*Streptococcus pneumoniae*

Source: Murray et al. (2022).

Supplementary Annexure 5: Antibiotic Classes Covered in the GRAM Study

	Antibiotic Class
1	Aminoglycosides
2	Aminopenicillin
3	Anti-pseudomonal penicillin/Beta-Lactamase inhibitors
4	Beta-lactam/Beta-lactamase inhibitors
5	Carbapenems
6	Extensive drug resistance in TB
7	Fluoroquinolones
8	Fourth-generation cephalosporins
9	Isoniazid mono-resistance
10	Macrolide
11	Methicillin
12	Multi-drug resistance excluding extensive drug resistance in TB
13	Multi-drug resistance in Salmonella Typhi and Paratyphi
14	Penicillin
15	Rifampicin mono-resistance
16	Third-generation cephalosporins
17	Trimethoprim-Sulfamethoxazole
18	Vancomycin

Source: Murray et al. (2022).

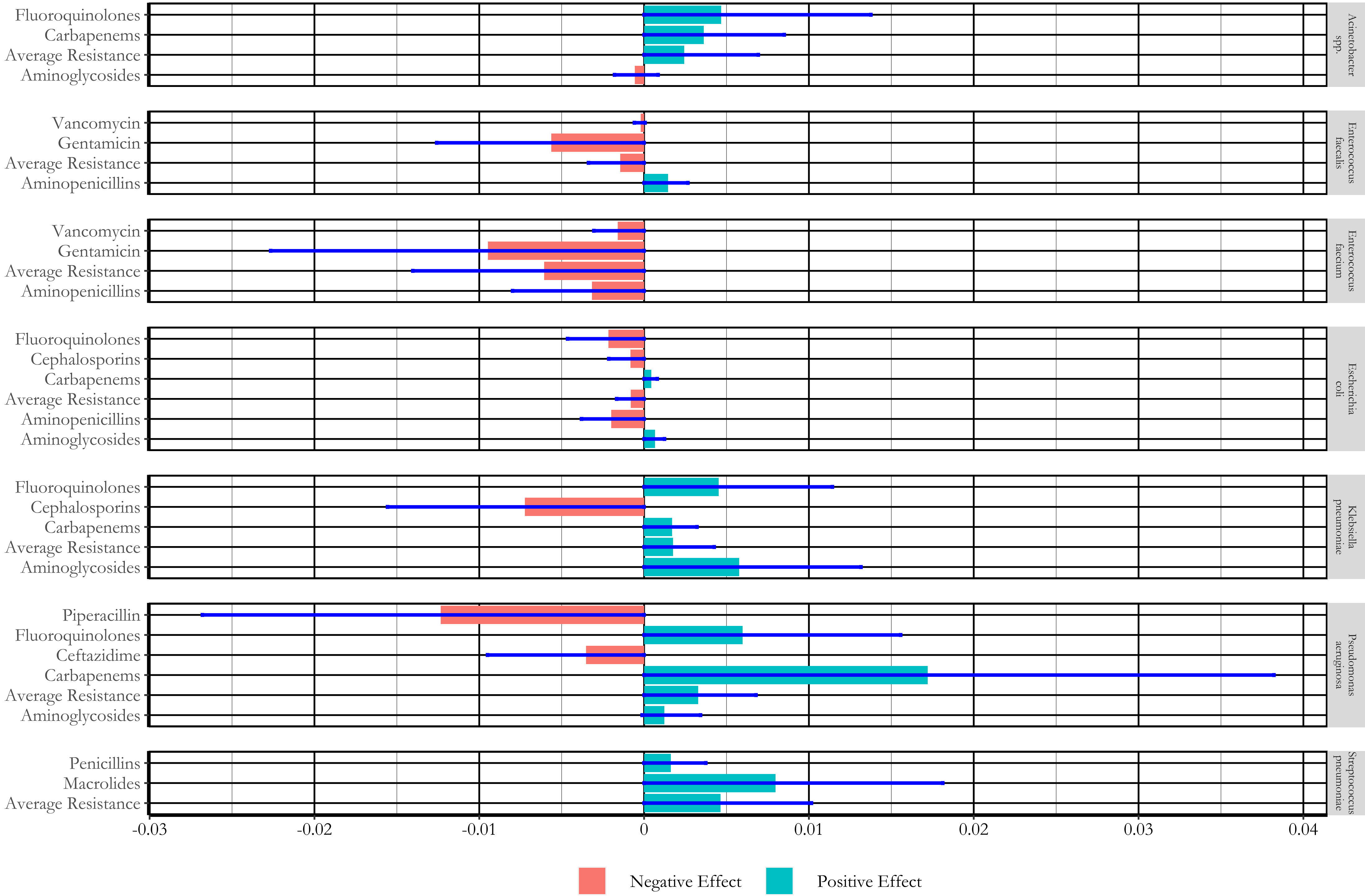
Supplementary Annexure 6: Antimicrobial Drug–Pathogen Combinations

	Pathogen	Antibiotic Class
1	*Acinetobacter baumannii*	Aminoglycosides
2	*Acinetobacter baumannii*	Anti-pseudomonal penicillin/Beta-Lactamase inhibitors
3	*Acinetobacter baumannii*	Beta-Lactam/Beta-lactamase inhibitors
4	*Acinetobacter baumannii*	Carbapenems
5	*Acinetobacter baumannii*	Fluoroquinolones
6	*Acinetobacter baumannii*	Fourth-generation cephalosporins
7	*Acinetobacter baumannii*	Third-generation cephalosporins
8	*Citrobacter spp.*	Aminoglycosides
9	*Citrobacter spp.*	Anti-pseudomonal penicillin/Beta-Lactamase inhibitors
10	*Citrobacter spp.*	Carbapenems
11	*Citrobacter spp.*	Fluoroquinolones
12	*Citrobacter spp.*	Fourth-generation cephalosporins
13	*Citrobacter spp.*	Third-generation cephalosporins
14	*Enterobacter spp.*	Aminoglycosides
15	*Enterobacter spp.*	Anti-pseudomonal penicillin/Beta-Lactamase inhibitors
16	*Enterobacter spp.*	Carbapenems
17	*Enterobacter spp.*	Fluoroquinolones
18	*Enterobacter spp.*	Fourth-generation cephalosporins
19	*Enterobacter spp.*	Trimethoprim-Sulfamethoxazole
20	*Enterococcus faecalis*	Fluoroquinolones
21	*Enterococcus faecalis*	Vancomycin
22	*Enterococcus faecium*	Fluoroquinolones
23	*Enterococcus faecium*	Vancomycin
24	*Escherichia coli*	Aminoglycosides
25	*Escherichia coli*	Aminopenicillin
26	*Escherichia coli*	Beta-Lactam/Beta-lactamase inhibitors
27	*Escherichia coli*	Carbapenems
28	*Escherichia coli*	Fluoroquinolones
29	*Escherichia coli*	Third-generation cephalosporins
30	*Escherichia coli*	Trimethoprim-Sulfamethoxazole
31	*Group A Streptococcus*	Macrolide
32	*Group B Streptococcus*	Fluoroquinolones
33	*Group B Streptococcus*	Macrolide
34	*Group B Streptococcus*	Penicillin
35	*Haemophilus influenzae*	Aminopenicillin
36	*Haemophilus influenzae*	Third-generation cephalosporins
37	*Klebsiella pneumoniae*	Aminoglycosides
38	*Klebsiella pneumoniae*	Beta-Lactam/Beta-lactamase inhibitors
39	*Klebsiella pneumoniae*	Carbapenems
40	*Klebsiella pneumoniae*	Fluoroquinolones
41	*Klebsiella pneumoniae*	Third-generation cephalosporins
42	*Klebsiella pneumoniae*	Trimethoprim-Sulfamethoxazole
43	*Morganella spp.*	Fluoroquinolones
44	*Morganella spp.*	Fourth-generation cephalosporins
45	*Morganella spp.*	Third-generation cephalosporins
46	*Mycobacterium tuberculosis*	Extensive drug resistance in TB
47	*Mycobacterium tuberculosis*	Isoniazid mono-resistance
48	*Mycobacterium tuberculosis*	Multi-drug resistance excluding extensive drug resistance in TB
49	*Mycobacterium tuberculosis*	Rifampicin mono-resistance
50	*Neisseria gonorrhoeae*	Fluoroquinolones
51	*Neisseria gonorrhoeae*	Third-generation cephalosporins
52	*Non-typhoidal Salmonella*	Fluoroquinolones
53	*Other enterococci*	Fluoroquinolones

54	*Other enterococci*	Vancomycin
55	*Proteus spp.*	Aminoglycosides
56	*Proteus spp.*	Aminopenicillin
57	*Proteus spp.*	Fluoroquinolones
58	*Proteus spp.*	Third-generation cephalosporins
59	*Proteus spp.*	Trimethoprim-Sulfamethoxazole
60	*Pseudomonas aeruginosa*	Aminoglycosides
61	*Pseudomonas aeruginosa*	Anti-pseudomonal penicillin/Beta-Lactamase inhibitors
62	*Pseudomonas aeruginosa*	Carbapenems
63	*Pseudomonas aeruginosa*	Fluoroquinolones
64	*Pseudomonas aeruginosa*	Fourth-generation cephalosporins
65	*Pseudomonas aeruginosa*	Third-generation cephalosporins
66	*Salmonella Paratyphi*	Fluoroquinolones
67	*Salmonella Paratyphi*	Multi-drug resistance in Salmonella Typhi and Paratyphi
68	*Salmonella Typhi*	Fluoroquinolones
69	*Salmonella Typhi*	Multi-drug resistance in Salmonella Typhi and Paratyphi
70	*Serratia spp.*	Aminoglycosides
71	*Serratia spp.*	Anti-pseudomonal penicillin/Beta-Lactamase inhibitors
72	*Serratia spp.*	Carbapenems
73	*Serratia spp.*	Fluoroquinolones
74	*Serratia spp.*	Fourth-generation cephalosporins
75	*Serratia spp.*	Third-generation cephalosporins
76	*Shigella spp.*	Fluoroquinolones
77	*Staphylococcus aureus*	Fluoroquinolones
78	*Staphylococcus aureus*	Macrolide
79	*Staphylococcus aureus*	Methicillin
80	*Staphylococcus aureus*	Trimethoprim-Sulfamethoxazole
81	*Staphylococcus aureus*	Vancomycin
82	*Streptococcus pneumoniae*	Beta-Lactam/Beta-lactamase inhibitors
83	*Streptococcus pneumoniae*	Carbapenems
84	*Streptococcus pneumoniae*	Fluoroquinolones
86	*Streptococcus pneumoniae*	Macrolide
86	*Streptococcus pneumoniae*	Penicillin
87	*Streptococcus pneumoniae*	Third-generation cephalosporins
88	*Streptococcus pneumoniae*	Trimethoprim-Sulfamethoxazole

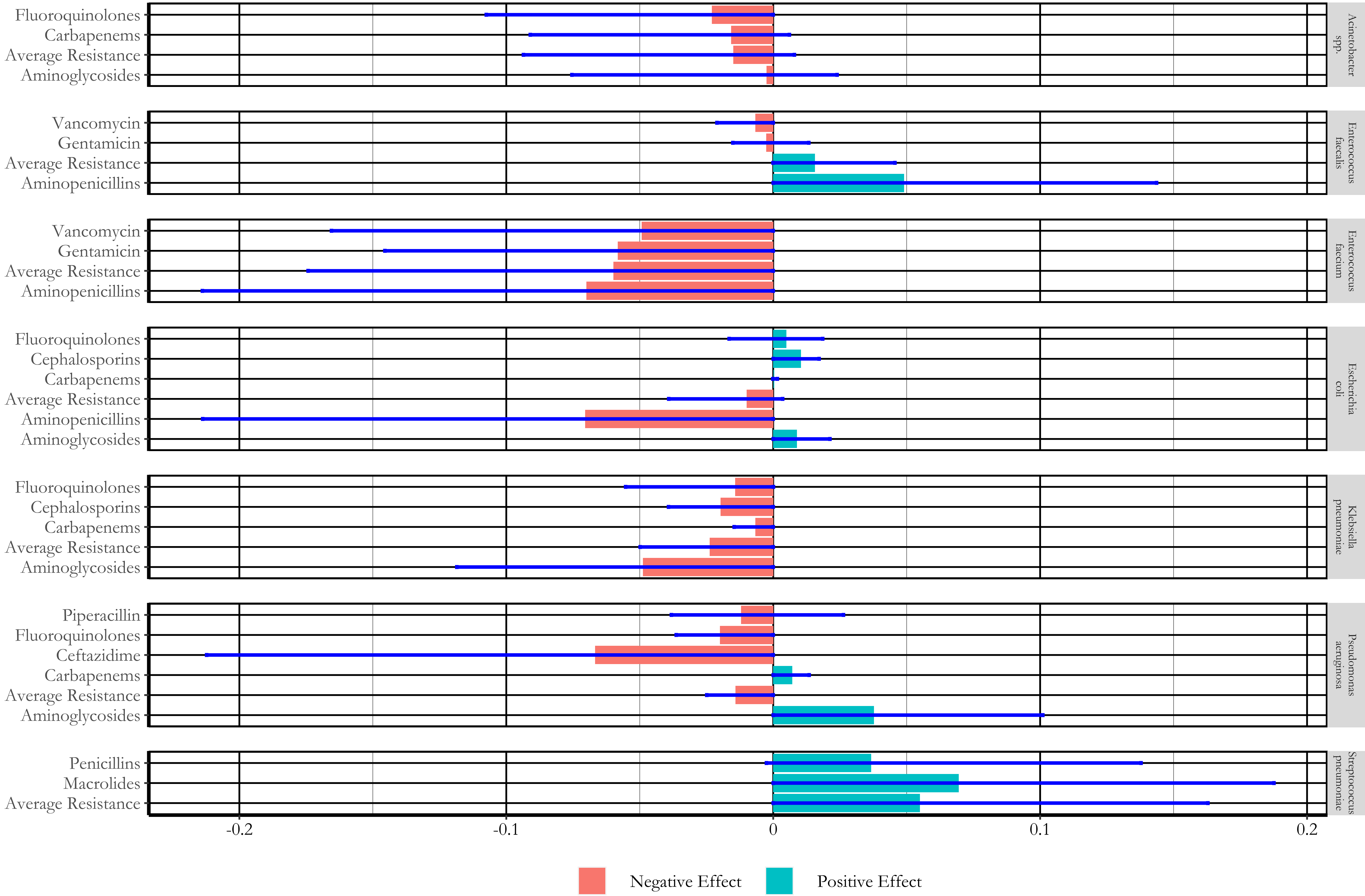
Source: Constructed by the Authors.

Supplementary Annexure 7A: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Growth in Antimicrobial Consumption



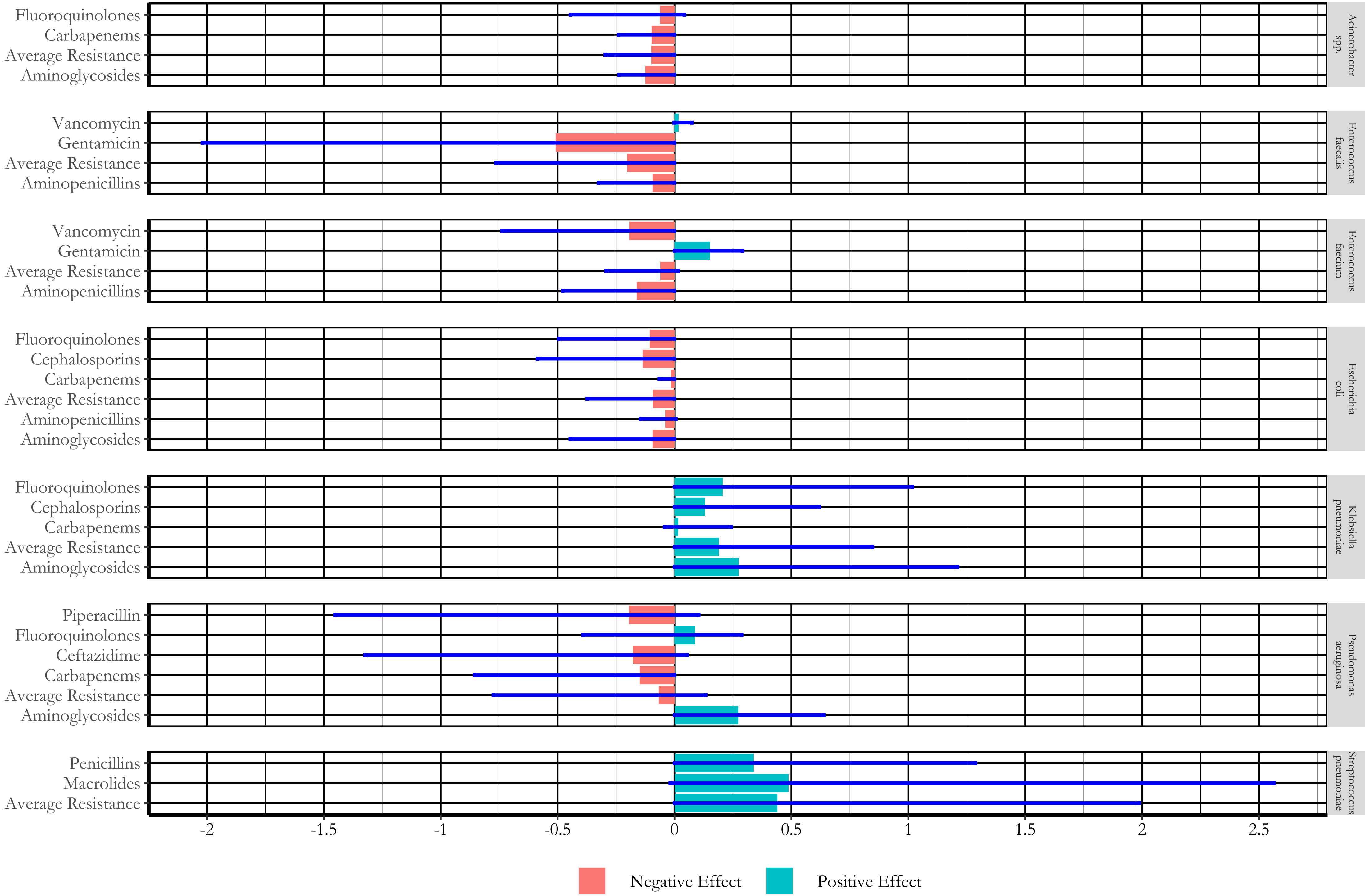
Source: Fernando (2023b).

Supplementary Annexure 7B: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Growth in GDP per capita



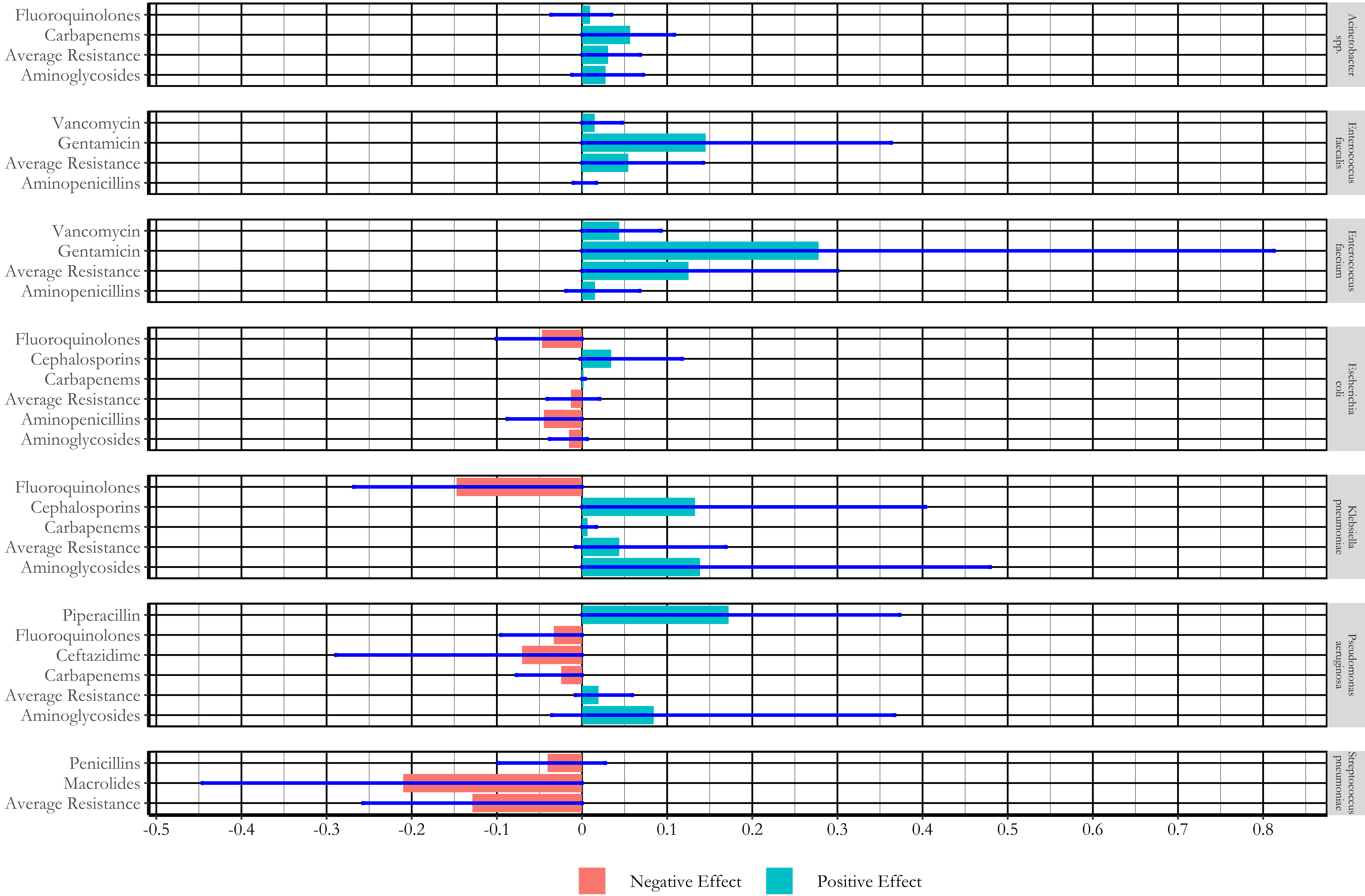
Source: Fernando (2023b).

Supplementary Annexure 7C: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Growth in Population



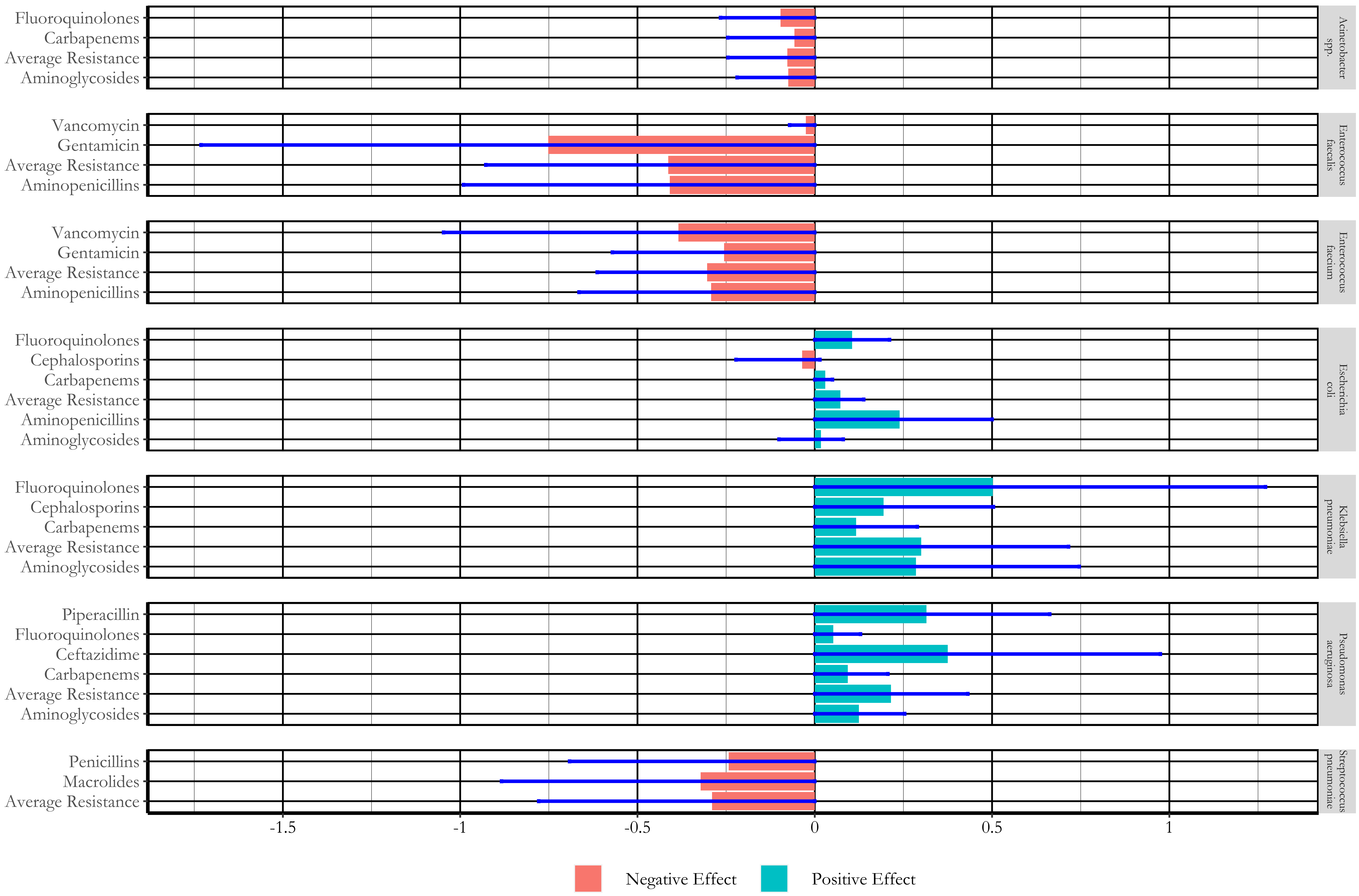
Source: Fernando (2023b).

Supplementary Annexure 7D: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Growth in Old-age Dependency Ratio



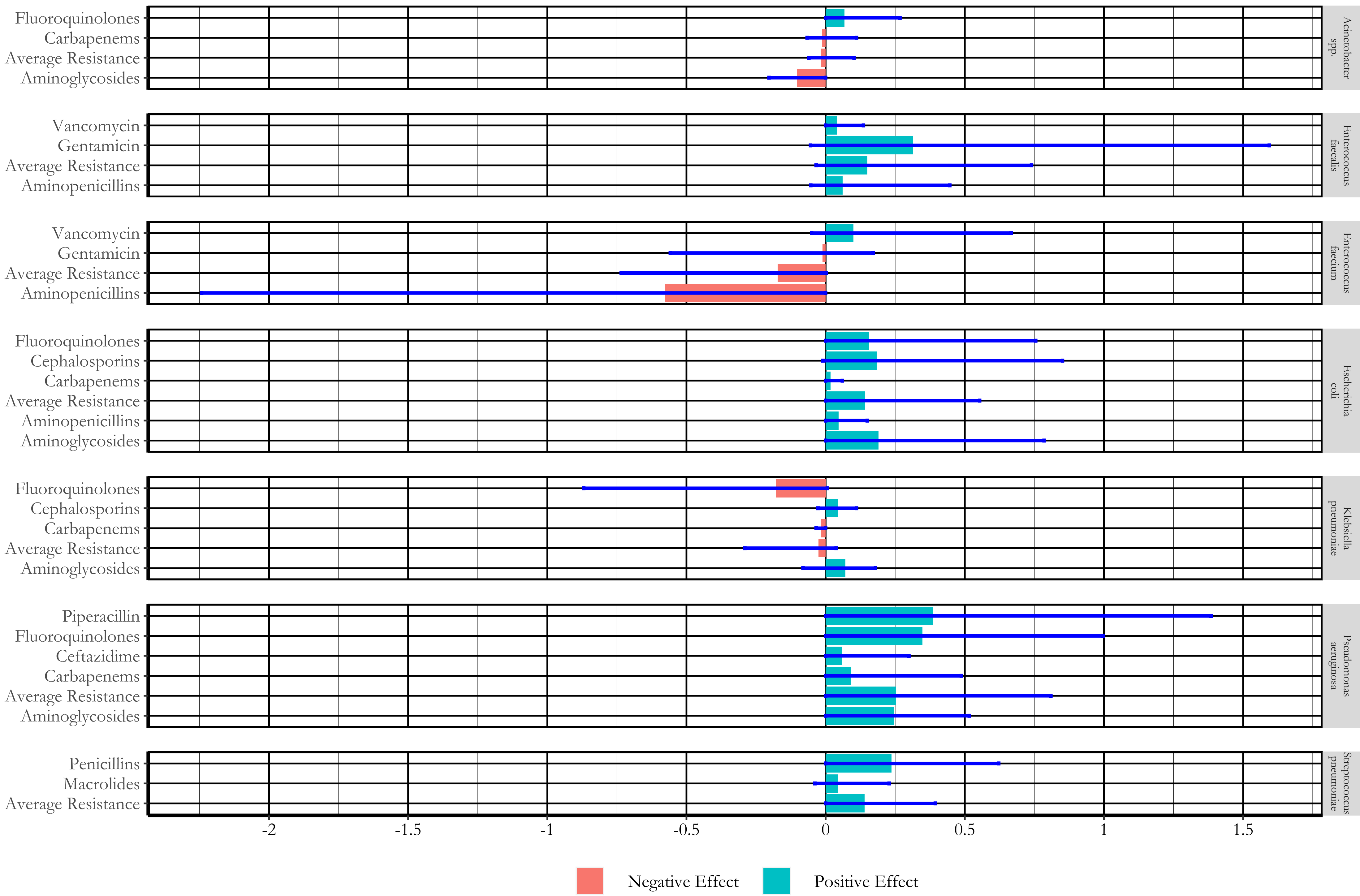
Source: Fernando (2023b).

Supplementary Annexure 7E: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Growth in Urban Population



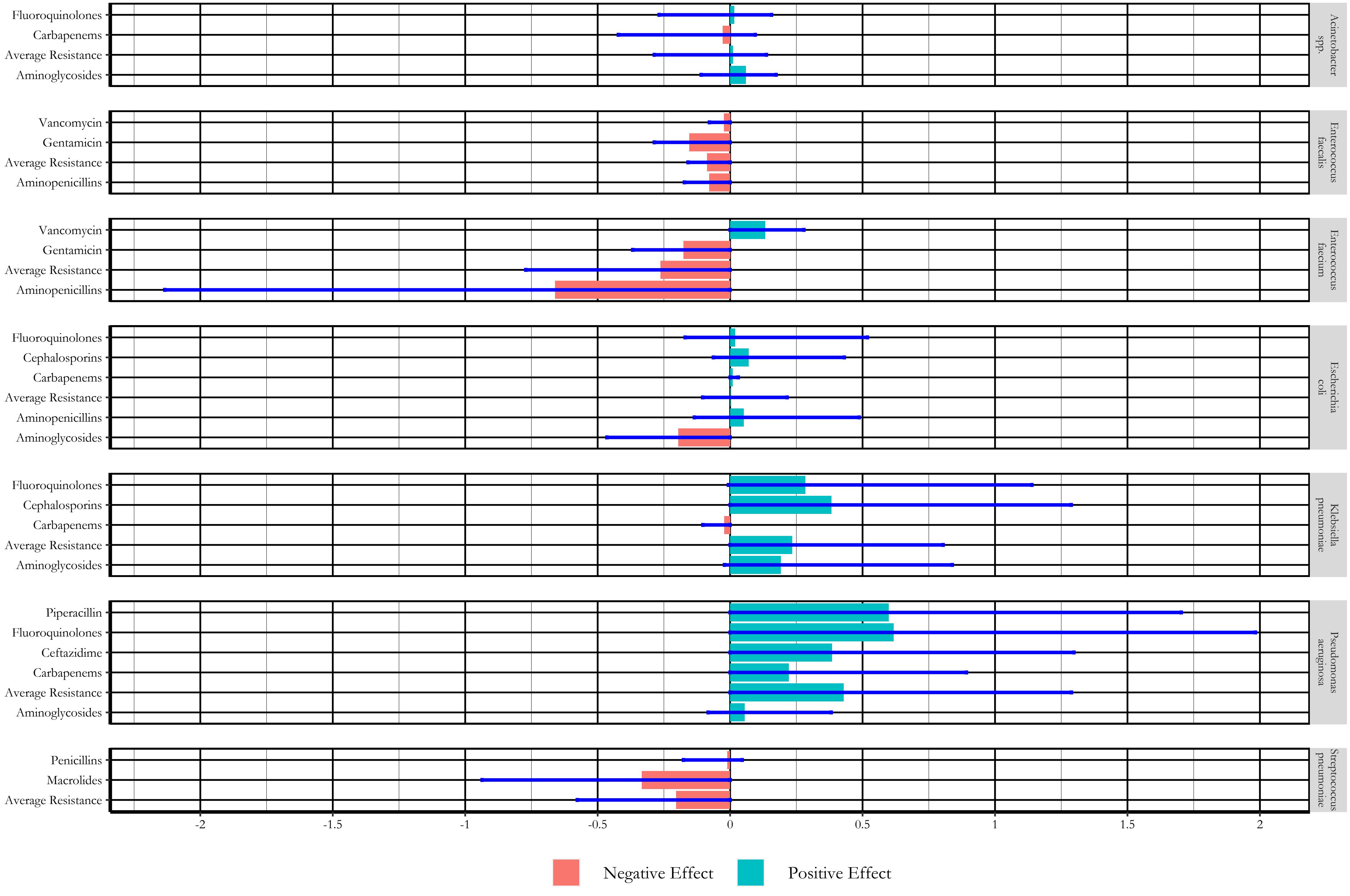
Source: Fernando (2023b).

Supplementary Annexure 7F: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Growth in Population Density



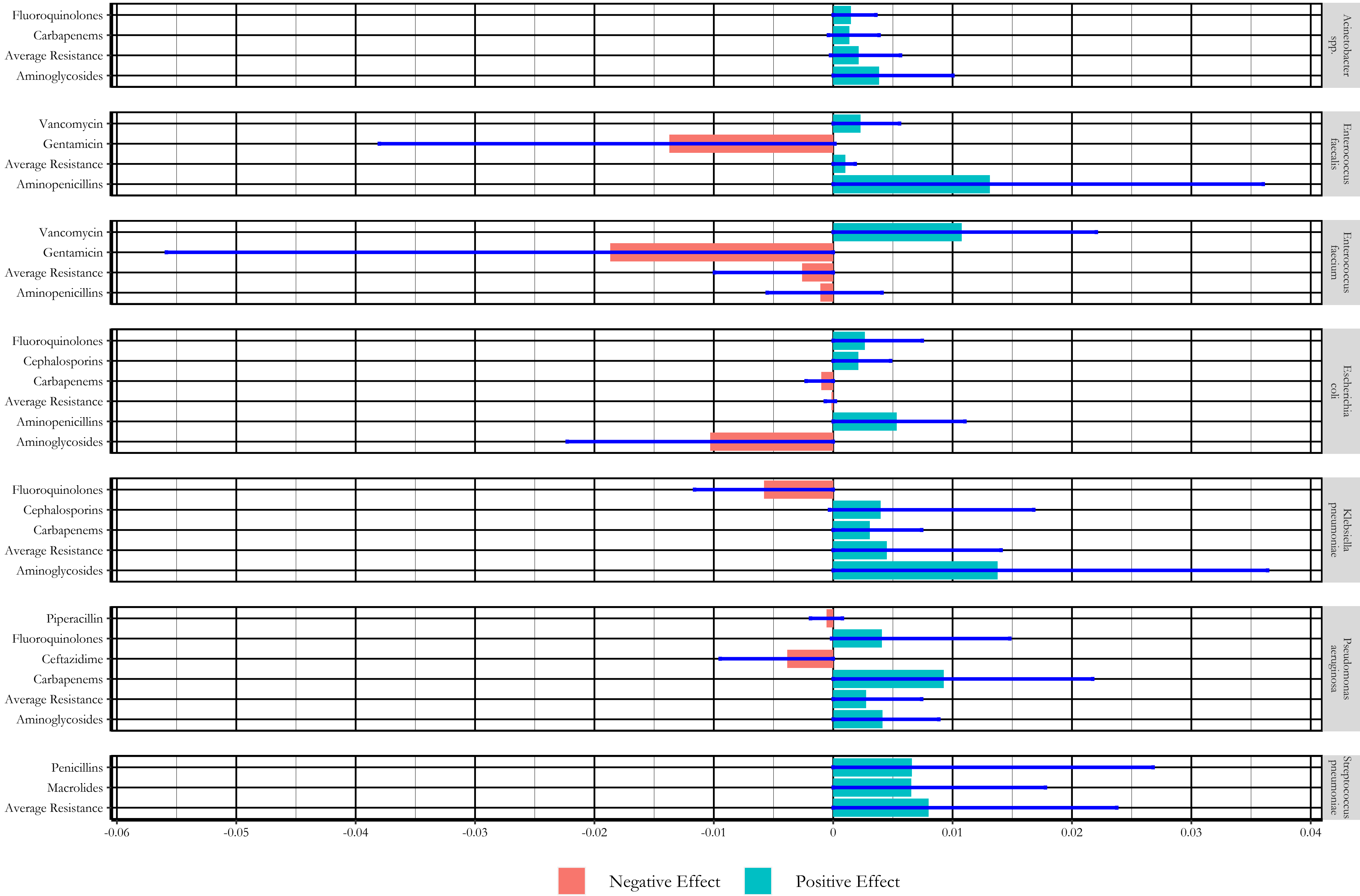
Source: Fernando (2023b).

Supplementary Annexure 7G: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Change in Mean Temperature from the Baseline



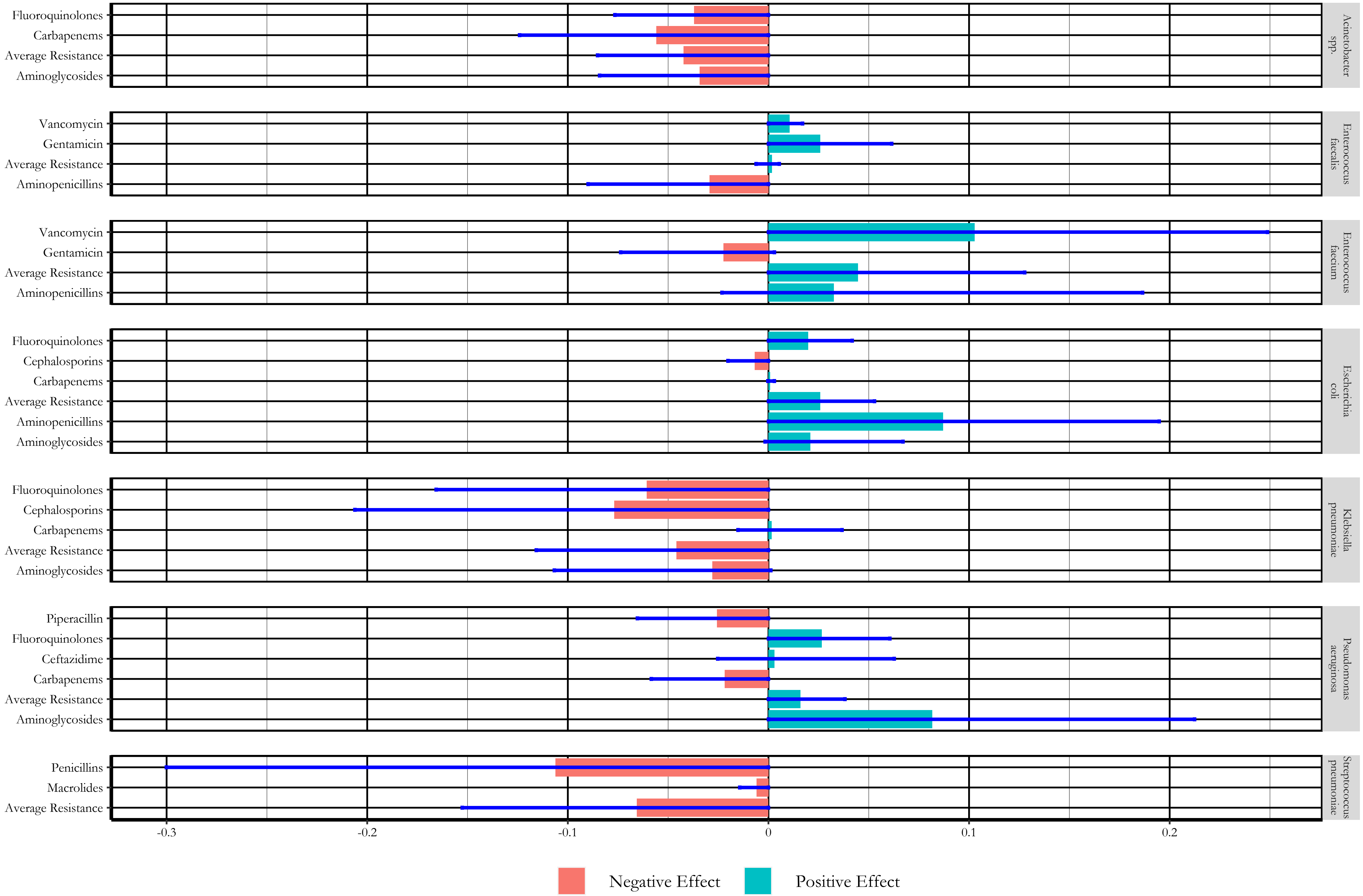
Source: Fernando (2023c).

Supplementary Annexure 7H: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Percentage Change in Precipitation from the Baseline



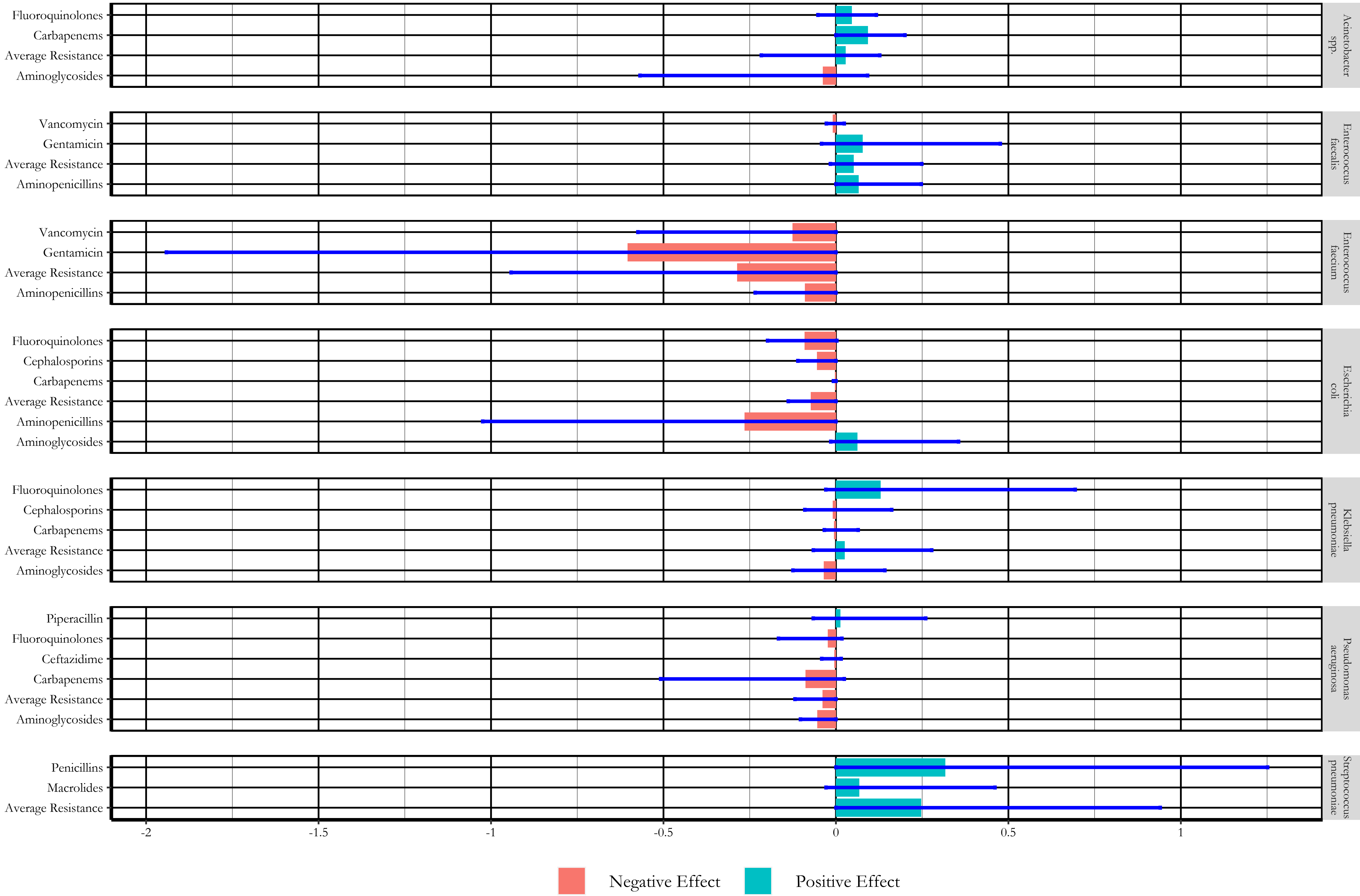
Source: Fernando (2023c).

Supplementary Annexure 7I: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Percentage Change in Relative Humidity from the Baseline



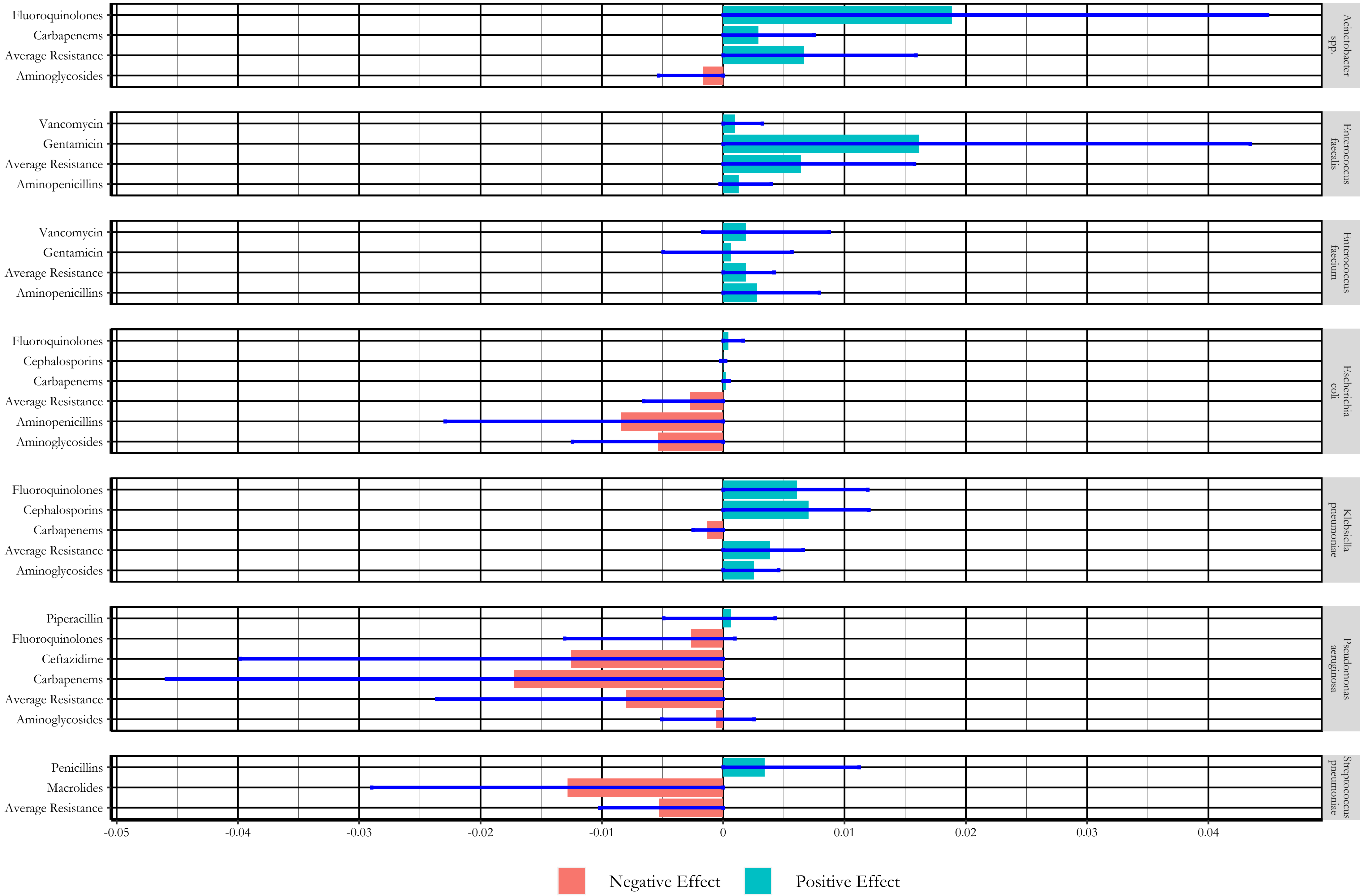
Source: Fernando (2023c).

Supplementary Annexure 7J: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Percentage Change in Extremely Warm Conditions during the Day from the Baseline



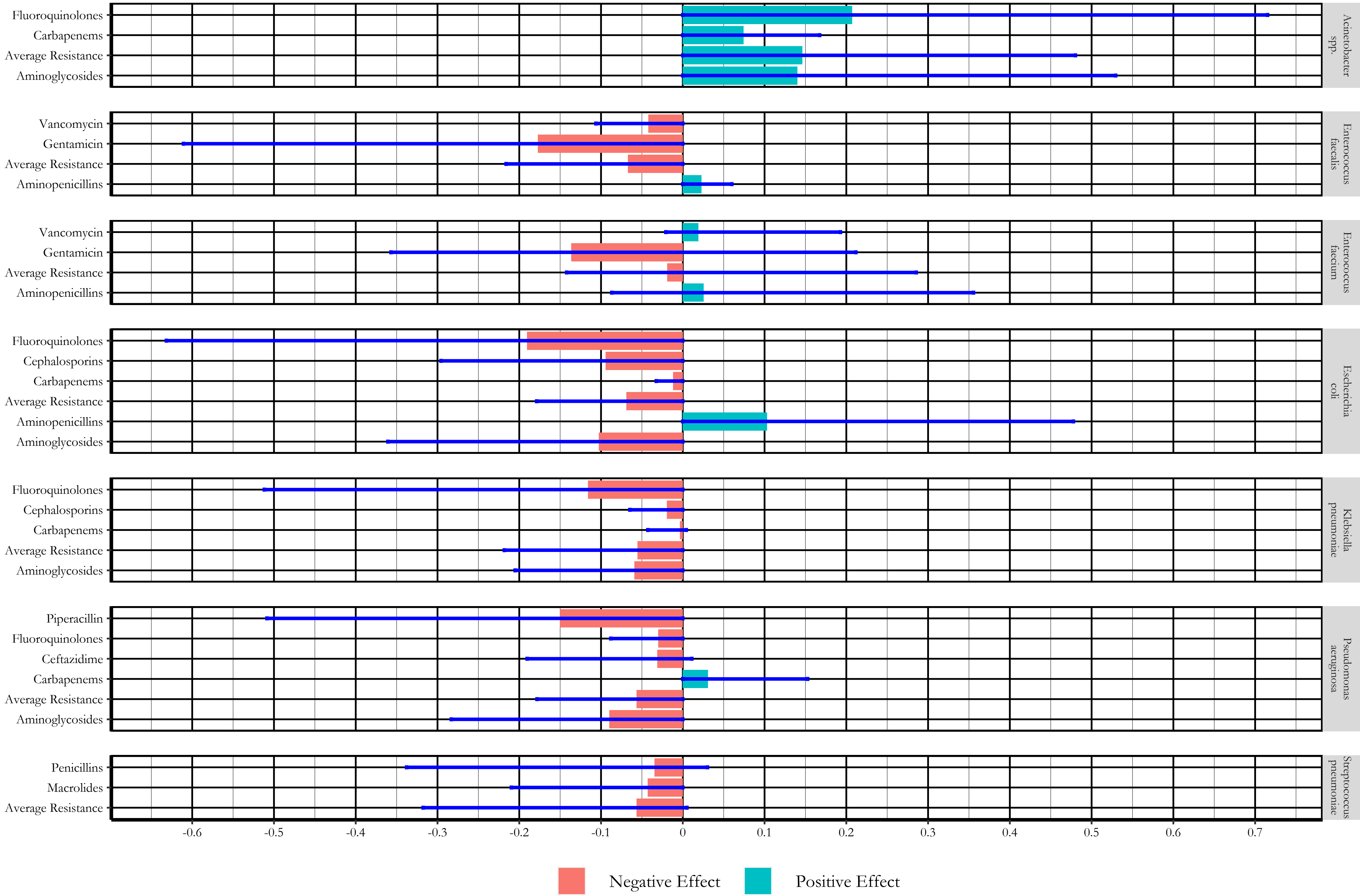
Source: Fernando (2023c).

Supplementary Annexure 7K: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Percentage Change in Extremely Cold Conditions during the Day from the Baseline



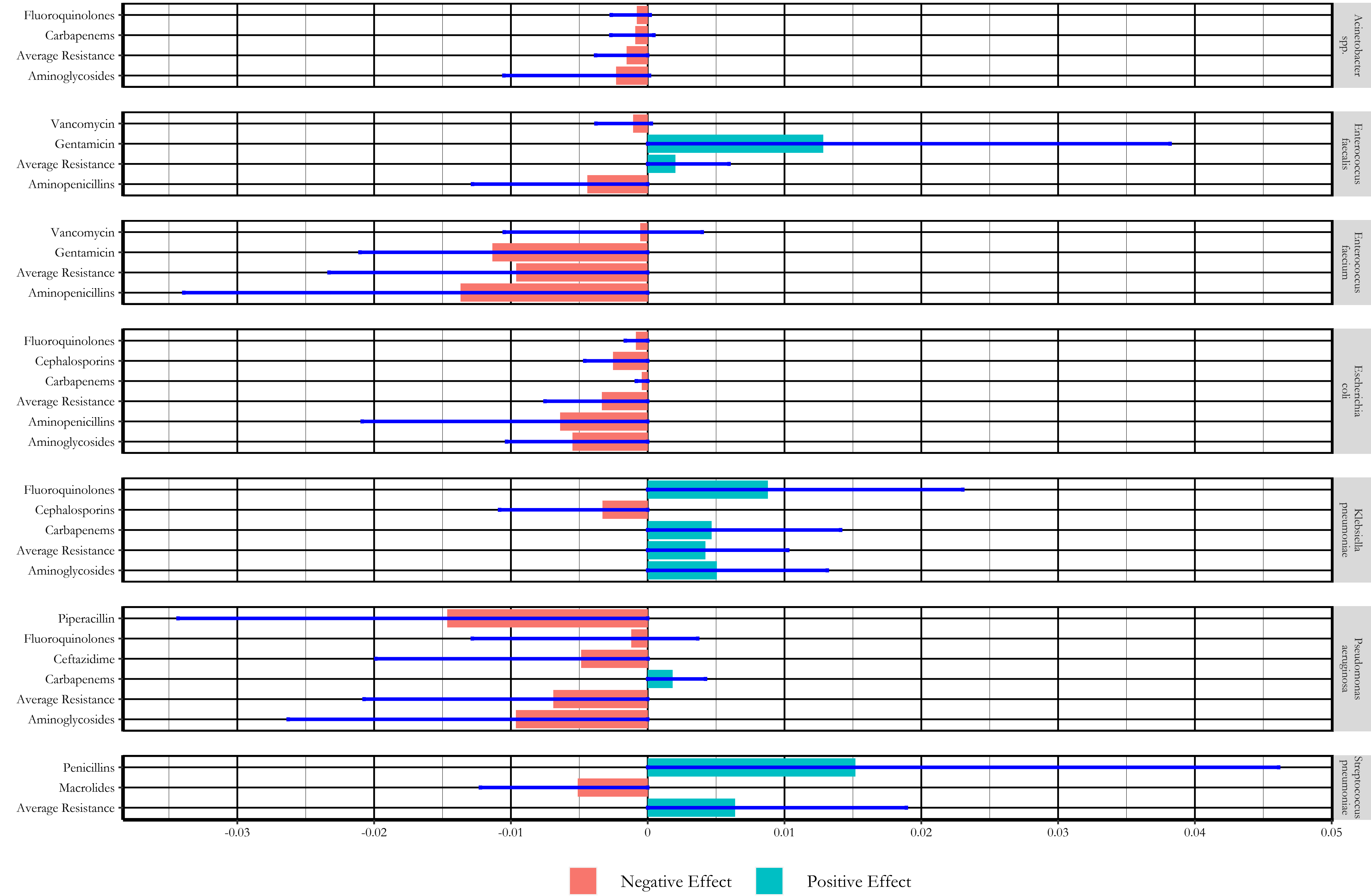
Source: Fernando (2023c).

Supplementary Annexure 7L: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Percentage Change in Extremely Warm Conditions during the Night from the Baseline



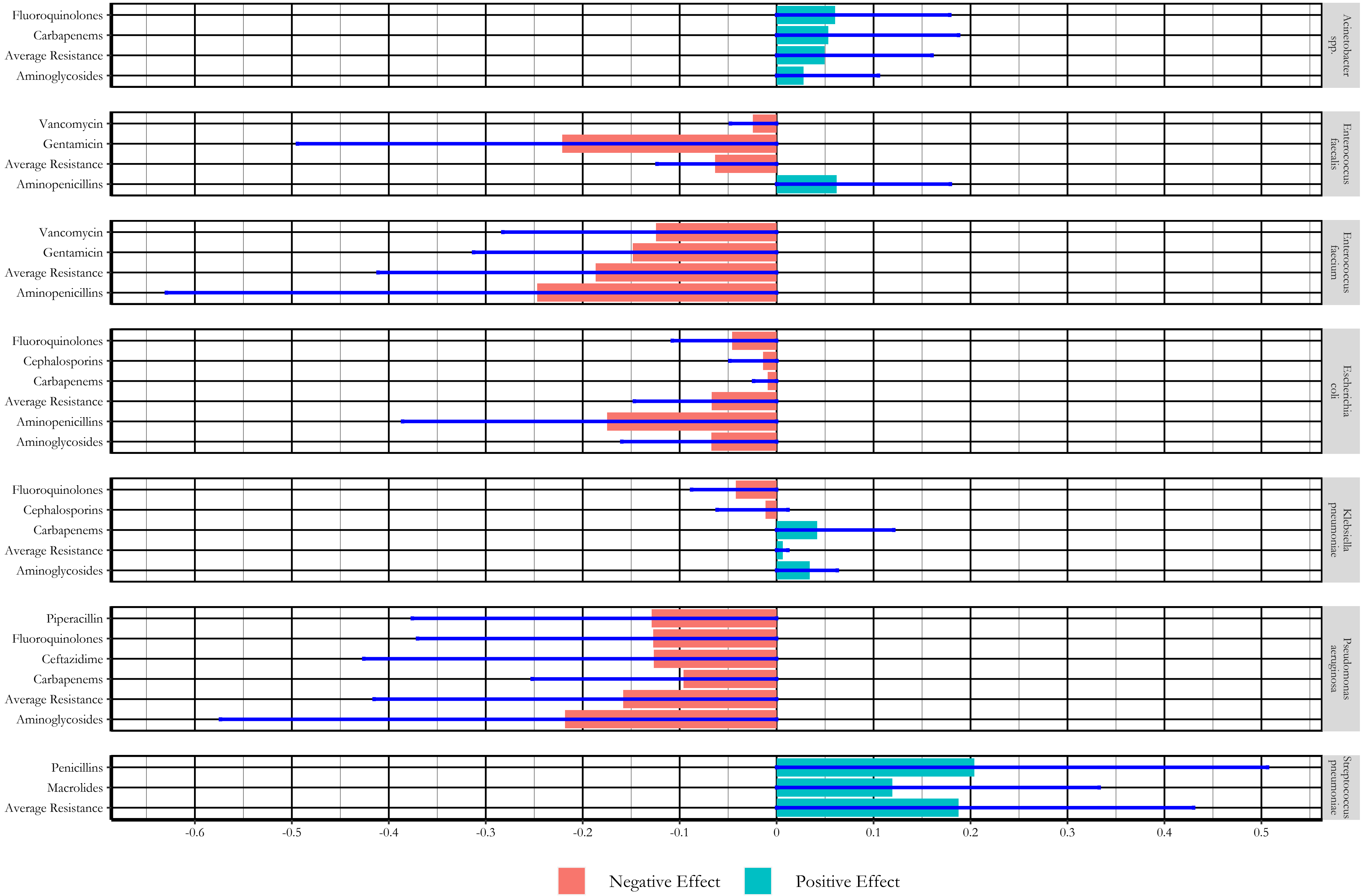
Source: Fernando (2023c).

Supplementary Annexure 7M: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Percentage Change in Extremely Cold Conditions during the Night from the Baseline



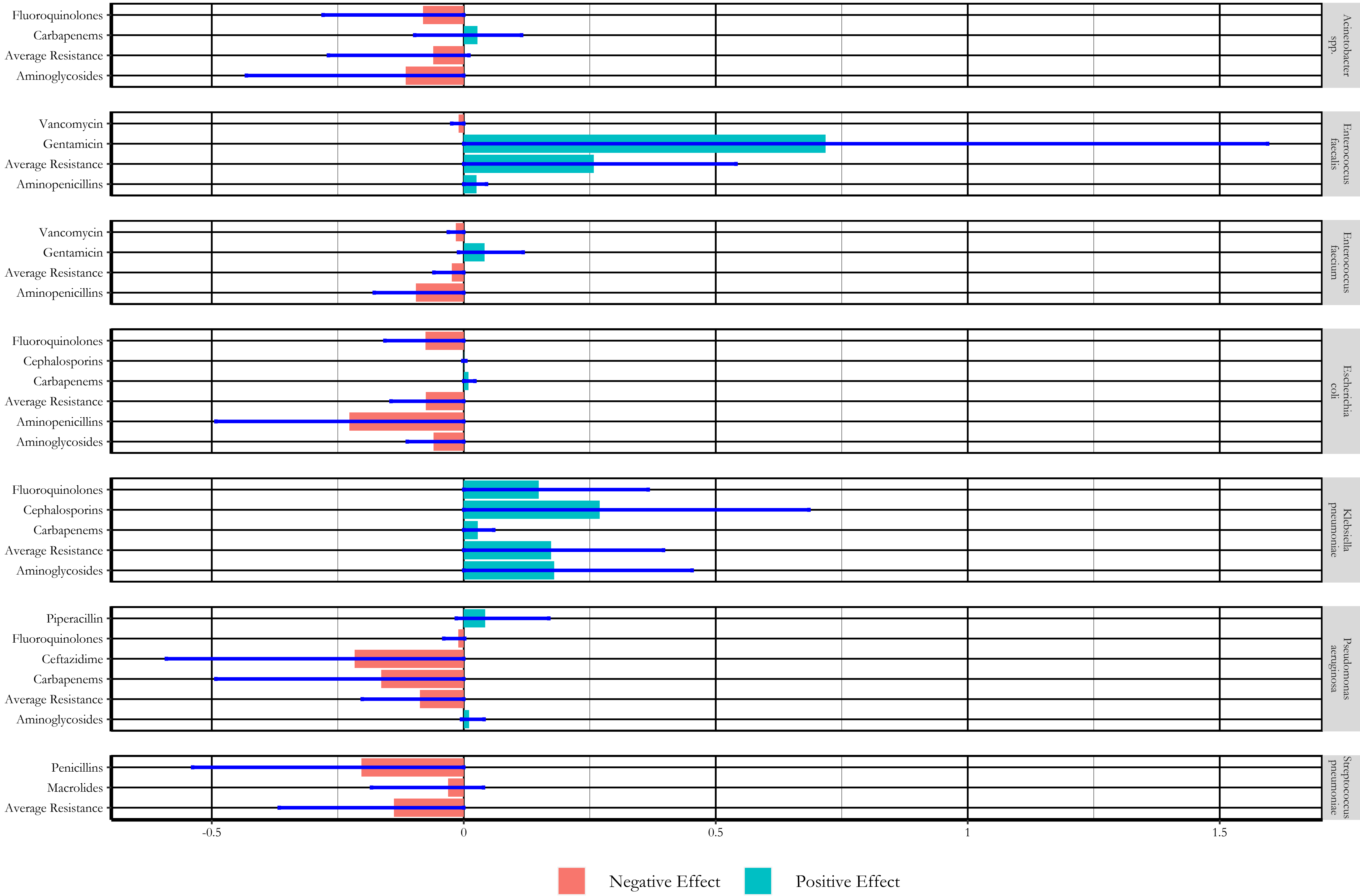
Source: Fernando (2023c).

Supplementary Annexure 7N: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Percentage Change in Extremely Dry Conditions from the Baseline



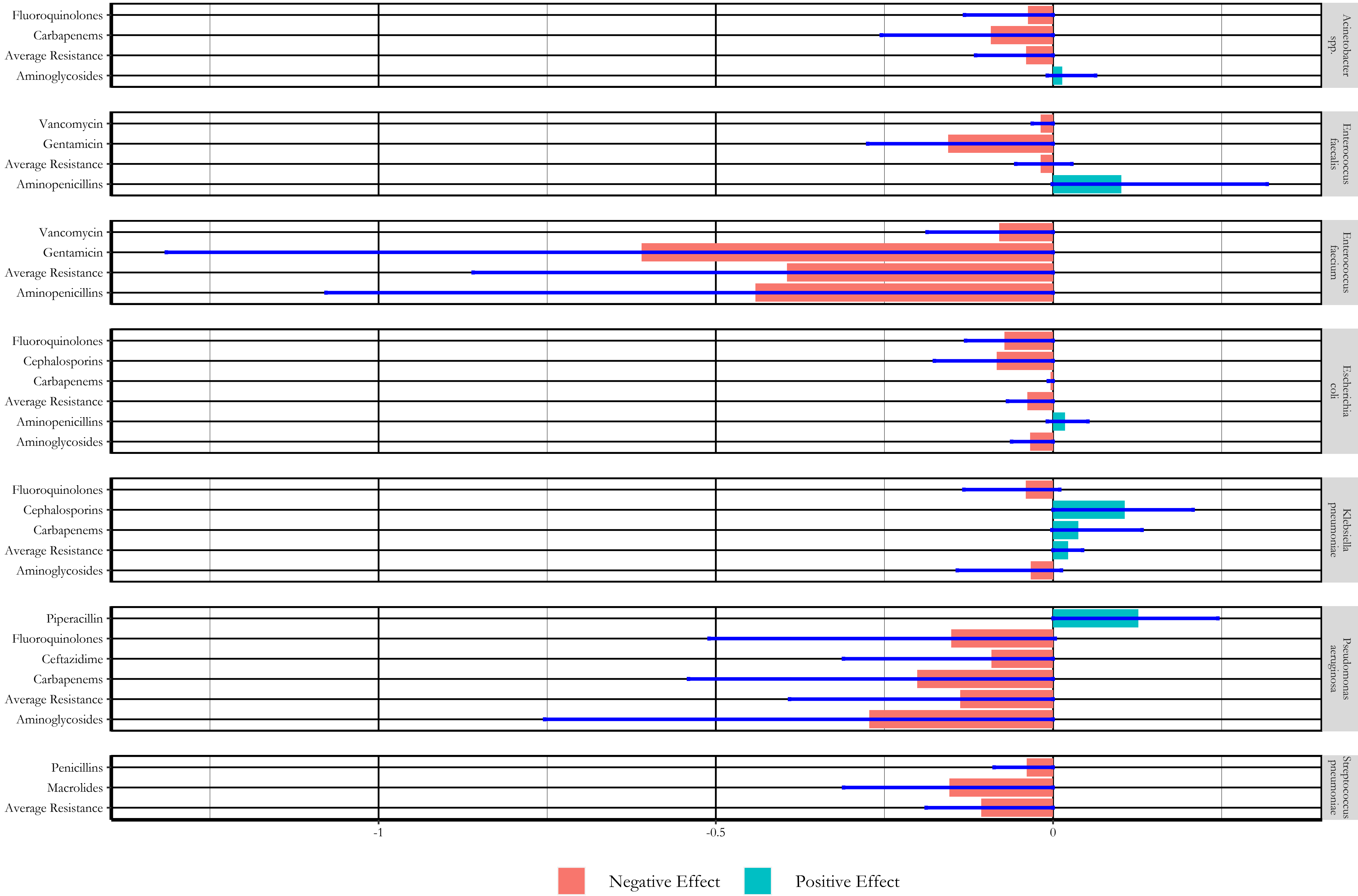
Source: Fernando (2023c).

Supplementary Annexure 7O: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Percentage Change in Extremely Wet Conditions from the Baseline

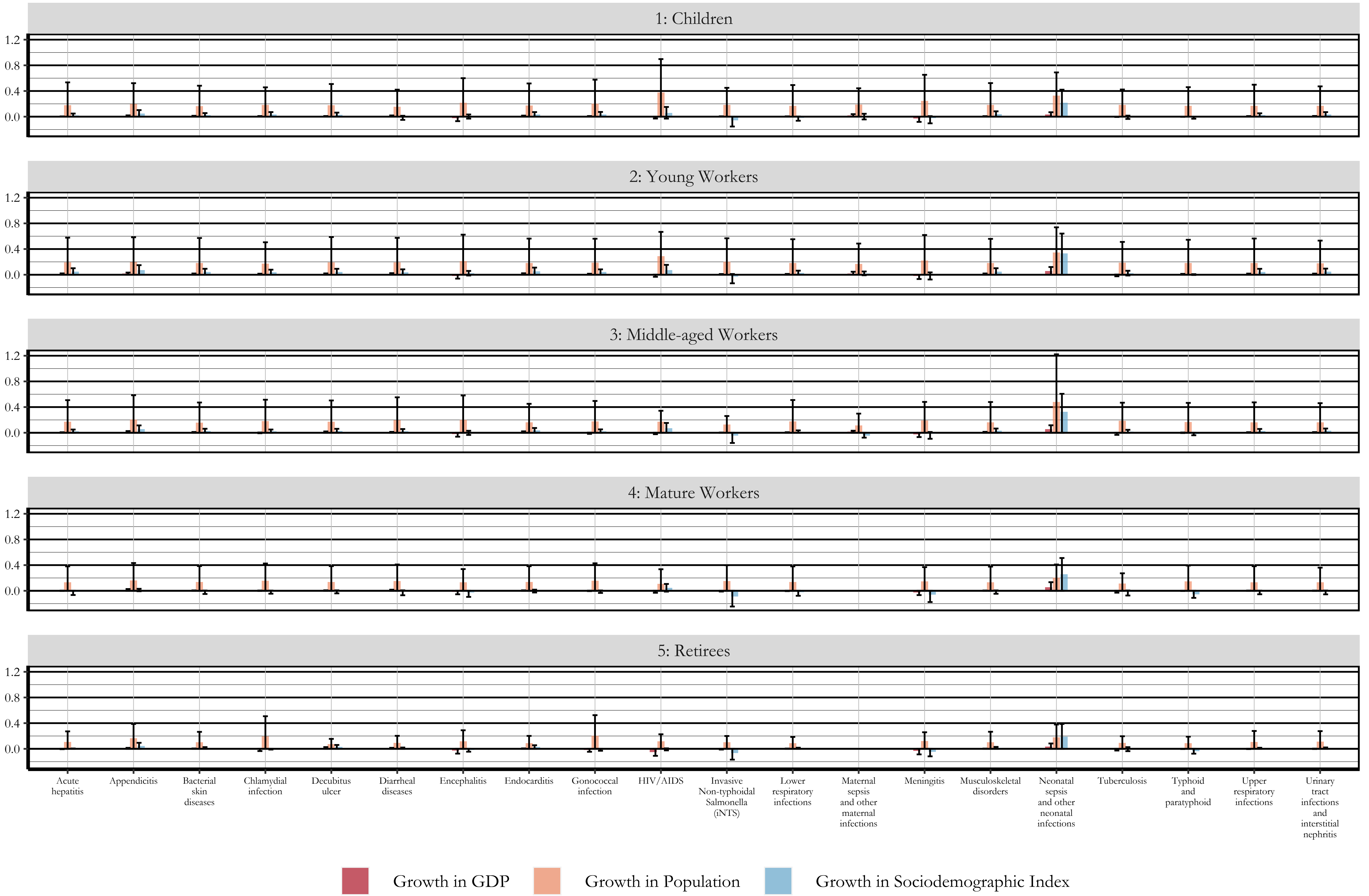


Source: Fernando (2023c).

Supplementary Annexure 7P: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Percentage Change in Extremely Windy Conditions from the Baseline

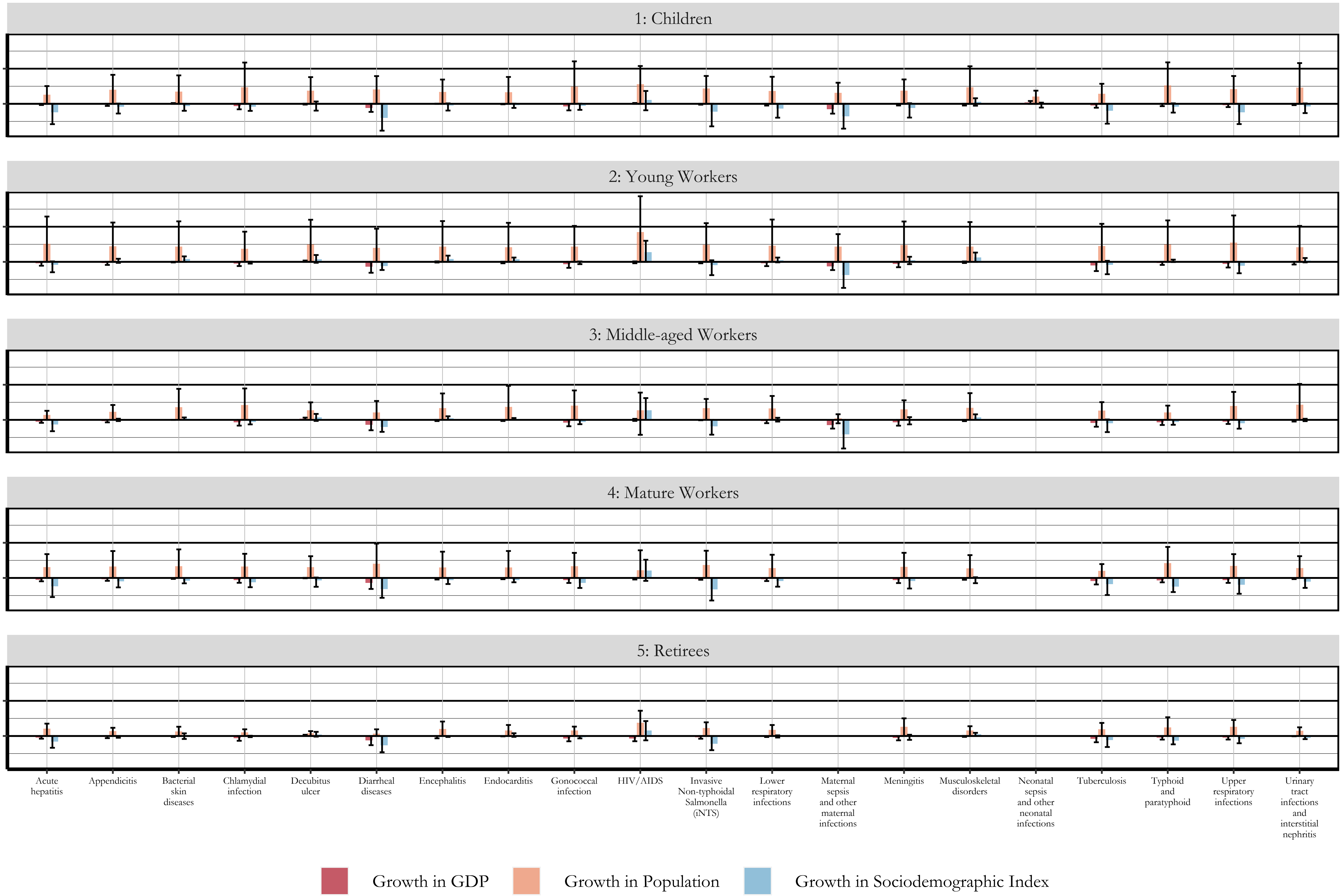


Source: Fernando (2023c).



Source: Authors' Calculations.

Supplementary Annexure 8B: Average Percentage Change in the Growth of Years of Life Lost due to Premature Mortality (YLLs) from 1990 to 2020



Source: Authors' Calculations.