

# ARC Centre of Excellence in Population Ageing Research

# Working Paper 2023/19

# Impact of Physical Climate Risks on Antimicrobial Resistance

Roshen Fernando

This paper can be downloaded without charge from the ARC Centre of Excellence in Population Ageing Research Working Paper Series available at <a href="http://www.cepar.edu.au">www.cepar.edu.au</a>



**Crawford School of Public Policy** 



**Centre for Applied Macroeconomic Analysis** 

# Impact of Physical Climate Risks on Antimicrobial Resistance

# CAMA Working Paper 61/2023 November 2023

#### **Roshen Fernando**

Centre for Applied Macroeconomic Analysis (CAMA), ANU Australian Research Centre of Excellence in Population Ageing Research (CEPAR), UNSW

# Abstract

Antimicrobial resistance (AMR) and climate change are interrelated complex challenges to humanity. We investigate the role of physical climate risks in the resistance growth of seven pathogens against twelve antimicrobials in 30 countries from 2000 to 2020. Our empirical assessment considers both chronic (gradual changes in temperature, precipitation, and relative humidity) and extreme climate risks (representing extreme precipitation events, droughts, heatwaves, coldwaves, and storms). We observe heterogeneous responses of different antimicrobial drug-pathogen combinations to physical climate risks. We observe that the physical climate risks could affect resistance growth more than antimicrobial consumption growth in some antimicrobial-drug pathogen combinations. We also illustrate stronger effects of extreme climate risks on resistance growth compared to chronic risks in some antimicrobial-drug pathogen combinations. We emphasize the importance of a broader exploration of factors affecting AMR evolution from a one-health approach and enhanced AMR surveillance, among others, to produce effective policy responses to tame AMR.

#### Keywords

Antimicrobial resistance, Infectious diseases, Climate Change, Econometrics, Machine Learning

#### **JEL Classification**

C51, C53, C54, C55, C68, F41, Q51, Q54

#### Address for correspondence:

(E) cama.admin@anu.edu.au

#### ISSN 2206-0332

<u>The Centre for Applied Macroeconomic Analysis</u> in the Crawford School of Public Policy has been established to build strong links between professional macroeconomists. It provides a forum for quality macroeconomic research and discussion of policy issues between academia, government and the private sector.

**The Crawford School of Public Policy** is the Australian National University's public policy school, serving and influencing Australia, Asia and the Pacific through advanced policy research, graduate and executive education, and policy impact.

# IMPACT OF PHYSICAL CLIMATE RISKS ON ANTIMICROBIAL RESISTANCE

#### Roshen Fernando<sup>1</sup>

Centre for Applied Macroeconomic Analysis (CAMA), The Australian National University Australian Research Centre of Excellence in Population Ageing Research (CEPAR)

#### ABSTRACT

Antimicrobial resistance (AMR) and climate change are interrelated complex challenges to humanity. We investigate the role of physical climate risks in the resistance growth of seven pathogens against twelve antimicrobials in 30 countries from 2000 to 2020. Our empirical assessment considers both chronic (gradual changes in temperature, precipitation, and relative humidity) and extreme climate risks (representing extreme precipitation events, droughts, heatwaves, coldwaves, and storms). We observe heterogeneous responses of different antimicrobial drug-pathogen combinations to physical climate risks. We observe that the physical climate risks could affect resistance growth more than antimicrobial consumption growth in some antimicrobial-drug pathogen combinations. We also illustrate stronger effects of extreme climate risks on resistance growth compared to chronic risks in some antimicrobial-drug pathogen combinations. We emphasize the importance of a broader exploration of factors affecting AMR evolution from a one-health approach and enhanced AMR surveillance, among others, to produce effective policy responses to tame AMR.

JEL Codes: C51, C53, C54, C55, C68, F41, Q51, Q54

Keywords: Antimicrobial resistance, Infectious diseases, Climate Change, Econometrics, Machine Learning

<sup>&</sup>lt;sup>1</sup> I am grateful to Professor Warwick McKibbin, Dr. Yixiao Zhou, and Dr. Weifeng Liu for their generous comments. I thank the Australian National University and the Australian Research Council Centre of Excellence in Population Ageing Research (ARC CEPAR) (CE170100005) for their funding to support my Ph.D. research. I am also thankful to the European Centre for Disease Prevention and Control for providing me with the data on antimicrobial consumption and resistance to be used for this research.

#### **1 INTRODUCTION**

Climate change and antimicrobial resistance (AMR) are two complex challenges to humanity. On the one hand, climate change, unequivocally driven by anthropogenic factors, such as greenhouse gas emissions and land-use changes, continues to disrupt the natural and social systems. The Intergovernmental Panel on Climate Change (IPCC), in its sixth Assessment Report (IPCC 2023), anticipates the future effects of climate change to multiply without substantial mitigation and irreversible effects on natural and social systems under continued warming. Conversely, AMR has been caused by subop-timal antimicrobial consumption in both healthcare and agriculture settings. It has cost at least 1.27 million lives in 2019 and threatens the viability of harnessing decades of medical advancements to prevent and cure diseases. Failing antimicrobials also endanger global food security due to livestock reliance on them for prevention, control, and treatment of diseases and growth promotion.

Microorganisms are the life-support system of the biosphere, and their roles in nutrient cycling, plant and animal health, agriculture, and global food chains are critical for life on Earth. Climate change alters the atmosphere, biosphere, cryosphere, and oceans and increases the intensity and frequency of extreme events, such as extreme precipitation, droughts, wildfires, and tropical cyclones, disrupting ecosystems and economies. As climate change stresses the native life of microorganisms, the possibility to benefit from their desirable effects reduces, and their undesirable effects on humanity worsen. Increased disease incidence both in terrestrial and marine ecosystems and the development, spread, and persistence of resistant genes exemplify such undesirable effects on humanity due to climate impacts on microorganisms (Cavicchioli et al. 2019; Altizer et al. 2013).

Accordingly, AMR is affected by a multitude of factors in addition to antimicrobial consumption. Identifying these different AMR risk factors within our socioeconomic systems and those arising from microbial interactions with the broader natural environment is imperative to addressing AMR effectively. The quadripartite initiative on AMR, which brings together the Food and Agriculture Organization (FAO), the World Organization for Animal Health (OIE), and the United Nations Environment Program (UNEP), alongside the World Health Organization (WHO), recognizes the importance of such a one-health approach to addressing AMR (WHO 2023).

This paper estimates the impact of physical climate risks on AMR. The rest of the paper is organized as follows. Section 2 discusses in depth how climate change affects AMR. Section 3 explains the data and empirical estimation approach used to derive the impact of physical climate risks on AMR. Section 4 discusses the empirical estimates with reference to the current knowledge on the climate impacts on AMR and the pathogen characteristics. We also project the near-term AMR variation under two climate scenarios. Section 5 concludes by outlining the implications and future directions for research.

#### 2 CLIMATE CHANGE AND AMR

Climate change and microorganisms share a two-way relationship. On one hand, microorganisms are instrumental in regulating the climate, both via the production and consumption of greenhouse gases.

For example, as part of their nutrient uptakes in carbon, methane, and nitrogen cycles, they consume  $CO_2$  via chemoautotrophic growth,  $CH_4$  via methanotrophy, and  $N_2O$  via denitrification, respectively (Tiedje et al. 2022; Cavicchioli et al. 2019).

On the other hand, climate change affects microorganisms. Climate change directly affects microbial survival and functions. As for all other living beings, an optimum environment is essential for the survival of microorganisms. The optimum temperature, humidity, and pH level of the environment on which microorganisms rely for their substrate are the fundamental determinants of their survival and a broad range of microbial activities, including metabolism, growth, and reproduction.

The optimum temperature is vital for microorganisms to survive, conduct their metabolism, and grow, reproduce, and incubate. Thus, increasing temperature or global warming could favor microorganisms that have higher optimum temperature ranges (thermophiles). At the same time, prolonged cold conditions could incentivize microbial activities of those with lower optimum temperature ranges (psychrophiles). Prolonged temperatures could also alter the diversity and composition of microbial communities, resulting in the extinction of vulnerable microorganisms and alterations of genes and traits of those who survive (Portier et al. 2013).

Cloud cover also impacts microbial activities. Sunshine affects temperature regulation, oxygen consumption, nutrient uptake, enzymatic activities, protein inhibition, and DNA synthesis of microorganisms. Thus, microbial activities change with changes in exposure to sunshine. Accordingly, cloud cover changes are vital for determining microbial exposure to sunlight and temperature (Wu et al. 2016).

Precipitation is another crucial aspect of the climate affecting microbial survival and functions. Notably, lower precipitation favors the microorganisms that prefer dry or less humid climate conditions. Precipitation after prolonged droughts also incentivizes faster growth of microorganisms, which prefer wet climate conditions. Thus, both the intensity and frequency of precipitation affect microbial activities (Jofre et al. 2010; Wilby et al. 2005).

Climate change further enables microorganisms with pathogenic potential (pathogens) to spread and develop AMR, leading to disease incidence changes. Temperature and precipitation changes and more frequent extreme climate events are the climate effects that have predominantly contributed to the increase in infectious diseases (Patz et al. 2000). Pathogens extend their range of hosts via insect vectors, floods, storms, and when hosts (humans, animals, or plants) become more vulnerable amidst exposure to droughts and extreme temperature events. Floods and storms causing sewage overflow or droughts with dry winds also result in the dispersion and mixing of pathogenic and resistant genes into the environment, enabling horizontal gene transfer across different pathogens. These increase the incidence and prevalence of infectious diseases and enable the emergence of new infectious diseases, mainly due to permafrost thawing (ASM 2022).

In addition, Rodriguez-Verdugo et al. (2020) identify two main pathways via which climate warming affects the pathogenic ability to develop resistance intrinsically. Firstly, temperature changes increase

the pathogenic ability to transiently tolerate antimicrobials and persist via their cellular structural changes. Secondly, temperature changes increase the pathogenic ability to develop genetic modifications, enabling withstanding higher antimicrobial concentrations.

The increased incidence of infections, both due to the climate effects and via increased AMR, also postulates the inability and insufficiency of the current antimicrobial medicine stock to prevent and treat infections. Further increasing the antimicrobial consumption frequency by treating those infections increases the selective pressure, leading to stronger resistance development. Thus, climate change becomes integral to the vicious cycle of pathogens developing resistance. However, the empirical estimates of the climate effects on AMR are scarce.

To the best of our knowledge, thus far, only three studies have estimated the effect of temperature on AMR. McGough et al. (2020) and Kaba et al. (2020) estimate the effect of temperature on AMR in Europe. McGough et al. (2020) found a positive relationship between AMR and temperature increases and that temperature increases substantially affect AMR more than antimicrobial consumption. Kaba et al. (2020) demonstrate that resistance of *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Escherichia coli* towards carbapenems is significantly associated with temperature and emphasize that seasonal temperature variations could be more significant than antimicrobial consumption in explaining AMR. MacFadden et al. (2018) explore how the resistance of *Escherichia coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus* to carbapenems changed with temperature changes in the US. They found that a temperature increase of 10°C could increase their resistance by 4.2, 2.2, and 2.7 percent, respectively.

Climate warming is not the sole climate impact pathway for AMR. While climate warming increases antimicrobial growth rates and incentivizes AMR acquisition mechanisms, humidity changes, extreme climate impacts, and their spill-over effects, such as environmental pollution, also affect AMR (Burnham 2021). However, the role of those effects on AMR is yet to be empirically estimated. This paper evaluates the responsiveness of AMR to a range of chronic (temperature, precipitation, and relative humidity) and extreme climate risk indicators (representative of extreme precipitation, droughts, heatwaves, coldwaves, and storms). The paper also extends the current knowledge by employing a wider group of antimicrobial drug classes and pathogens to evaluate their heterogeneous responses to physical climate risks.

#### **3 THE IMPACT OF PHYSICAL CLIMATE RISKS ON AMR**

#### 3.1 Data on Antimicrobial Consumption and Resistance

Systematic global surveillance of AMR commenced only in 2015 (WHO 2015). Therefore, the availability of global AMR data is limited. However, the European Centre for Disease Prevention and Control (ECDC) (2023a, b) has been gathering data on the resistance of eight pathogens to 12 antimicrobial drugs across 30 countries from 2000 to 2020<sup>2</sup>. Even though some data for several other developed countries outside Europe, such as Australia, Canada, and the US, are available, they are not for comparable pathogens and antimicrobial drugs ECDC covers. Therefore, this paper focuses on the 30 countries ECDC covers to assess the impact of physical climate risks on AMR using the consistent data available from the ECDC.

One of the main approaches to measuring a pathogen's resistance to a given antimicrobial drug involves observing the antimicrobial drug concentration required to inhibit the growth of a desired proportion of the pathogen population. Depending on the inhibitory concentration levels, pathogens will be identified with different levels of susceptibilities to the antimicrobial drugs. The proportion of the population that requires extensive antimicrobial concentrations is drug-resistant.

Observing pathogenic molecular structures could also reveal whether a pathogen is no longer responsive to a drug. Furthermore, resistance could be identified by monitoring different pathogenic activities, such as their reproduction patterns, responsiveness to external disturbances, etc. Ultimately, these experiments produce the percentage of a pathogen population resistant to a given drug.

ECDC (2023b) data on AMR distinguishes three categories of pathogens: (1) the proportion of the population that is susceptible to a given drug; (2) the proportion of the population that is susceptible and has received increased exposure to a given drug, and (3) the proportion of the population resistant to a given drug. This paper uses the data on the proportion of pathogens resistant to a given drug out of these three categories. The data covers the resistance of eight pathogens to 12 antimicrobial drug classes.

ECDC (2023a) data covers the consumption of Antibacterials for Systemic Use (J01 class), according to the Anatomical Therapeutic Chemical (ATC) Classification System. The data is expressed in Daily Defined Dosages per 1,000 inhabitants per day and, hence, is already adjusted for the populations of the countries covered. Following the guidelines from the WHO Collaborating Centre for Drug Statistics Methodology (WHO 2023), we map the antimicrobial consumption data for 1,284 drugs to the 12 antimicrobial drug classes covered in the ECDC data.

Tables 1 and 2 summarize the pathogens and antimicrobial drugs. The pathogens and antimicrobial drugs result in 26 combinations. However, we avoid the resistance of Methicillin against *Staphylococcus aureus* (MRSA) due to the lack of availability of antimicrobial consumption data<sup>3</sup>.

<sup>&</sup>lt;sup>2</sup> Supplementary Annexure 1 lists the 30 countries covered in the paper, the five United Nations (UN) subregion they belong to, and their ISO codes. It is noteworthy that geographically, the countries belong to Northern, Eastern, Southern, and Western Europe, as well as Western Asia.

<sup>&</sup>lt;sup>3</sup> Supplementary Annexure 2 lists the 25 antimicrobial drug-pathogen combinations considered in this paper. Supplementary Annexures 3 and 4 present the descriptive statistics for historical antimicrobial consumption and resistance, respectively. The <u>online dashboard</u> illustrates and Supplementary Annexures 5 and 6 discuss the historical variation in antimicrobial consumption and resistance, respectively, across the 30 countries this paper focuses on.

	Pathogen		Pathogen
1	Acinetobacter spp	5	Klebsiella pneumoniae
2	Enterococcus faecalis	6	Pseudomonas aeruginosa
3	Enterococcus faecium	7	Staphylococcus aureus
4	Escherichia coli	8	Streptococcus pneumoniae
C	ECDC(2022L)		

Source: ECDC (2023b).

	Antimicrobial Drug	Corresponding ATC-4 Drug Classes
1	Aminoglycoside	J01GA and J01GB (excluding High-level gentamicin)
2	Aminopenicillin	J01CA
3	Carbapenem	J01DH
4	Ceftazidime	J01DD
5	Fluoroquinolone	J01MA
6	High-level gentamicin	J01GB
7	Macrolide	J01FA
8	Methicillin	J01CF
0	Penicillin	J01CE, J01CF (excluding Methicillin),
)	I ememin	J01CG, and J01CR
10	Piperacillin Tazobactam	J01CA
11	Third-generation cephalosporin	J01DD
12	Vancomycin	J01XA
C	ECDC(2022)	

Source: ECDC (2023a).

#### 3.2 Climate Variables and Indicators

#### 3.2.1 Climate Data

We use historical data on six climate variables: Mean Temperature, Maximum Temperature, Minimum Temperature, Precipitation, Relative Humidity, and Wind Speed. We obtain the historical gridded monthly data for the first four variables from the Climate Research Unit of the University of East Anglia (2023) for the period from 1961 to 2020<sup>4</sup> at 0.5<sup>o</sup> x 0.5<sup>o</sup> resolution. The historical gridded daily data on the remaining variables (i.e., Relative Humidity and Wind Speed) for the same period (1961–2020) are obtained from the Earth System Model of the Geophysical Fluid Dynamics Library as reported by the Intersectoral Impact Model Intercomparison Project (Potsdam Institute for Climate Impact Research 2022). We then aggregate the gridded data for 256 countries recognized in the Database of Global Administrative Areas (GADM) (2023) and extract the data for the 30 countries this paper focuses on. We use the climate variables at monthly and annual frequencies to construct ten physical climate risk indicators indicative of three chronic and seven extreme climate risks, following the approach in Fernando (2023).

<sup>&</sup>lt;sup>4</sup> The Climate Research Unit of the University of East Anglia (2023) provides the historical gridded data from 1901 to 2020 for Cloud cover, Diurnal Temperature Range, Frost Day Frequency, Mean Temperature, Maximum Temperature, Minimum Temperature, Potential Evapotranspiration, Precipitation, Vapor Pressure, and Wet Day Frequency.

#### 3.2.2 Chronic and Extreme Climate Indicators

When constructing the climate indicators, we use the period from 1961 to 1990 as the climatological baseline following the guidelines of the World Meteorological Organization (WMO) (2017). Table 3 summarizes the climate indicators constructed and used in this paper.

Our approaches to constructing the indicators of extreme temperature conditions are similar to those of Lai and Dzombak (2019). We use the Standardized Precipitation Index (SPI) developed by McKee et al. (1993) to identify precipitation-related extreme conditions. Following the insights in the literature<sup>5</sup> using indicators of extreme conditions, our indicators relate to heat and cold waves, droughts, extreme precipitation events, and storms<sup>6,7</sup>.

The indicators of extreme temperature conditions evaluate how the monthly maximum (or minimum) temperature of a given month has deviated from the 90<sup>th</sup> and 10<sup>th</sup> percentiles of the historical baseline distribution (1961-90) of monthly maximum (or minimum) temperatures. Assuming the maximum temperature of a day would be experienced during the day, a maximum temperature exceeding the 90<sup>th</sup> percentile of the baseline maximum temperature distribution indicates a month with warmer days on average, and a maximum temperature experienced below the 10<sup>th</sup> percentile of the baseline maximum temperature distribution indicates a month with colder days on average. Similarly, assuming the minimum temperature of a day would be experienced during the night, a minimum temperature exceeding the 90<sup>th</sup> percentile of the baseline minimum temperature distribution indicates a month with colder days on average. Similarly, assuming the minimum temperature of a day would be experienced during the night, a minimum temperature of a day would be experienced during the night, a minimum temperature distribution indicates a month with colder days on average. Similarly, assuming the minimum temperature of a day would be experienced during the night, a minimum temperature exceeding the 90<sup>th</sup> percentile of the baseline minimum temperature distribution indicates a month with colder days on average.

We construct these short-term extreme temperature indicators for each month for each country and obtain the annual average percentage deviation of the maximum (or minimum) temperatures from the 90<sup>th</sup> and 10<sup>th</sup> percentiles of the historical baseline distribution (1961-90).

The indicators of extreme precipitation conditions evaluate how monthly precipitation patterns for a given country have changed compared to the historical baseline distribution (1961-90). SPI is one such statistical indicator widely used in meteorology to identify dry and wet conditions. SPI compares the total precipitation observed at a particular location during a period of n months with the long-term rainfall distribution for the same period at the same location. SPI is calculated monthly for a

<sup>&</sup>lt;sup>5</sup> Russo et al. (2014) use short-term indicators of extreme temperature conditions to project heat and cold waves. A few recent studies using SPI to predict droughts and/or extreme precipitation events include Ekwezuo et al. (2020) for West Africa, Ali et al. (2020) for Pakistan, Bhunia et al. (2020) for India, Golian et al. (2015) for Iran, Wang and Cao (2011) for China, and Manasta et al. (2010) for Zimbabwe.

<sup>&</sup>lt;sup>6</sup> The indicators of extreme conditions should not be interpreted as indicators of extreme events as the occurrence of extreme events would depend on a complex set of other factors, including local weather conditions and land-use management practices, which we do not account for when constructing the indicators of extreme conditions.

<sup>&</sup>lt;sup>7</sup> The <u>online dashboard</u> illustrates and Supplementary Annexure 7 discusses the average behavior of the historical climate indicators for the five UN regions, covering the 30 countries this paper focuses on from 2000 to 2020.

moving window of n months, where n indicates the rainfall accumulation period, typically 1, 3, 6, 9, 12, 24, or 48 months (European Commission 2013).

Following the procedure in McKee et al. (1993), we calculate the monthly SPI for all the countries. We then obtain the percentage deviation of those values from extremely dry and wet conditions, defined as SPI values lower than -2 and higher than 2, respectively<sup>8</sup>. We use the annual average of the monthly values to obtain the indicators.

#### 3.3 Empirical Estimation Approach

In this paper, using the data on antimicrobial consumption and resistance for 30 countries, we first calculate the consumption growth for 12 antimicrobial drug classes and resistance growth for seven pathogens against the 12 antimicrobial drug classes. We aim to understand how the chronic and extreme climate indicators (introduced in Section 3.3) historically affected antimicrobial consumption and resistance growth in those countries. There, we encounter two challenges.

Firstly, some of the climate indicators are linked to the same distributions, although their methods of construction are independent<sup>9</sup>. Secondly, we have a considerably higher number of climate indicators as predictors (especially compared to existing studies that mostly use temperature). Accordingly, both accounting for collinearity and retaining the features were central to our estimations. Therefore, we estimate a regularized panel regression model, the Ridge regression model, illustrated in Equation 1<sup>10</sup>.

We control for the GDP per capita growth in the regression model to account for the impact of the national economic growth adjusted for the population on AMR. Per capita economic growth also acts as a proxy to indicate the level of private and public healthcare expenditure, the existence of public health and sanitation infrastructure, and the development of the health and sanitation practices, standards, and policies, including those targeting AMR, in the absence of consistent measures for them for all the countries across the period.

We include drug-specific fixed effects ( $\alpha_i$ ) to control for unobserved time-invariant heterogeneity in resistance growth. We also include additional country- and year-specific fixed effects ( $\gamma_j$  and  $\delta_k$  respectively) to control for unobserved time-invariant heterogeneities, such as those in climate indicators, and any additional unobserved time-variant effects. These fixed effects also account for the effect of any time-variant and/or time-invariant historical health policies and climate adaptation measures on AMR growth<sup>11</sup>.

<sup>&</sup>lt;sup>8</sup> Following McKee et al. (1993), World Meteorological Organization (2012) defines SPI ranges as below: Extremely wet: SPI > 2; Very wet: 1.5 < SPI < 1.99; Moderately wet: 1.0 < SPI < 1.49; Near Normal: -0.99 < SPI 0.99; Moderately Dry: -1.0 < SPI < -1.49; Severely Dry: -1.5 < SPI < -1.99; Extremely Dry: SPI < -2.

<sup>&</sup>lt;sup>9</sup> For example, while a chronic climate indicator could measure the deviation in mean temperature in a given year from baseline, an extreme climate indicator could measure the average deviations of the monthly maximum temperature from a percentile of the distribution. Accordingly, both indicators could be related to the same distribution, yet the method of construction enables identifying mean vs. extreme values.

<sup>&</sup>lt;sup>10</sup> Supplementary Annexure 8 introduces regularized regression models and illustrates how they help overcome certain limitations of linear regression models.

<sup>&</sup>lt;sup>11</sup> The objective of the empirical estimation in this paper is not to comprehensively explain the AMR growth patterns of a pathogen towards an antimicrobial drug but to estimate the sensitivity of AMR growth to physical climate risks. Therefore, the omitted variables (that could contribute to explaining AMR growth patterns) could

	Indicator	Description					
Chr	onic Climate Indi	cators					
1	Mean Temperature	Change in the mean annual temperature compared to the mean annual temperature of the baseline period (1961–1990).	<sup>0</sup> C				
2	Precipitation	Percentage change in annual total precipitation compared to the mean annual total precipitation of the baseline period (1961–1990).	%				
3	Relative Change in the mean annual relative humidity compared to the mean annual relative humidity of the baseline period (1961–1990).						
Ext	eme Climate Ind	icators					
4	MaxTemp90P	In a given year, the average percentage change of the monthly maximum temperature from the 90 <sup>th</sup> percentile of the baseline (1961–1990) monthly maximum temperature distribution.	%				
5	MaxTemp10P	In a given year, the average percentage change of the monthly maximum temperature from the 10 <sup>th</sup> percentile of the baseline (1961–1990) monthly maximum temperature distribution.	%				
6	MinTemp90P	In a given year, the average percentage change of the monthly minimum temperature from the 90 <sup>th</sup> percentile of the baseline (1961–1990) monthly minimum temperature distribution.	%				
7	MinTemp10P	In a given year, the average percentage change of the monthly minimum temperature from the 10 <sup>th</sup> percentile of the baseline (1961-1990) monthly minimum temperature distribution.	%				
8	Extremely Dry Conditions	In a given year, the average percentage deviation of the SPI index from -2 (SPI Index < -2 indicates Extreme Dry conditions).	%				
9	Extremely Wet Conditions	In a given year, the average percentage deviation of the SPI index from 2 (SPI Index > 2 indicates Extreme Wet conditions).	%				
10	Extremely Windy Conditions	In a given year, the average percentage change of the monthly maximum wind speed from the 90 <sup>th</sup> percentile of the baseline (1961-1990) monthly maximum wind speed distribution.	%				

#### **Table 3: Chronic and Extreme Climate Indicators**

Source: Constructed by the Author, following Fernando (2023).

# Equation 1: Estimated Model for AMR Growth in a Given Pathogen against Antimicrobial Drug *i* in Country *j* and Year *k*.

$$AMR \ Growth_{i,j,k} = \beta_0 + \beta_{AMC} * Antimicrobial \ Consumption \ Growth_{i,j,k} + \beta_{GDP} * GDP \ Per \ Capita \ Growth_{j,k} + \sum_{n=1}^{10} \beta_n * Growth \ in \ the \ Climate \ Indicator_{n,j,k} + \alpha_i + \gamma_j + \delta_k + \varepsilon_{i,j,k}$$

We estimate the same regression model for individual antimicrobial drug-pathogen combinations, omitting the drug-specific fixed effects. Equation 2 presents the specific model we estimate. This allows us to break down the average resistance of a given pathogen against multiple antimicrobial drugs for individual antimicrobial drugs.

#### Equation 2: Estimated Model for AMR Growth for a Given Pathogen-Antimicrobial Drug Combination in Country *j* and Year *k*.

$$\begin{aligned} AMR \; Growth_{j,k} &= \beta_0 \; + \beta_{AMC} \; * \; Antimicrobial \; Consumption \; Growth_{j,k} + \; \beta_{GDP} \; * \; GDP \; Per \; Capita \; Growth_{j,k} \\ &+ \sum_{n=1}^{10} \beta_n \; * \; Growth \; in \; the \; Climate \; Indicator_{n,j,k} + \gamma_j + \; \delta_k + \varepsilon_{j,k} \end{aligned}$$

affect the estimates only to the extent they are correlated with the climate indicators. As climate risks are largely exogenous, we assume the omitted variables do not significantly affect the current estimates.

#### 4 RESULTS & DISCUSSION

#### 4.1 Associations between AMR and Physical Climate Risks

Figure 1 presents the average Pearson's correlation coefficients among AMR, physical climate risks, antimicrobial consumption, and GDP per capita for the 25 antimicrobial drug-pathogen combinations. Notably, the correlation coefficients illustrate the average relationship AMR had with its confounders from 2001 to 2020 and all 30 countries. Therefore, while the correlation coefficients capture the resistance heterogeneity a pathogen may illustrate towards various antimicrobial drugs, those do not reflect the heterogeneity across time and countries.

Different physical climate risks affect pathogens differently. For example, while for thermophiles, or microorganisms that prefer higher temperatures, a temperature increase may catalyze their activities up to the upper bound of its optimum range, a temperature increase may be inhibitive for psychotrophs that prefer cold to moderate temperatures. Correlation analyses illustrate the directionality of the association between the resistance growth of a pathogen against a given drug and physical climate risks.

Overall, the correlation coefficients of AMR and physical climate risks lie within those of AMR and antimicrobial consumption. The correlation coefficients vary between 0.2 and -0.15. However, the correlations are quite heterogeneous. For example, the mean temperature increases are positively associated with the resistance growth in *Acinetobacter spp.*, while they are negatively associated with the resistance growth of *Escherichia coli*. against Fluoroquinolones. Extremely warm conditions during the day and night illustrate similar directionality, while extremely cold conditions demonstrate opposite correlations. Precipitation, in general, is negatively associated with the resistance growth of all the pathogens, except for the resistance growth of *Enterococcus faecium* against Vancomycin, *Enterococcus faecalis*, and *Escherichia coli*, against Aminopenicillins and *Klebsiella pneumoniae* against Aminoglycosides which are positively correlated with precipitation. Extremely windy conditions are also negatively associated with the resistance growth of all the pathogens, except for the resistance growth of all the pathogens, except for the resistance growth of all the pathogens, except for the resistance growth of all the pathogens, except for the resistance growth of all the pathogens, except for the resistance growth of all the pathogens, except for the resistance growth of all the pathogens, except for the resistance growth of all the pathogens, except for the resistance growth of all the pathogens, except for the resistance growth of all the pathogens, except for the resistance growth of all the pathogens, except for the resistance growth of *Klebsiella pneumoniae* against Cephalosporins, *Pseudomonas aeruginosa* against Piperacillin, and *Enterococcus faecalis* against Aminopenicillins.

Figure 1 also illustrates that antimicrobial consumption growth may not always be negatively associated with AMR growth. Resistance growth of *Pseudomonas aeruginosa* is particularly observed to be positively affected by the consumption growth of carbapenems. The GDP per capita growth is also differently associated with the resistance growth different pathogens demonstrate towards different antimicrobials. In general, the resistance growth of *Acinetobacter spp.* and *Escherichia coli*. are positively associated with GDP per capita growth. It is negatively associated with the resistance growth of *Klebsiella pneumoniae*.

#### 4.2 Impact of Physical Climate Risks on AMR

#### 4.2.1 Overview

As explained in Section 3.3, we estimate empirical models to capture the impact of physical climate risks on the resistance growth of pathogens against specific antimicrobial drugs and the average resistance growth across all the antimicrobial drugs. The empirical results are presented in the <u>online</u> <u>dashboard</u> for each indicator and pathogen and in Figures 2A to 2F for each pathogen<sup>12</sup>. Sections 4.2.2 to 4.2.7 discuss the empirical estimates, and where available, we incorporate existing evidence from microbiological studies about the preferential climate conditions for pathogens to reinforce the impact of physical climate risks on AMR.

#### 4.2.2 Acinetobacter spp.

Acinetobacter spp. survives at moderate temperatures such as 30°C and continues to grow at temperatures as high as 42°C (Percival & Williams 2014). As observed in Figure 2A, within the existing temperature ranges, an increase in temperature from the 1961-90 baseline incentivizes its resistance growth. A breakdown of the effects across different antimicrobial drugs illustrates that the resistance growth towards Aminoglycosides and Carbapenems experiences more substantial positive and mild negative effects, respectively, compared to the average. Extremely warm conditions during the day and night also have positive and more significant effects on resistance growth than mean temperature. The effect during the night is more substantial than that during the day. Extremely cold conditions have very mild effects on resistance growth.

An increase in relative humidity and extremely wet conditions adversely affects the resistance growth of *Acinetobacter spp*, and extremely dry conditions incentivize its growth. These observations agree with the evidence from Jawad et al. (1996), who illustrate that *Acinetobacter spp*. prefers drier and less humid environments. Extremely windy conditions also adversely affect its resistance growth. However, precipitation has a very mild positive effect on its resistance growth.

Growth in antimicrobial consumption and GDP per capita have very mild, yet statistically significant, effects on the resistance growth of *Acinetobacter spp*. While antimicrobial consumption growth incentivizes resistance growth, on average, GDP per capita growth reduces resistance growth.

#### 4.2.3 Enterococcus faecalis & Enterococcus faecium

Enterococci bacteria grow within a temperature range of 10 to 42°C and prefer higher levels of humidity (Microbe Wiki 2022a; Blanco et al. 2017). As observed in Figure 2B, mean temperature increments reduce resistance growth in both *Enterococcus faecalis* and *Enterococcus faecium*. *Enterococcus faecium* is also negatively affected by increases in extremely warm conditions during the day and night. While extremely warm conditions during the night still reduce the resistance growth of *Enterococcus faecalis*, extremely warm conditions during the day incentivize its resistance growth.

<sup>&</sup>lt;sup>12</sup> The diagnostics for the empirical models and the Variance Inflation Factors for the confounders are available from Supplementary Annexures 9 and 10, respectively.

Also, in line with the existing microbiological evidence, increases in relative humidity incentivize the resistance growth of Enterococci, in general. Extremely dry conditions inhibit their resistance growth. While precipitation has very mild effects on the resistance growth of Enterococci, extremely wet conditions have, in general, considerably higher positive effects on the resistance growth of *Enterococcus faecalis* and negative effects on the resistance growth of *Enterococcus faecalis* and negative effects on the resistance growth of *Enterococcus faecalis*. Extremely windy conditions inhibit the resistance growth in both bacteria.

Growth in antimicrobial consumption, although very small, favors the resistance growth in both bacteria. Growth in GDP per capita, however, has mixed effects on the bacteria: it favors resistance growth in *Enterococcus faecalis* and negatively affects that in *Enterococcus faecium*.

#### 4.2.4 Escherichia coli

Being a mesophile, *Escherichia coli* can survive between 10 and 45°C even though its optimum temperature remains at 37°C (Gonthier et al. 2001). As observed in Figure 2C, the resistance growth in *Escherichia coli* is incentivized mainly by increases in temperature, although the average effect is very low. The resistance growth against Aminoglycosides could even reduce amidst mean temperature increases. Extremely warm conditions have negative effects on average, while extremely cold conditions have positive yet mild effects on resistance growth.

While *Escherichia coli* demonstrates mixed responses to humidity changes, on average, less humid environments are lethal (Chew 2008). Thus, even though temperature rises could favor it, lower precipitation and relative humidity are undesirable for its microbial activities, including resistance development. *Escherichia coli* is positively affected by precipitation and relative humidity increases. Conversely, it is negatively affected by extremely dry conditions. Though precipitation is favorable, extremely wet and windy conditions are detrimental to its resistance growth.

Antimicrobial consumption growth encourages resistance growth of *Escherichia coli*, though the effect is much smaller than those of physical climate risks. GDP per capita growth has similar positive effects across most antimicrobial drugs, though the average effect is negative.

#### 4.2.5 Klebsiella pneumoniae

The optimum temperature for the survival of *Klebsiella pneumoniae* ranges between 28 and 37°C (Bengoecha & Sa Pesoa 2018), although it could survive temperatures as low as 5°C and as high as 45°C (Ajayasree & Borkar 2018). As observed in Figure 2D, mean temperature increases incentivize its resistance growth. The average resistance growth is 0.25 percent per 1°C increase in mean temperature, which is also closer to the estimate of MacFadden et al. (2018) for the US. Extremely warm conditions during the day and night have positive and negative effects on resistance growth, respectively. Extremely cold conditions have mild positive effects, on average.

Anderson et al. (2008) indicate that *Klebsiella pneumoniae* prefers higher humidity levels. Thus, increased precipitation is desirable for their survival. Although mild, our estimates align with this observation, on average, and extremely wet conditions have a much higher positive impact, also quite close to that

of mean temperature. However, changes in relative humidity and extremely windy conditions have very mild mixed effects on the resistance growth of *Klebsiella pneumoniae*.

Antimicrobial consumption growth has a positive, though mild, effect on resistance growth of *Klebsiella pneumoniae*. GDP per capita growth contributes to reducing its resistance growth.

#### 4.2.6 Pseudomonas aeruginosa

Even though some virulent activities of *Pseudomonas aeruginosa* are not effective under temperatures below 30°C, it could survive within 4°C to 42°C (LaBauve & Wargo 2012). The optimum temperature for its growth lies at 37°C, similar to other mesophiles. As observed in Figure 2E, mean temperature increases have notable positive effects on resistance growth, where a 1°C increment increases its resistance by 0.5 percent. Extremely warm and cold conditions have mixed, though mild, effects on its resistance growth.

Higher humidity levels incentivize microbial activities of *Pseudomonas aeruginosa* (Limaylla et al. 2019; Ramos et al. 2013). Thus, higher precipitation could be desirable for its resistance growth. Aligning with those microbiological foundations, *Pseudomonas aeruginosa* experiences positive, though mild, effects on resistance growth from precipitation and relative humidity increases, and extremely dry and windy conditions are detrimental. Extremely wet conditions have mixed effects, although the average effect is mildly negative.

Antimicrobial consumption growth promotes resistance growth in *Pseudomonas aeruginosa*, although the effects are very mild. GDP per capita growth has similar positive effects across most antimicrobial drugs, although the average effect is negative.

#### 4.2.7 Streptococcus pneumoniae

Similar to other mesophiles, the optimum temperature range for microbial activities of *Streptococcus pneumoniae* lies between 30 and 35°C (Microbe Wiki 2022b). As observed in Figure 2F, it is adversely affected by mean temperature increases, where a 1°C increase reduces its resistance growth by approximately 0.25 percent. However, extremely warm conditions during the day have an equally positive effect on its resistance growth. Extreme temperature conditions during the night have mixed, yet mild, effects on its resistance growth. Warmer nights also reduce its resistance growth.

*Streptococcus pneumoniae* also prefers lower humidity levels (Liu et al. 2015). Thus, precipitation reductions may encourage microbial activities, including resistance growth. Although precipitation increases have very low positive effects on resistance growth, in line with microbiological evidence, relative humidity increments reduce resistance growth, and extremely dry conditions increase resistance growth. Extremely wet and windy conditions reduce the resistance growth of *Streptococcus pneumoniae*.

Similar to other pathogens, antimicrobial consumption growth positively affects the resistance growth of *Streptococcus pneumoniae*. GDP per capita growth also contributes to its resistance growth.

#### 4.2.8 Summary

Overall, we observe that the impact of physical climate risks on resistance growth varies across pathogens and, within pathogens, across antimicrobial drugs. Our empirical estimates align with the existing microbiological evidence on the effects of climate variables on different pathogenic activities. The impacts could be either positive or negative depending on the evidence from the historical data, which covers antimicrobial consumption and resistance across 30 countries from 2000 to 2020. We illustrate that extreme climate risks could also have dominant effects on resistance growth in addition to chronic climate risks, and hence, the importance of incorporating both physical climate risk categories when estimating the effect of physical climate risks on resistance growth.

We also assess the effects of antimicrobial consumption and GDP per capita on resistance growth alongside physical climate risks. Most of our estimates agree with the general notion of the effect of selective pressure on AMR exerted by antimicrobial consumption. However, the physical climate risks have more substantial effects on AMR growth. We also observe that the GDP per capita could have mixed effects on AMR, although most effects on resistance growth are adverse. The positive effects of GDP per capita growth are attributable to antimicrobial consumption outside the healthcare sector, such as livestock. Resistance growth could still increase if it increases in parallel to the GDP per capita growth.

#### 4.3 Near-term AMR Growth Projections under SSPs

#### 4.3.1 Climate Scenarios

We project the near-term AMR growth variations under two climate scenarios. The climate scenarios are referred to as the Shared Socioeconomic Pathways (SSPs) and have been used by the IPCC since its fifth Assessment Report (Riahi et al. 2017). SSPs illustrate how a given greenhouse gas concentration pathway could be achieved under a given set of socioeconomic and technological growth assumptions and some climate mitigation and/or adaptation policies<sup>13</sup>. We focus on the first two SSPs, SSP 1-2.6 and SSP 2-4.5, representing low and intermediate greenhouse gas emission and concentration trajectories.

Given the enormous evolutionary power and adaptability of pathogens, we only project the nearterm variation in AMR growth rates for the 30 years from 2021 to 2050. Although highly probable, we do not assume any additional adaptation of pathogens to physical climate risks other than historical adaptation trends built into the empirical estimates through historical observations. We do not assume any additional effects on AMR from GDP per capita and antimicrobial consumption growth.

Most importantly, we do not attribute any likelihood to any of the scenarios and consider any of them to be a counterfactual case. Given the high uncertainty involved also in climate projections, this exercise is highly speculative. Notwithstanding the limitations, in order to contribute to the discussions

<sup>&</sup>lt;sup>13</sup> The five widely used SSPs and their complete narratives are presented in Supplementary Annexure 11.

on taming both climate risks and AMR, we illustrate how the changing physical climate risks could influence the near-term AMR growth trajectories.

#### 4.3.2 Projected AMR Growth

We apply the empirical estimates obtained in Section 3.3 and discussed in Section 4.2 to the projected climate indicators illustrated in the <u>online dashboard</u> and discussed in Supplementary Annexure 12 to project the near-term AMR growth variations under SSP 1-2.6 and SSP 2-4.5. The <u>online dashboard</u> presents the AMR growth variations for the seven pathogens we focus on in this paper. Tables 4 and 5 summarize the projected average resistance growth of the pathogens by the end of 2030, 2040, and 2050 in each region for SSP 1-2.6 and SSP 2-4.5, respectively.

Region	Pathogen	2030	2040	2050
	Acinetobacter spp.	0.13	0.13	0.13
	Enterococcus faecalis	-0.44	-0.43	-0.42
	Enterococcus faecium	-2.22	-2.27	-2.31
Eastern Europe	Escherichia coli	-0.27	-0.28	-0.29
	Klebsiella pneumoniae	0.45	0.45	0.45
	Pseudomonas aeruginosa	0.72	0.71	0.71
	Streptococcus pneumoniae	-0.22	-0.18	-0.14
	Acinetobacter spp.	0.60	0.58	0.57
	Enterococcus faecalis	-0.37	-0.38	-0.38
	Enterococcus faecium	-2.08	-2.22	-2.36
Northern Europe	Escherichia coli	-0.47	-0.48	-0.49
	Klebsiella pneumoniae	0.48	0.49	0.50
	Pseudomonas aeruginosa	0.48	0.43	0.39
	Streptococcus pneumoniae	-0.25	-0.28	-0.32
	Acinetobacter spp.	0.27	0.31	0.35
	Enterococcus faecalis	-0.23	-0.22	-0.21
	Enterococcus faecium	-0.79	-0.90	-1.02
Southern Europe	Escherichia coli	-0.16	-0.20	-0.24
	Klebsiella pneumoniae	0.27	0.30	0.34
	Pseudomonas aeruginosa	0.56	0.53	0.50
	Streptococcus pneumoniae	-0.24	-0.12	0.00
	Acinetobacter spp.	0.20	0.23	0.27
	Enterococcus faecalis	-0.14	-0.14	-0.15
	Enterococcus faecium	-0.85	-0.89	-0.94
Western Asia	Escherichia coli	-0.11	-0.14	-0.16
	Klebsiella pneumoniae	0.36	0.35	0.34
	Pseudomonas aeruginosa	0.59	0.57	0.55
	Streptococcus pneumoniae	-0.03	-0.01	0.01
	Acinetobacter spp.	0.14	0.15	0.15
	Enterococcus faecalis	-0.27	-0.27	-0.28
	Enterococcus faecium	-1.56	-1.57	-1.58
Western Europe	Escherichia coli	-0.17	-0.18	-0.19
-	Klebsiella pneumoniae	0.40	0.41	0.41
	Pseudomonas aeruginosa	0.56	0.55	0.53
	Streptococcus pneumoniae	-0.58	-0.58	-0.58

Table 4: Changes in Average Resistance by 2030, 2040, and 2050 under SSP 1-2.6

Source: Constructed by the Author.

The average resistance growth variations are derived from aggregating the effects of individual climate indicators on the average resistance each pathogen demonstrates to the respective antimicrobial drugs. Specifically, the projections are based on the empirical estimates from the model presented in

Equation 1. The <u>online dashboard</u> also illustrates the decomposition of the aggregate effect to identify the individual contribution from the ten climate indicators.

The resistance growth variations across SSPs are primarily influenced by three factors: (1) the nonlinear variation in climate indicators across SSPs, (2) the differential exposure of a given region to different climate indicators under different SSPs, and (3) the differential responsiveness of resistance growth to different climate indicators. Therefore, the ultimate resistance growth variations could vastly differ from the results expected from a linear extrapolation involving one or few climate indicators.

Region	Pathogen	2030	2040	2050
	Acinetobacter spp.	0.30	0.37	0.43
	Enterococcus faecalis	-0.35	-0.38	-0.40
	Enterococcus faecium	-3.50	-3.51	-3.51
Eastern Europe	Escherichia coli	-0.58	-0.61	-0.64
	Klebsiella pneumoniae	0.42	0.40	0.37
	Pseudomonas aeruginosa	-0.35	-0.37	-0.39
	Streptococcus pneumoniae	-0.50	-0.53	-0.56
	Acinetobacter spp.	0.39	0.37	0.35
	Enterococcus faecalis	-0.36	-0.36	-0.37
	Enterococcus faecium	-2.22	-2.38	-2.54
Northern Europe	Escherichia coli	-0.38	-0.39	-0.41
*	Klebsiella pneumoniae	0.60	0.61	0.61
	Pseudomonas aeruginosa	0.50	0.45	0.39
	Streptococcus pneumoniae	-0.47	-0.51	-0.55
	Acinetobacter spp.	0.44	0.53	0.63
	Enterococcus faecalis	-0.32	-0.37	-0.42
	Enterococcus faecium	-1.29	-1.41	-1.53
Southern Europe	Escherichia coli	-0.35	-0.41	-0.46
1	Klebsiella pneumoniae	0.14	0.20	0.26
	Pseudomonas aeruginosa	0.25	0.31	0.36
	Streptococcus pneumoniae	-0.30	-0.33	-0.37
	Acinetobacter spp.	0.30	0.29	0.29
	Enterococcus faecalis	-0.16	-0.16	-0.16
	Enterococcus faecium	-0.78	-0.80	-0.82
Western Asia	Escherichia coli	-0.21	-0.22	-0.22
	Klebsiella pneumoniae	0.12	0.12	0.12
	Pseudomonas aeruginosa	0.38	0.37	0.37
	Streptococcus pneumoniae	-0.06	-0.06	-0.07
	Acinetobacter spp.	0.07	0.09	0.10
	Enterococcus faecalis	-0.25	-0.25	-0.25
	Enterococcus faecium	-2.08	-2.10	-2.11
Western Europe	Escherichia coli	-0.26	-0.26	-0.27
I	Klebsiella pneumoniae	0.29	0.30	0.32
	Pseudomonas aeruginosa	0.15	0.14	0.14
	Streptococcus pneumoniae	-0.59	-0.57	-0.55

Table 5: Changes in Average Resistance by 2030, 2040, and 2050 under SSP 2-4.5

Source: Constructed by the Author.

The resistance growth of *Acinetobacter spp.* generally increases across SSPs, mainly driven by the increase in extremely warm conditions during the night and the favorable responsiveness of resistance growth to them. However, the resistance growth in Northern Europe decreases and converges with its peers, mainly driven by the increase in extremely windy conditions and the adverse responsiveness of resistance growth to them.

*Enterococcus faecalis* experiences a net resistance growth reduction across all the regions under the SSPs. However, some regions experience (such as Northern, Eastern, and Western Europe) a positive shift in resistance growth, driven by the favorable effect of extremely warm conditions during the day. Western Asia experiences minimal resistance growth changes, while Southern Europe experiences a further resistance growth reduction driven by the increasing extremely warm conditions during the night and the adverse responsiveness of resistance growth to them.

Similar to *Enterococcus faecalis*, overall, the resistance growth of *Enterococcus faecium* reduces across all the regions with warming. On average, these changes are mainly driven by the increasing extremely warm conditions during both the day and night and extremely windy and dry conditions. Among the regions, Eastern and Western Europe experience the most prominent negative effects on resistance growth.

*Escherichia coli.*, also, overall, experiences a net resistance growth reduction as the warming increases under SSPs. However, Northern Europe experiences a positive shift in resistance growth mainly driven by the extremely warm conditions during the night. The increase in the adverse effect on resistance growth in the other regions is primarily driven by the increasing extremely warm conditions during the day and the negative responsiveness of resistance growth.

The resistance growth in *Klebsiella pneumoniae* illustrates mixed patterns across the regions amidst warming. Eastern and Western Europe and Western Asia experience an overall reduction in resistance growth. In Western Asia, the resistance growth reduction is due to reducing precipitation combined with favorable responsiveness of resistance growth to precipitation changes. The other regions experience a resistance growth increase. In Northern Europe, the resistance growth increase is driven by the rise in mean temperature across SSPs and the favorable responsiveness of resistance growth to mean temperature changes.

*Pseudomonas aeruginosa*, overall, experiences a net resistance growth reduction. Eastern Europe experiences the most substantial reduction, primarily driven by the increasing extremely windy conditions and the adverse responsiveness of resistance growth. Northern Europe experiences a mild upward shift in resistance growth mainly driven by the rising mean temperature.

*Streptococcus pneumoniae* illustrates mixed resistance growth patterns across the regions under the SSPs. While the overall resistance in Western Asia remains unchanged, resistance growth trajectories in Eastern and Southern Europe change from positive to negative. The changes in Eastern Europe are driven by the increasing extremely windy conditions and the vulnerability of resistance growth. In Southern Europe, the mean temperature increases also reduce resistance growth. Western Europe experiences an increasing resistance growth trajectory, mainly due to the increasing extremely warm conditions and the favorable responsiveness of resistance growth.

#### 4.4 Summary

Section 4 discussed two sets of results from this paper. Firstly, we discussed the results from the empirical estimation of the impact of physical climate risks on resistance growth. The results included

the impacts on the average resistance of a given pathogen and specific resistance to different antimicrobial drugs. We illustrated that the responsiveness of resistance growth could differ across various climate risks. The responsiveness of the specific resistance growth in a given pathogen towards different antimicrobial drugs could also be different from the average resistance growth. Where available, we also compared our estimates with the existing understanding of the responsiveness of microbial activities to temperature, precipitation, and humidity. We also demonstrated that the role of physical climate risks is crucial for explaining the resistance growth in most pathogens, in addition to antimicrobial consumption, which is currently considered the primary driver of AMR.

Secondly, we applied the empirical estimates to projected climate indicators to speculate how the resistance growth of different pathogens could change under two SSPs. We illustrated the net effect on resistance growth as the climate risks evolve differently, changing their proportional contribution to net resistance growth. However, given the uncertainty in climate projections and the potential of pathogens to adapt to evolving climate conditions, we restricted our projections to a 30-year horizon (2021-2050). In discussing those projections, we illustrated that, given the historical adaptation of pathogens to climate conditions and without additional growth changes in antimicrobial consumption and GDP per capita, the resistance patterns could change positively or negatively<sup>14</sup>. While these patterns were diverse across pathogens, the climate drivers of those changes were also diverse. Therefore, we reiterated the importance of considering a more comprehensive range of climate indicators when assessing the impacts of physical climate risks on AMR and that the holistic variation in resistance growth may be much different from what could be linearly predicted using a single climate risk indicator (such as temperature).

#### 5 CONCLUSION & POLICY IMPLICATIONS

#### 5.1 Summary

Climate change and AMR are two complex challenges humanity is facing. The human footprint in aggravating both issues is unequivocal. While anthropogenic greenhouse gas emissions have caused climate change in the Anthropocene, AMR has been caused by the suboptimal consumption of antimicrobials, primarily for healthcare and agriculture applications. The consequences of both climate change and AMR are already widely felt. Continuing challenges and their possible interactions may further aggravate the already dire consequences. Given the criticality of those linkages to mitigation and adaptation policies for both challenges, this paper investigates the impact of physical climate risks on AMR.

Section 2 sets the context for the paper exploring the current evidence of how physical climate risks interact with pathogens and infectious diseases, given the limited evidence on the impact of physical climate risks on AMR. Section 3 explained the data sources used to obtain antimicrobial consumption

<sup>&</sup>lt;sup>14</sup> This observation should not be interpreted as a positive effect of climate change on health consequences. We refer to Fernando et al. (2021) and Fernando and Lepore (2023) for discussing the broader economic consequences of climate change.

and resistance data and climate variables. The antimicrobial consumption and resistance data covered the resistance of eight pathogens to 12 antimicrobial drugs in 30 countries from 2000 to 2020. It further explains the construction of climate indicators to reflect chronic and extreme physical climate risks, following Fernando (2023). The empirical estimation approach of penalized regressions coupled with machine learning was also introduced there.

Section 4 discussed the results from empirical estimations and projected the near-term variation in the resistance growth of different pathogens under two climate scenarios: SSP 1-2.6 and SSP 2-4.5. The results illustrate a wider heterogeneity in the responsiveness of AMR to different climate risks. The responsiveness also varies for different antimicrobial drugs a given pathogen is resisting. Different regions are exposed to physical climate risks differently, and the ultimate effect is determined both by the responsiveness of resistance to various physical climate risks and the exposure of the given regions to those physical climate risks.

#### 5.2 Implications for Research

This paper has four main implications for AMR research. Firstly, it illustrates the importance of considering a wider group of factors when modeling AMR growth. Specifically, this paper demonstrates the more substantial effects physical climate risks could have on resistance, even compared to antimicrobial consumption, which is currently considered the primary driver of AMR. Fernando and McKibbin (2022) summarize several other factors, such as demographic trends (Fernando (Forthcoming)), that should be considered when understanding the evolution of AMR.

Secondly, this paper highlights the importance of incorporating a broader range of physical climate risks, going beyond chronic risks (or temperature, which most existing studies consider) to understand the effect of physical climate risks on AMR. We particularly demonstrate that extreme risks also influence the resistance growth changes in some pathogens.

Thirdly, we emphasize the importance of preserving heterogeneity. Specifically, we observe the different responsiveness of antimicrobial drug-specific resistance compared to the average resistance of a pathogen to different physical climate risks. In our near-term projections under SSPs, we also illustrate how the resistance growth could differ across various regions despite their geographical similarities.

Fourthly, we illustrate the potential of penalized regression coupled with machine learning to help alleviate some of the limitations in conventional estimation techniques to handle high dimensionality and multicollinearity.

#### 5.3 Implications for Policy

We identify four main policy implications arising from this paper. Firstly, it highlights the importance of perceiving global challenges from a systems perspective and appreciating the broad linkages between and within natural and socioeconomic systems. A one-health approach of recognizing the interactions between the environment, plants, animals, and humans pioneered by the Quadripartite Initiative (WHO-FAO-OIE-UNEP) is a significant step towards that. As Fernando and McKibbin (Forthcoming) argue, via the illustration of the global economic impacts of AMR, the initiative should be extended to include development institutions and other economic policy institutions, given the transboundary nature of AMR and its development, growth, and welfare consequences. The consequences of AMR are disproportionately felt by the fractions of the world, which are already struggling with poverty, poor institutions, and many other development challenges, including climate change and infectious diseases.

Secondly, we illustrate the importance of strengthening AMR surveillance and making AMR data widely available and accessible. Our ability to extend the study is constrained by the lack of consistent data from other developed countries and the lack of antimicrobial consumption and resistance observations from developing countries. With informal pharmaceutical markets and disproportionate vulnerabilities to physical climate risks, developing countries will continue to aggravate AMR risks, which will spill over to the rest of the world, given its transboundary nature. Thus, developing their institutional capabilities, including those for AMR surveillance, and improving their climate and health system resilience will be vital for taming AMR.

Thirdly, physical climate risks have implications for the design and operation of antimicrobial supply chains. Given the anticipated more frequent and adverse changes in climate, research and development into pharmaceuticals and alternatives to antimicrobial drugs should consider how the physical climate risks could alter the pathogenic resistance patterns and thrive on reducing such implications on the efficacy of antimicrobial medicine. Furthermore, the production, storage, and distribution of antimicrobials should be undertaken within settings that minimize their exposure to physical climate risks and inhibit pathogenic functions.

Fourthly, this paper reiterates various sources of uncertainty AMR (and climate change) involves. These are primarily related to the pathways via which climate risks affect AMR, data availability, and the methodologies used to process and model the data to derive estimates. Thus, research into factors affecting AMR and, notably, the effects of climate risks on AMR should be expanded. The access to AMR and antimicrobial consumption data should be widened, enabling further studies. Furthermore, studies employing a variety of methodologies should be accommodated and considered to navigate through methodological uncertainties.

#### 5.4 Suggestions for Future Research

Future research could extend this paper to other parts of the world, particularly developing countries, incorporating additional antimicrobial drugs and pathogens, as far as the data warrants. Future studies could also incorporate other factors (such as demographic, health, sanitation, and economic and governance indicators) affecting AMR to measure the contemporaneous effects as well as persistent effects of all factors through dynamic estimations.

#### References

Ajayasree, T. & Borkar, S. 2018. Survival of Klebsiella pneumoniae Strain in Pomegranate Orchard Soil and its Tolerance to Temperature and pH. Journal of Applied Biotechnology & Bioengineering, 5, 299-301.

- Ali, S., Khalid, B., Akhter, A., Islam, A. & Adnan, S. 2020. Analyzing the Occurrence of Floods and Droughts in Connection with Climate Change in Punjab Province, Pakistan. Natural Hazards, 103, 2533-59.
- Altizer, S., Ostfeld, R., Johnson, P., Kutz, S. & Harvel, C. 2013. Climate Change and Infectious Diseases: From Evidence to a Predictive Framework. Science, 341, 514-9.
- American Society for Microbiology. 2022. Microbes and Climate Change Science, People and Impacts. In: MICROBIOLOGY, A. S. F., ed. American Academy of Microbiology Virtual Colloquium, 5 November 2021. Washington DC. American Society for Microbiology.
- Anderson, D., Richet, H., Chen, L., Spelman, D., Hung, Y., Huang, A., Sexton, D. & Raoul, D. 2008. Seasonal Variation in Klebsiella pneumoniae Bloodstream Infection on 4 Continents. Journal of Infectious Diseases, 197, 752-6.
- Bengoechea, J. & Pessoa, J. 2018. Klebsiella pneumoniae Infection Biology: Living to Counteract Host Defences. FEMS Microbiology Reviews, 43, 123-44.
- Bhunia, P., Das, P. & Maiti, R. 2020. Meteorological Drought Study through SPI in Three Drought Prone Districts of West Bengal, India. Earth Systems and Environment, 4, 43-55.
- Blanco, N., Perencevich, E., Li, S. & Morgan, D. 2017. Effect of Meteorological Factors and Geographic Location on Methicillin-Resistant Staphylococcus aureus and Vancomycin-Resistant Enterococci Colonization in the US. PLoS ONE, 12, 1-13.
- Burnham, J. 2021. Climate Change and Antibiotic Resistance: A Deadly Combination. Therapeutic Advances in Infectious Disease, 15, 1-7.
- Chew, W. 2008. Correlation of In-field Survival of Escherichia coli 0157:H7 with Rainfall, Relative Humidity, and Soil Moisture. Master's Thesis, Oklahoma State University.
- Climate Research Unit of the University of East Anglia. 2023. High-Resolution Gridded Datasets (and Derived Products) [Online]. Norwich: Climate Research Unit of the University of East Anglia. Available: https://crudata.uea.ac.uk/cru/data/hrg/ [Accessed 15 September 2023].
- Database of Global Administrative Areas. 2023. GADM Maps and Data [Online]. Database of Global Administrative Areas. Available: https://gadm.org/ [Accessed 15 September 2023].
- Ekwezuo, C. & Ezeh, C. 2020. Regional Characterisation of Meteorological Drought and Floods over West Africa. Sustainable Water Resources Management, 6.
- European Centre for Disease Prevention and Control. 2023. Antimicrobial Consumption Database (ESAC-Net) [Online]. European Centre for Disease Prevention and Control. Available: http://ecdc.europa.eu/en/antimicrobial-consumption/surveillance-and-disease-data/database [Accessed 15 September 2023].
- European Centre for Disease Prevention and Control. 2023. Antimicrobial Resistance in Europe Data Visualization Tool [Online]. European Centre for Disease Prevention and Control. Available: https://www.ecdc.europa.eu/en/publications-data/antimicrobial-resistance-europe-data-visualisation-tool [Accessed 15 September 2023].
- European Commission. 2013. Standardized Precipitation Index (SPI) [Online]. European Commission. Available: https://edo.jrc.ec.europa.eu/documents/factsheets/factsheet\_spi.pdf [Accessed 15 September 2023].
- Fernando, R. 2019. Global Economic Consequences of an Escalation of Antimicrobial Resistance. Master's Thesis, Australian National University.
- Fernando, R. 2023. Global Economic Consequences Arising from the Impacts of Physical Climate Risks on Agriculture and Energy. 26th Annual Conference on Global Economic Analysis. Bordeaux: Global Trade Analysis Project.
- Fernando, R. & Lepore, C. 2023. Global Economic Impacts of Physical Climate Risks. IMF Working Papers. Washington, DC: The International Monetary Fund.
- Fernando, R., Liu, W. & McKibbin, W. 2021. Global Economic Impacts of Climate Shocks, Climate Policy and Changes in Climate Risk Assessment. Climate and Energy Economics Discussion Paper. Washington DC: The Brookings Institution.
- Fernando, R. & McKibbin, W. 2022. Antimicrobial Resistance: Designing a Comprehensive Macroeconomic Modeling Strategy. Washington DC: The Brookings Institution.
- Fernando, R. & McKibbin, W. Forthcoming. Global Economic Impacts of Antimicrobial Resistance. Canberra: Centre for Applied Macroeconomic Analysis.

- Golian, S., Mazdiyasni, O. & AghaKouchak, A. 2015. Trends in Meteorological and Agricultural Droughts in Iran. Theoretical and Applied Climatology, 119, 679-88.
- Gonthier, A., Guerin-Faublee, V., Tilly, B. & Delignette-Muller, M. 2001. Optimal Growth Temperature of O157 and Non-O157 Escherichia coli Strains. Letters in Applied Microbiology, 33, 352-6.
- Hastie, T., Tibshirani, R. & Friedman, J. 2017. Statistical Learning: Data Mining, Inference, and Prediction, Springer.
- Intergovernmental Panel on Climate Change 2023. AR6 Synthesis Report: Climate Change 2023. Intergovernmental Panel on Climate Change.
- Jawad, A., Heritage, J., Snelling, A., Gascoyne-Binzi, D. & Hawkey, P. 1996. Influence of Relative Humidity and Suspending Menstrua on Survival of Acinetobacter spp. on Dry Surfaces. Journal of Clinical Microbiology, 34, 2881-7.
- Jofre, J., Blanch, A. & Lucena, F. (eds.) 2010. Water-Borne Infectious Disease Outbreaks Associated with Water Scarcity and Rainfall Events, Berlin, Heidelberg: Springer.
- Kaba, H., Kuhlmannb, E. & Scheithauer, S. 2020. Thinking Outside the Box: Association of Antimicrobial Resistance with Climate Warming in Europe - a 30 Country Observational Study. International Journal of Hygiene and Environmental Health, 223, 151-8.
- LaBauve, A. & Wargo, M. 2012. Growth and Laboratory Maintenance of Pseudomonas aeruginosa. Current Protocols in Microbiology, 6, 1-11.
- Lai, Y. & Dzombak, D. 2019. Use of Historical Data to Assess Regional Climate Change. Journal of Climate, 32, 4299-320.
- Limaylla, D., Silva, M. & Fortaleza, C. 2019. Temperature, Humidity and Climate Control in Hospital Units: a Clue for Understanding the Seasonality of Healthcare-associated Pathogens. Infection Control & Hospital Epidemiology, 40, 829-30.
- Liu, Y., Liu, J., Chen, F., Shamsi, B., Wang, Q., Jiao, F., Qiao, Y. & Shi, Y. 2015. Impact of Meteorological Factors on Lower Respiratory Tract Infections in Children. Journal of International Medical Research, 44, 30-41.
- MacFadden, D., McGough, S., Fisman, D., Santillana, M. & Brownstein, J. 2018. Antibiotic Resistance Increases with Local Temperature. Nature Climate Change, 8, 510-5.
- Manatsa, D., Mukwada, G., Siziba, E. & Chinyanganya, T. 2010. Analysis of Multidimensional Aspects of Agricultural Droughts in Zimbabwe Using the Standardized Precipitation Index (SPI). Theoretical and Applied Climatology, 102, 287-305.
- McGough, S., MacFadden, D., Hattab, M., Molbak, K. & Santillana, M. 2020. Rates of Increase of Antibiotic Resistance And Ambient Temperature in Europe: a Cross-National Analysis of 28 Countries between 2000 and 2016. Euro Surveillance, 25, 1-12.
- McKee, T., Doesken, N. & Kleist, J. The Relationship of Drought Frequency and Duration to Time Scales. 8th Conference on Applied Climatology, 1993. 179-83.
- Microbe Wiki. 2022. Enterococcus fecal [Online]. Available: https://microbewiki.kenyon.edu/index.php/Enterococcus\_faecalis [Accessed 10 June 2022].
- Microbe Wiki. 2022. Streptococcus pneumoniae [Online]. Available: https://microbewiki.kenyon.edu/index.php/Streptococcus\_pneumoniae#:~:text=(5)%20S.,30%20and%2035%20degrees%20Celsius. [Accessed 10 June 2022].
- MSD Manuals. 2020. Acinetobacter Infections [Online]. MSD Manuals. Available: https://www.msdmanuals.com/professional/infectious-diseases/gram-negative-cocci-and-coccobacilli/acinetobacter-infections?query=acinetobacter%20species [Accessed 10 June 2020].
- MSD Manuals. 2020. Enterococcal Infections [Online]. Available: https://www.msdmanuals.com/professional/infectious-diseases/gram-positive-cocci/enterococcal-infections?query=enterococcal [Accessed 10 June 2020].
- MSD Manuals. 2020. Escherichia coli Infections [Online]. Available: https://www.msdmanuals.com/professional/infectious-diseases/gram-negative-bacilli/escherichia-coli-infections?query=escherichia%20coli [Accessed 10 June 2020].
- MSD Manuals. 2020. Klebsiella, Enterobacter, and Serratia Infections [Online]. Available: https://www.msdmanuals.com/professional/infectious-diseases/gram-negative-bacilli/klebsiella,enterobacter,-and-serratia-infections?query=klebsiella%20pneumoniae [Accessed 10 June 2020].

- MSD Manuals. 2020. Pneumococcal Infections [Online]. Available: https://www.msdmanuals.com/professional/infectious-diseases/gram-positive-cocci/pneumococcal-infections?query=streptococcus%20pneumoniae [Accessed 10 June 2020].
- MSD Manuals. 2020. Pseudomonas and Related Infections [Online]. Available: https://www.msdmanuals.com/professional/infectious-diseases/gram-negative-bacilli/pseudomonas-and-related-infections?query=pseudomonas%20aeruginosa [Accessed 10 June 2020].
- MSD Manuals. 2020. Staphylococcal Infections [Online]. Available: https://www.msdmanuals.com/professional/infectious-diseases/gram-positive-cocci/staphylococcal-infections?query=staphylococcus%20aureus [Accessed 10 June 2020].
- O'Neil, J. C. 2016. Tackling Drug-resistant Infections Globally: Final Report and Recommendations. United Kingdom: AMR Review.
- Patz, J., Graczyk, T., Geller, N. & Vittor, A. 2000. Effects of Environmental Change on Emerging Parasitic Diseases. International Journal for Parasitology, 30, 1395-405.
- Percival, S., Yates, M., Williams, D., Chalmers, R. & Gray, N. 2004. Microbiology of Waterborne Diseases, Berlin, Heidelberg, Academic Press.
- Portier, C., Tart, K., Carter, S., Dilworth, C. & Grambsch, A. 2013. A Human Health Perspective on Climate Change: a Report Outlining the Research Needs on the Human Health Effects of Climate Change. Journal of Current Issues in Globalization, 6, 621-710.
- Potsdam Institute for Climate Impact Research. 2022. Intersectoral Impact Model Intercomparison Project [Online]. Potsdam-Institute for Climate Impact Research. Available: https://esg.pik-potsdam.de/search/isimip/ [Accessed 10 June 2022].
- Ramos, G., Rocha, J. & Tuon, F. 2013. Seasonal Humidity may Influence Pseudomonas Aeruginosa Hospital-Acquired Infection Rates. International Journal of Infectious Diseases, 17, 757-61.
- Rodriguez-Verdugo, A., Lozano-Huntelman, N., Cruz-Loya, M., Savage, V. & Yeh, P. 2020. Compounding Effects of Climate Warming and Antibiotic Resistance. iScience, 23, 1-16.
- Russo, S., Dosio, A., Graversen, R., Sillmann, J., Carrao, H., Dunbar, M., Singleton, A., Montagna, P., Barbola, P. & Vogt, J. 2014. Magnitude of Extreme Heat Waves in Present Climate and Their Projection in a Warming World. Journal of Geophysical Research-Atmospheres, 119, 12500-12.
- Tiedje, J., Bruns, M., Casadevall, A., Criddle, C., Eloe-Fadrosh, E., Karl, D., Nguyen, N. & Zhou, J. 2022. Microbes and Climate Change: a Research Prospectus for the Future. Environmental Microbiology, 13, 1-9.
- Wang, Z. & Cao, L. 2011. Analysis on Characteristics of Droughts and Floods of Zhengzhou City based on SPI in Recent 60 Years. Journal of North China Institute of Water Conservancy and Hydroelectric Power, 6, 1-14.
- Wilby, R., Hedger, M. & Orr, H. 2005. Climate Change Impacts and Adaptation: a Science Agenda for the Environment Agency of England and Wales. Weather, 60, 206-11.
- World Health Organization 2015. Global Antimicrobial Resistance Surveillance Systems (GLASS). World Health Organization.
- World Health Organization. 2023. J01 Antibacterials for Systemic Use [Online]. World Health Organization. Available: https://www.whocc.no/atc\_ddd\_index/?code=J01&showdescription=no [Accessed 15 September 2023].
- World Health Organization. 2023. Quadripartite Call to Action for One Health for a Safer World [Online]. World Health Organization. Available: https://www.who.int/news/item/27-03-2023-quadripartitecall-to-action-for-one-health-for-a-safer-world#:~:text=The%20Quadripartite%20aims%20to%20achieve,for%20Animal%20Health%20(WOAH) [Accessed 15 September 2023].
- World Meteorological Organization 2017. WMO Guidelines on the Calculation of Climate Normals. Geneva, Switzerland: World Meteorological Organization.
- Wu, X., Lu, Y., Zhou, S., Chen, L. & Xu, B. 2016. Impact of Climate Change on Human Infectious Diseases: Empirical Evidence and Human Adaptation. Environment International, 86, 14-23.



Figure 1: Association between Physical Climate Risks and AMR



Figure 1 (Contd.): Association between Physical Climate Risks and AMR

#### Figure 2A: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Acinetobacter spp.



#### Figure 2B: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Enterococcus faecalis



#### Figure 2C: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Enterococcus faecium



Figure 2D: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Escherichia coli



#### Figure 2E: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Klebsiella pneumoniae



#### Figure 2F: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Pseudomonas aeruginosa



Figure 2G: Average Responsiveness of AMR Percentage Growth from 2001 to 2020: Streptococcus pneumoniae



Negative Effect

#### IMPACT OF PHYSICAL CLIMATE RISKS ON ANTIMICROBIAL RESISTANCE

#### **Roshen Fernando**

Centre for Applied Macroeconomic Analysis, Crawford School of Public Policy, The Australian National University

#### SUPPLEMENTARY ANNEXURES

	Name	ISO-3	ISO-2	UN Region
1	Austria	AUT	АТ	Western Europe
2	Belgium	BEL	BE	Western Europe
3	Bulgaria	BGR	BG	Eastern Europe
4	Croatia	HRV	HR	Southern Europe
5	Cyprus	CYP	CY	Western Asia
6	Czechia	CZE	CZ	Eastern Europe
7	Denmark	DNK	DK	Northern Europe
8	Estonia	EST	EE	Northern Europe
9	Finland	FIN	FI	Northern Europe
10	France	FRA	FR	Western Europe
11	Germany	DEU	DE	Western Europe
12	Greece	GRC	GR	Southern Europe
13	Hungary	HUN	HU	Eastern Europe
14	Iceland	ISL	IS	Northern Europe
15	Ireland	IRL	IE	Northern Europe
16	Italy	ITA	IT	Southern Europe
17	Latvia	LVA	LV	Northern Europe
18	Lithuania	LTU	LT	Northern Europe
19	Luxembourg	LUX	LU	Western Europe
20	Malta	MLT	MT	Southern Europe
21	Netherlands	NLD	NL	Western Europe
22	Norway	NOR	NO	Northern Europe
23	Poland	POL	PL	Eastern Europe
24	Portugal	PRT	PT	Southern Europe
25	Romania	ROU	RO	Eastern Europe
26	Slovakia	SVK	SK	Eastern Europe
27	Slovenia	SVN	SI	Southern Europe
28	Spain	ESP	ES	Southern Europe
29	Sweden	SWE	SE	Northern Europe
30	United Kingdom	GBR	GB	Northern Europe

Supplementary Annexure 1: Countries Considered in the Study and their ISO Codes

	Pathogen	Drug
1	Acinetobacter spp.	Aminoglycosides
2	Acinetobacter spp.	Carbapenems
3	Acinetobacter spp.	Fluoroquinolones
4	Enterococcus faecalis	Aminopenicillins
5	Enterococcus faecalis	Gentamicin
6	Enterococcus faecalis	Vancomycin
7	Enterococcus faecium	Aminopenicillins
8	Enterococcus faecium	Gentamicin
9	Enterococcus faecium	Vancomycin
10	Escherichia coli	Aminoglycosides
11	Escherichia coli	Aminopenicillins
12	Escherichia coli	Carbapenems
13	Escherichia coli	Cephalosporins
14	Escherichia coli	Fluoroquinolones
15	Klebsiella pneumoniae	Aminoglycosides
16	Klebsiella pneumoniae	Carbapenems
17	Klebsiella pneumoniae	Cephalosporins
18	Klebsiella pneumoniae	Fluoroquinolones
19	Pseudomonas aeruginosa	Aminoglycosides
20	Pseudomonas aeruginosa	Carbapenems
21	Pseudomonas aeruginosa	Ceftazidime
22	Pseudomonas aeruginosa	Fluoroquinolones
23	Pseudomonas aeruginosa	Piperacillin
24	Streptococcus pneumoniae	Macrolides
25	Streptococcus pneumoniae	Penicillins

#### Supplementary Annexure 2: Antimicrobial Drug-Pathogen Combinations

	Pathogen	Drug	Mean	SD	Min	Max
1	Acinetobacter spp.	Aminoglycosides	1.29	20.21	-99.45	93.75
2	Acinetobacter spp.	Carbapenems	1.88	21.49	-97.57	100.00
3	Acinetobacter spp.	Fluoroquinolones	-0.26	18.85	-99.64	80.00
4	Enterococcus faecalis	Aminopenicillins	-0.28	19.04	-99.61	100.00
5	Enterococcus faecalis	Gentamicin	-0.97	24.12	-99.84	100.00
6	Enterococcus faecalis	Vancomycin	0.35	23.93	-99.07	100.00
7	Enterococcus faecium	Aminopenicillins	-0.28	19.04	-99.61	100.00
8	Enterococcus faecium	Gentamicin	-0.97	24.12	-99.84	100.00
9	Enterococcus faecium	Vancomycin	0.35	23.93	-99.07	100.00
10	Escherichia coli	Aminoglycosides	1.66	20.46	-99.45	100.00
11	Escherichia coli	Aminopenicillins	-0.28	19.04	-99.61	100.00
12	Escherichia coli	Carbapenems	2.05	21.46	-97.57	100.00
13	Escherichia coli	Cephalosporins	0.04	17.90	-99.75	100.00
14	Escherichia coli	Fluoroquinolones	-0.18	18.06	-99.64	80.00
15	Klebsiella pneumoniae	Aminoglycosides	1.66	20.46	-99.45	100.00
16	Klebsiella pneumoniae	Carbapenems	2.05	21.46	-97.57	100.00
17	Klebsiella pneumoniae	Cephalosporins	0.04	17.90	-99.75	100.00
18	Klebsiella pneumoniae	Fluoroquinolones	-0.18	18.06	-99.64	80.00
19	Pseudomonas aeruginosa	Aminoglycosides	1.66	20.46	-99.45	100.00
20	Pseudomonas aeruginosa	Carbapenems	2.05	21.46	-97.57	100.00
21	Pseudomonas aeruginosa	Ceftazidime	0.79	23.58	-99.92	100.00
22	Pseudomonas aeruginosa	Fluoroquinolones	-0.18	18.06	-99.64	80.00
23	Pseudomonas aeruginosa	Piperacillin	-0.58	14.70	-99.90	100.00
24	Streptococcus pneumoniae	Macrolides	-0.88	16.57	-99.80	81.25
25	Streptococcus pneumoniae	Penicillins	-0.17	17.20	-99.66	82.14

## Supplementary Annexure 3: Descriptive Statistics on Antimicrobial Consumption

	Pathogen	Drug	Mean	SD	Min	Max
1	Acinetobacter spp.	Aminoglycosides	-0.13	5.55	-21.15	22.88
2	Acinetobacter spp.	Carbapenems	-0.24	5.32	-31.82	22.08
3	Acinetobacter spp.	Fluoroquinolones	-0.42	4.97	-22.75	27.73
4	Enterococcus faecalis	Aminopenicillins	0.09	4.63	-26.43	32.25
5	Enterococcus faecalis	Gentamicin	-0.55	8.84	-42.27	50.00
6	Enterococcus faecalis	Vancomycin	0.02	2.00	-21.97	31.09
7	Enterococcus faecium	Aminopenicillins	1.03	9.14	-37.87	39.29
8	Enterococcus faecium	Gentamicin	0.38	12.03	-49.23	59.71
9	Enterococcus faecium	Vancomycin	0.72	5.61	-27.65	46.60
10	Escherichia coli	Aminoglycosides	0.40	2.91	-13.42	25.19
11	Escherichia coli	Aminopenicillins	0.45	4.38	-23.34	23.91
12	Escherichia coli	Carbapenems	0.00	0.42	-3.03	3.03
13	Escherichia coli	Cephalosporins	0.68	2.91	-16.43	24.36
14	Escherichia coli	Fluoroquinolones	0.75	3.51	-19.87	32.16
15	Klebsiella pneumoniae	Aminoglycosides	0.07	5.66	-20.89	29.06
16	Klebsiella pneumoniae	Carbapenems	0.52	2.40	-8.98	19.07
17	Klebsiella pneumoniae	Cephalosporins	0.45	6.10	-27.94	30.33
18	Klebsiella pneumoniae	Fluoroquinolones	1.29	5.90	-29.26	28.45
19	Pseudomonas aeruginosa	Aminoglycosides	-0.60	5.92	-26.67	25.00
20	Pseudomonas aeruginosa	Carbapenems	0.17	6.44	-32.86	33.75
21	Pseudomonas aeruginosa	Ceftazidime	-0.03	7.38	-32.12	33.12
22	Pseudomonas aeruginosa	Fluoroquinolones	-0.65	6.55	-33.69	32.95
23	Pseudomonas aeruginosa	Piperacillin	-0.26	6.16	-34.13	36.38
24	Streptococcus pneumoniae	Macrolides	0.08	6.80	-37.47	27.60
25	Streptococcus pneumoniae	Penicillins	-0.36	6.82	-45.45	31.62

#### Supplementary Annexure 4: Descriptive Statistics on Antimicrobial Resistance

#### Supplementary Annexure 5: Historical Variation of Antimicrobial Consumption

The <u>online dashboard</u> presents the historical antimicrobial consumption growth variation in the 30 countries this paper focuses on from 2000 to 2020, aggregated for the 12 ATC-4 drug classes and five UN regions. For better presentation and interpretation of the consumption trends, the growth rates have been normalized relative to 2000. Accordingly, a five percent consumption growth rate in a given region should be interpreted as seven percent if the consumption growth rate in that particular region was two percent in 2000. The consumption trends are discussed by ATC-3 drug classes: J01C, J01D, J01F, J01G, J01M, and J01X.

J01C refers to Beta-lactam Antibacterials and Penicillins. J01C encompasses Penicillins with Extendedspectrum (J01CA), Beta-lactamase Sensitive Penicillins (J01CE), Beta-lactamase Resistant Penicillins (J01CF), Beta-lactamase Inhibitors (J01CG), and Combinations of Penicillins, including Beta-lactamase Inhibitors (J01CR). Consumption growth increased in almost all the regions for most of these drugs, except for J01CA. Southern Europe recorded the highest growth among all the regions, except for J01CA, where all the regions had minimal consumption growth changes. Western Europe experienced minimal consumption growth changes across all the drugs, except for J01CF, where the consumption growth almost gained a ten percentage point increase by 2020, compared to 2000. Northern Europe experienced minimal consumption growth changes across all the drugs.

J01D refers to Other Beta-lactam Antibacterials, which mainly include Cephalosporins (J01DB, J01DC, J01DD, and J01DE), Monobactams (J01DF), and Carbapenems (J01DH). Out of these, ECDC data covers J01DD (Third generation Cephalosporins) and J01DH. Eastern Europe experienced an increasing consumption growth of Cephalosporins (J01DD), which reached an increase of about ten percentage points by 2020 compared to 2000. All other regions experienced minimal consumption growth changes compared to 2000. In contrast, all the regions, except Northern Europe, experienced an increasing consumption growth of carbapenems (J01H). Similar to Cephalosporins, Eastern Europe dominated the consumption growth trends, and other regions experienced moderate movements, reaching a five to ten percentage point increase in consumption growth by 2020 compared to 2000.

J01F encompasses Macrolides, Lincosamides, and Streptogramins. ECDC data includes consumption data for J01FA, which refers to Macrolides. All the regions experienced minimal consumption growth changes in Macrolides compared to 2000.

J01G consists of Streptomycins (J01GA) and Other Aminoglycosides (J01GB), data for both of which is available from ECDC. Most regions experienced minimal consumption growth changes in Streptomycins compared to 2000. Notably, Eastern Europe experienced a decreasing consumption growth, reaching almost a five percentage point reduction compared to 2000 by 2020. All the regions, except Eastern Europe and Western Asia, experienced minimal consumption growth changes in Other Aminoglycosides. Eastern Europe and Western Asia reached about a ten percentage point increase in consumption growth by 2020, compared to 2000. J01M includes Quinolone Antibacterials: Fluoroquinolones (J01MA) and Other Quinolones (J01MB). ECDC data is available for J01MA. Consumption of Fluoroquinolones was similar to Other Aminoglycosides (J01GB), where Eastern Europe and Western Asia experienced the highest consumption growth. In contrast, the other regions experienced minimal consumption growth changes compared to 2000.

J01X refers to Antibacterials not covered in other classes, i.e., J01A-G, M, and R. J01X includes Glycopeptide Antibacterials (J01XA), which ECDC data covers. All the regions experienced consumption growth in J01XA, except Northern Europe. Southern Europe experienced almost a 13 percentage point increase in consumption growth compared to 2000. Consumption in other regions grew steadily to reach increments between 9 to 12 percentage points by 2020, compared to 2000.

Overall, we observe that the consumption growth patterns were quite heterogeneous across the regions and the drug classes from 2000 to 2020. Eastern and Southern Europe experienced consumption growth increases, compared to 2000, across most of the drug classes, while Northern Europe experienced the least consumption growth variation.

#### Supplementary Annexure 6: Historical Variation of Antimicrobial Resistance

The <u>online dashboard</u> presents the historical antimicrobial resistance growth variations in the 30 countries this paper focuses on, aggregated for five UN regions, from 2000 to 2020. The variations cover the resistance of eight pathogens to 12 antimicrobial drugs, totaling 26 antimicrobial drug-pathogen combinations. Similar to antimicrobial consumption growth variations, the growth rates have been normalized relative to those of 2000 for better presentation and interpretation of the resistance trends.

Acinetobacter spp. mostly cause respiratory diseases, which include bronchiolitis and pneumoniae (especially within healthcare settings). They also cause wound infections, suppurative infections in the lungs, skin, soft tissues, and urinary tract, and rarely meningitis (MSD Manuals 2020a). The data for the resistance growth of *Acinetobacter spp.* towards Aminoglycosides, Carbapenems, and Fluoroquinolones is available. The resistance growth of *Acinetobacter spp.* notably increased in Western Asia across all the drugs, except for Aminoglycosides, where the resistance growth decreased in Western Asia compared to 2000. Western Europe also experienced an increasing resistance growth across all the drugs. The other regions experienced minimal resistance growth changes compared to their respective resistance growth rates in 2000.

*Enterococcus faecalis* and *Enterococcus faecium* commonly cause skin and wound infections, endocarditis, bacteremia, intra-abdominal infections, and urinary tract infections (MSD Manuals 2020b). Resistance growth variations of *Enterococcus faecalis* to Aminopenicillins, Gentamicin, and Vancomycin were relatively lower than their respective resistance growth in 2000 and other antimicrobial drug-pathogen combinations. Yet, their variations were diverse across the regions and drugs. While the resistance growth of *Enterococcus faecalis* and *Enterococcus faecium* against Gentamicin increased in Western Asia, it decreased in Southern Europe compared to 2000. While Southern Europe also experienced a decreasing resistance growth from both the pathogens against Vancomycin, Western Asia experienced an increasing resistance growth from both pathogens, while Western Asia experienced an increasing resistance growth from both pathogens, while Western Asia experienced an increasing resistance growth from both pathogens demonstrated minimal resistance growth changes, compared to 2000, across all the drugs.

*Escherichia coli* mainly causes diarrheal infections, urinary tract infections, wound infections, and bacteremia (MSD Manuals 2020c). The data for its resistance growth variations towards Aminoglycosides, Aminopenicillins, Carbapenems, Fluoroquinolones, and Third generation Cephalosporins is available. Overall, the resistance growth minimally changed for Carbapenems across all the regions. Resistance growth towards Aminopenicillins, Cephalosporins, and Fluoroquinolones notably increased in Western Asia, which exceeded a three percentage point increase in growth compared to 2000. Resistance growth decreased against Aminopenicillins and Fluoroquinolones in several regions compared to 2000. Eastern and Southern Europe experienced the highest resistance growth declines for Aminopenicillins, while Southern and Western Europe experienced the highest declines for Fluoroquinolones.

*Klebsiella pneumoniae* causes pneumoniae (especially in healthcare settings), urinary tract infections, wound infections, and various bloodstream infections (MSD Manuals 2020d). The data for its resistance growth

variations towards Aminoglycosides, Carbapenems, Fluoroquinolones, and Third-generation Cephalosporins is available. The resistance growth changes were minimal for Carbapenems and Cephalosporins. At the same time, the regions illustrated mixed patterns for Fluoroquinolones, where Eastern and Western Europe experienced increasing resistance growth, and Northern Europe and Western Asia experienced decreasing resistance growth. Notably, in Western Asia, the resistance growth against Fluoroquinolones decreased by six percentage points compared to 2000.

*Pseudomonas aeruginosa* is responsible for malignant external otitis and most hospital-acquired infections. It also causes urinary tract infections, skin and soft-tissue infections, ear infections, and bacteremia (MSD Manuals 2020e). The data for its resistance growth variations towards Aminoglycosides, Carbapenems, Ceftazidime, Fluoroquinolones, and Piperacillin Tazobactam is available. The resistance growth against Carbapenems did not change noticeably in any regions. The resistance growth against Ceftazidime increased in Western Asia and decreased in Southern Europe. Several regions experienced decreases in resistance growth against Aminoglycosides, with Western Asia reaching a 15 percentage point decrease by 2020 compared to 2000. The resistance growth against Piperacillin Tazobactam decreased in Southern Europe and Western Asia, while the resistance growth against Fluoroquinolones decreased in Western Europe.

*Staphylococcus aureus* mainly causes complex skin infections (MSD Manuals 2020f). The data for its resistance growth variations against Methicillin is available. All the regions did not experience any resistance growth changes, compared to their respective growth in 2000.

*Streptococcus pneumoniae* mainly causes pneumoniae (both within the community and healthcare settings), sinusitis, meningitis, bacterial conjunctivitis, and skin infections (MSD Manuals 2020g). The data for its resistance growth variations against Macrolides and Penicillins is available. The resistant growth against Macrolides and Penicillins is growth in 2000 across all the regions except Western Asia, where it experienced a decreasing resistance growth against both Macrolides and Penicillins.

Similar to antimicrobial consumption growth variations, the resistance growth against different drug classes illustrated heterogeneous patterns across the regions from 2000 to 2020. Eastern and Southern Europe and Western Asia generally experienced notable resistance growth changes compared to 2000. Similar to antimicrobial consumption growth patterns, Northern Europe experienced minimal resistance growth changes compared to its resistance growth in 2000.

#### Supplementary Annexure 7: Historical Variation in Climate Indicators

#### **Chronic Climate Indicators**

As observed in the <u>online dashboard</u>, the mean temperature remained above the 1961-90 baseline across all the regions, with Eastern and Western Europe experiencing temperature differences close to 1.6°C. Western Asia experienced the lowest increase, close to 0.4°C, above the 1961-90 baseline. In contrast to temperature, precipitation patterns were vastly different across the regions. Western Europe experienced a gradual decrease in precipitation, while Eastern and Southern Europe observed an increase. Similar to temperature, relative humidity changes remained constant across most regions, except for Eastern Europe, which experienced a gradual decrease.

#### **Extreme Climate Indicators**

As observed in the <u>online dashboard</u>, the deviation of the maximum temperature from the 90<sup>th</sup> percentile of the baseline distribution (which is representative of months with warmer days on average) remained above the baseline across all the regions between 2000 and 2020. Western Asia experienced a moderate decline in extremely warm conditions during the day by 2020, compared to 2000. The deviation of the minimum temperature from the 90<sup>th</sup> percentile of the baseline distribution (which is representative of months with warmer nights on average) demonstrated similar variations. Western Asia and Western Europe experienced the highest and lowest increases in extremely warm conditions during the night from the 1961-90 baseline, respectively.

The deviation of the maximum temperature from the 10<sup>th</sup> percentile of the baseline distribution (which is representative of months with colder days on average) did not change much for most regions. Western Europe experienced a gradual increase in extremely cold conditions during the day, compared to 2000 by 2020, though they remained below the 1961-90 baseline. Eastern Europe experienced a decline in extremely cold conditions during the day, although the levels remained constant, close to 10 percent below the 1961-90 baseline. The deviation of the minimum temperature from the 10<sup>th</sup> percentile of the baseline distribution (which is representative of months with colder nights on average) illustrated mixed patterns across the regions. Southern Europe and Western Asia observed an increase in extremely cold conditions during the 1961-90 baseline, while Northern and Western Europe experienced a reduction. Eastern Europe remained below the 1961-90 baseline at the same level throughout the period.

Extremely dry conditions increased, though differently, across all the regions. Western Europe experienced the highest increase, where the extremely dry conditions were one percent higher than the 1961-90 baseline. Southern Europe experienced the lowest change. Extremely wet conditions noticeably reduced in Western Europe. It experienced an increase in extremely wet conditions in 2000, although the extremely wet conditions reached below the baseline towards 2020. Eastern Europe experienced an increase in extremely wet conditions, while Northern and Southern Europe remained at the same level throughout the period.

Extremely windy conditions also remained at the same level across almost all the regions, except in Western Europe, which experienced an increase by 2020 compared to 2000.

Despite geographical similarities, the historical variation in chronic and extreme climate conditions across the regions was heterogeneous. Eastern, Southern, and Western Europe demonstrated notable changes in climate indicators. Mean temperature and extremely windy conditions fairly remained with minimal fluctuations from 2000 to 2020.

#### Supplementary Annexure 8: Regularized Regression Methods

Linear regression and its variants are widely used in estimating the empirical relationships between variables. Linear regression, in general, attempts to find the magnitudes of the coefficients that minimize the residual error between the actual observations and their predicted counterparts. The general representation of a linear regression model is presented in Equation 1, and the objective function is shown in Equation 2<sup>1</sup>.

Equation 1: General Form of a Linear Regression Model

$$Y_i = \beta_0 + \sum_{j=1}^n \beta_j X_{ij} + \varepsilon$$

Equation 2: Objective Function of a Linear Regression Problem

$$\operatorname{argm} in\left(\sum_{i=1}^{N} (Y_{i} - \widehat{Y}_{i})^{2} = \sum_{i=1}^{N} \left[Y_{i} - \beta_{0} - \sum_{j=1}^{n} \beta_{j} X_{ij}\right]^{2}\right)$$

2

However, when using linear regression models for predictions, two major problems could occur: overfitting and underfitting. Overfitting occurs when the regression model performs well on the training data but poorly on the testing data. Underfitting occurs when the regression model does not perform well on either data. Regularization prevents overfitting in regression models without changing the number of features or predictor variables. LASSO (Least Absolute Shrinkage and Selection Operator) and Ridge are widely used regularization algorithms. The objective functions of LASSO and Ridge are presented in Equations 3 and 4<sup>2</sup>.

Equation 3: Objective Function of a LASSO Regression Problem

$$\operatorname{argmin}\left(\sum_{i=1}^{N} \left[Y_{i} - \beta_{0} - \sum_{j=1}^{n} \beta_{j} X_{ij}\right]^{2} + \alpha \sum_{j=1}^{n} |\beta_{j}|\right)$$

Equation 4: Objective Function of a Ridge Regression Problem

$$\operatorname{argmin}\left(\sum_{i=1}^{N} \left[Y_{i} - \beta_{0} - \sum_{j=1}^{n} \beta_{j} X_{ij}\right]^{2} + \alpha \sum_{j=1}^{n} \beta_{j}^{2}\right)$$

As illustrated in Equations 3 and 4, both LASSO and Ridge regressions start with the conventional objective function of linear regression and impose a non-negative penalty on the coefficients of the predictors. The

<sup>&</sup>lt;sup>1</sup> The notation in the equations follows the standard interpretation of an OLS regression problem, where  $Y_i$  is the dependent variable and  $X_{ij}$  is an independent variable with  $\beta_j$  as its coefficient.  $\beta_0$  is the intercept of the regression equation.

<sup>&</sup>lt;sup>2</sup> The notation in the equations follows the standard interpretation of an OLS regression problem, where  $Y_i$  is the dependent variable and  $X_{ij}$  is an independent variable with  $\beta_j$  as its coefficient.  $\beta_0$  is the intercept of the regression equation and  $\alpha$  is the regularization parameter.

penalty prevents the coefficients from being too large when optimizing the conventional objective function. The penalty in LASSO regression works with the linear summation of coefficients and, thus, could shrink some coefficients to zero. However, Ridge regression works with the squared summation of the coefficients and does not necessarily reduce the coefficients to zero. This characteristic qualifies LASSO as a feature selection algorithm that could identify the optimum set of predictors from a large group of predictors.

The two algorithms also behave differently when there are correlated predictors. While LASSO would shrink some of the coefficients of correlated variables to zero, Ridge regression would treat all the correlated variables the same. Given these differences across LASSO and Ridge, a generalized form of regularized regression combining both approaches could also be used. Equation 5<sup>3</sup> presents the objective function of the generalized form<sup>4</sup>.

Equation 5: Objective Function of a General Regularized Regression Problem

$$\operatorname{argmin}\left(\sum_{i=1}^{N} \left[Y_{i} - \beta_{0} - \sum_{j=1}^{n} \beta_{j} X_{ij}\right]^{2} + \alpha \sum_{j=1}^{n} ((1-\theta) \beta_{j}^{2} + \theta |\beta_{j}|)\right)$$

<sup>&</sup>lt;sup>3</sup> The notation in the equations follows the standard interpretation of an OLS regression problem, where  $Y_i$  is the dependent variable and  $X_{ij}$  is an independent variable with  $\beta_j$  as its coefficient.  $\beta_0$  is the intercept of the regression equation,  $\alpha$  is the regularization parameter, and  $\theta$  is the weight.

<sup>&</sup>lt;sup>4</sup> See Hastie et al. (2017) for a detailed discussion on linear, LASSO, and Ridge regression models.

Pathogen	Drug	Lambda	Variance	Bias	MSE	F Statistic	R-Squared	Adjusted R-Squared	DF	Residual Effective DF	Effective- ness Index	AIC	BIC
		0.00	2861.30	0.01	2861.31	6.01	0.43	0.36	54.98	445.00	967.89	1514.79	4853.83
		0.11	956.24	1051.37	2007.60	5.97	0.34	0.26	46.72	447.63	1.83	1504.86	4809.05
		0.22	709.76	1603.30	2313.06	5.88	0.29	0.20	41.92	449.80	1.36	1504.47	4788.44
		0.33	575.80	1987.53	2563.33	5.79	0.25	0.16	38.23	451.86	1.17	1507.27	4775.68
Acinetobacter	Aminogly-	0.44	485.42	2300.15	2785.57	5.70	0.21	0.12	35.22	453.82	1.05	1511.67	4767.41
spp.	cosides	0.56	418.73	2571.00	2989.73	5.61	0.19	0.09	32.69	455.67	0.97	1516.85	4761.95
		0.67	366.98	2812.59	3179.57	5.52	0.17	0.06	30.53	457.42	0.90	1522.34	4758.33
		0.78	325.46	3031.42	3356.88	5.44	0.15	0.04	28.66	459.07	0.85	1527.88	4755.98
		0.89	291.35	3231.44	3522.79	5.36	0.13	0.03	27.01	460.61	0.81	1533.33	4754.48
		1.00	262.80	3415.40	3678.20	5.29	0.12	0.01	25.55	462.05	0.77	1538.60	4753.60
		0.00	2547.68	0.00	2547.69	7.43	0.47	0.41	55.98	464.00	5045.02	1507.31	4997.45
		0.11	851.36	327.68	1179.04	7.39	0.38	0.31	47.63	466.63	5.22	1496.36	4950.95
		0.22	635.40	628.77	1264.17	7.27	0.32	0.24	42.75	468.82	3.08	1497.35	4931.19
		0.33	518.24	907.94	1426.18	7.13	0.27	0.19	38.99	470.90	2.27	1502.46	4920.31
Acinetobacter	Car-	0.44	439.18	1171.20	1610.38	6.98	0.24	0.15	35.92	472.89	1.83	1509.48	4914.29
spp.	bapenems	0.56	380.74	1419.30	1800.04	6.84	0.21	0.11	33.35	474.78	1.56	1517.31	4911.17
		0.67	335.23	1652.44	1987.67	6.70	0.18	0.09	31.15	476.57	1.37	1525.36	4909.84
		0.78	298.58	1871.01	2169.59	6.57	0.16	0.06	29.23	478.24	1.23	1533.32	4909.66
		0.89	268.32	2075.65	2343.98	6.46	0.14	0.04	27.55	479.81	1.12	1541.00	4910.19
		1.00	242.90	2267.15	2510.05	6.35	0.13	0.03	26.06	481.29	1.04	1548.33	4911.18
		0.00	2311.38	0.52	2311.91	6.22	0.43	0.37	54.98	445.00	18.22	1407.92	4746.96
		0.11	812.10	17574.71	18386.81	5.87	0.32	0.23	46.71	447.63	0.09	1423.10	4727.28
		0.22	607.03	21030.31	21637.34	5.75	0.26	0.17	41.91	449.80	0.08	1426.26	4710.21
		0.33	493.26	22517.69	23010.95	5.65	0.22	0.13	38.22	451.86	0.08	1429.89	4698.29
Acinetobacter	Fluoroquin-	0.44	415.85	23395.65	23811.50	5.56	0.19	0.09	35.22	453.82	0.08	1434.32	4690.05
spp.	olones	0.56	358.51	24001.92	24360.42	5.47	0.17	0.07	32.69	455.68	0.08	1439.21	4684.29
		0.67	313.92	24460.45	24774.37	5.39	0.15	0.04	30.53	457.43	0.08	1444.26	4680.24
		0.78	278.11	24827.71	25105.82	5.32	0.13	0.03	28.66	459.07	0.08	1449.29	4677.37
		0.89	248.69	25133.34	25382.03	5.25	0.12	0.01	27.01	460.61	0.08	1454.20	4675.34
		1.00	224.08	25394.57	25618.65	5.18	0.10	0.00	25.55	462.05	0.08	1458.92	4673.91
		0.00	3384.48	0.03	3384.50	0.70	0.07	-0.03	57.98	502.00	569.77	1766.80	5561.39
		0.11	1128.56	939.41	2067.97	0.70	0.05	-0.05	49.45	504.64	2.42	1751.86	5509.53
Enterococcus	Aminopeni-	0.22	832.48	1202.26	2034.74	0.70	0.04	-0.06	44.42	506.86	2.13	1743.71	5479.59
faecalis	cillins	0.33	666.64	1350.74	2017.38	0.70	0.04	-0.07	40.52	508.99	2.02	1737.77	5456.80
~		0.44	553.43	1455.84	2009.27	0.70	0.03	-0.08	37.34	511.04	1.95	1733.16	5438.41
		0.56	469.79	1537.67	2007.47	0.70	0.03	-0.08	34.67	513.00	1.90	1729.44	5423.12
		0.67	405.22	1604.73	2009.94	0.70	0.02	-0.09	32.37	514.85	1.86	1/26.37	5410.13

# Supplementary Annexure 9: Diagnostics for Empirical Models

		0.78	353.88	1661.43	2015.30	0.70	0.02	-0.09	30.38	516.59	1.83	1723.80	5398.94
		0.89	312.17	1710.41	2022.57	0.70	0.02	-0.09	28.64	518.22	1.80	1721.60	5389.18
		1.00	277.70	1753.38	2031.08	0.70	0.02	-0.10	27.09	519.75	1.78	1719.71	5380.58
		0.00	11742.37	0.10	11742.47	1.03	0.11	0.00	57.98	502.00	508.28	2463.56	6258.15
		0.11	3918.60	3928.07	7846.67	1.03	0.08	-0.02	49.45	504.64	2.00	2449.05	6206.73
		0.22	2893.10	5019.83	7912.93	1.03	0.07	-0.04	44.42	506.86	1.77	2441.31	6177.20
		0.33	2319.16	5617.44	7936.60	1.03	0.05	-0.05	40.53	508.99	1.69	2435.91	6154.94
Enterococcus	- ··	0.44	1927.47	6040.86	7968.33	1.03	0.05	-0.06	37.34	511.04	1.63	2431.90	6137.16
faecalis	Gentamicin	0.56	1638.07	6375.56	8013.64	1.03	0.04	-0.07	34.67	513.00	1.59	2428.82	6122.51
·		0.67	1414.53	6655.03	8069.56	1.03	0.04	-0.07	32.38	514.84	1.56	2426.39	6110.16
		0.78	1236.67	6895.78	8132.45	1.03	0.03	-0.08	30.39	516.58	1.53	2424.43	6099.58
		0.89	1092.06	7107.28	8199.34	1.03	0.03	-0.08	28.64	518.21	1.51	2422.82	6090.41
		1.00	972.46	7295.61	8268.08	1.03	0.02	-0.09	27.09	519.74	1.48	2421.49	6082.36
		0.00	694.12	0.00	694.12	0.48	0.05	-0.06	57.98	502.00	2241.21	879.82	4674.42
		0.11	230.97	47.84	278.81	0.48	0.04	-0.07	49.45	504.64	9.73	863.46	4621.13
		0.22	170.04	63.05	233.09	0.48	0.03	-0.07	44.42	506.86	8.34	854.23	4590.12
		0.33	135.94	72.68	208.62	0.48	0.03	-0.08	40.52	508.99	7.71	847.36	4566.39
Enterococcus		0.44	112.69	80.11	192.80	0.48	0.03	-0.08	37.34	511.04	7.28	841.93	4547.19
faecalis	Vancomycin	0.56	95.54	86.31	181.85	0.48	0.02	-0.09	34.67	513.00	6.96	837.50	4531.18
		0.67	82.31	91.69	174.00	0.48	0.02	-0.09	32.38	514.85	6.69	833.81	4517.58
		0.78	71.81	96.46	168.27	0.48	0.02	-0.09	30.39	516.58	6.47	830.69	4505.84
		0.89	63.30	100.74	164.04	0.49	0.02	-0.10	28.64	518.22	6.28	828.00	4495.59
		1.00	56.26	104.63	160.89	0.49	0.01	-0.10	27.09	519.75	6.11	825.68	4486.55
		0.00	10645.75	0.03	10645.78	1.81	0.17	0.08	57.98	502.00	1726.41	2408.54	6203.13
		0.11	3555.87	2222.00	5777.88	1.81	0.14	0.04	49.45	504.64	3.21	2394.54	6152.21
		0.22	2630.97	3270.82	5901.79	1.81	0.11	0.01	44.42	506.86	2.47	2388.10	6123.98
		0.33	2114.00	3944.71	6058.71	1.80	0.10	-0.01	40.52	508.99	2.18	2384.06	6103.08
Enterococcus	Aminopeni-	0.44	1761.16	4457.27	6218.42	1.80	0.08	-0.02	37.34	511.04	2.01	2381.41	6086.66
faecium	cillins	0.56	1500.26	4878.03	6378.28	1.79	0.07	-0.03	34.67	513.00	1.89	2379.66	6073.33
		0.67	1298.48	5237.70	6536.18	1.79	0.06	-0.04	32.37	514.85	1.80	2378.51	6062.27
		0.78	1137.70	5552.66	6690.36	1.78	0.06	-0.05	30.38	516.59	1.72	2377.77	6052.92
		0.89	1006.75	5832.84	6839.59	1.78	0.05	-0.06	28.64	518.22	1.66	2377.33	6044.91
		1.00	898.28	6084.86	6983.14	1.78	0.05	-0.06	27.09	519.75	1.61	2377.11	6037.98
		0.00	19132.96	0.11	19133.07	1.22	0.12	0.02	57.98	502.00	776.84	2736.95	6531.55
		0.11	63/8.63	4285.63	10664.27	1.23	0.10	0.00	49.45	504.64	2.99	2721.89	64/9.5/
		0.22	4706.71	5617.85	10324.56	1.23	0.08	-0.02	44.42	506.86	2.58	2/13.84	6449.73
-		0.33	3//1.28	63/3.54	10144.82	1.23	0.07	-0.03	40.53	508.99	2.42	2708.18	6427.22
Enterococcus faecium	Gentamicin	0.44	3133.33	6918.42	10051.75	1.23	0.06	-0.04	37.34	511.04	2.32	2704.00	6409.26
		0.56	2662.36	/355.70	10018.06	1.23	0.06	-0.05	54.67	513.00	2.25	2700.81	6394.49
		0.67	2298.83	7/26.35	10025.18	1.23	0.05	-0.06	32.38	514.84	2.19	2698.33	6382.09
		0.78	2009.78	8050.36	10060.14	1.23	0.05	-0.06	30.39	516.58	2.14	2696.36	63/1.52
		0.89	1774.88	8339.07	10113.94	1.23	0.04	-0.07	28.64	518.21	2.09	2694.80	6362.38
		1.00	1580.70	8599.61	10180.31	1.23	0.04	-0.07	27.09	519.74	2.05	2693.53	6354.40

		0.00	1100.10	0.00	1100.10		0.4.4	0.05	<b>FF</b> 00	500.00	5 4 4 5 4	4050.04	5 (50.44
		0.00	4132.12	0.00	4132.12	1.46	0.14	0.05	57.98	502.00	5414.74	18/8.81	56/3.41
		0.11	1378.89	426.32	1805.21	1.46	0.11	0.01	49.45	504.64	6.50	1864.04	5621.72
		0.22	1019.30	702.93	1722.23	1.46	0.09	-0.01	44.42	506.86	4.45	1857.10	5592.98
		0.33	818.27	902.80	1721.07	1.46	0.08	-0.03	40.52	508.99	3.69	1852.56	5571.59
Enterococcus	<b>V</b> /	0.44	681.07	1062.97	1744.04	1.46	0.07	-0.04	37.34	511.04	3.27	1849.39	5554.65
faecium	vancomychi	0.56	579.63	1197.83	1777.46	1.45	0.06	-0.05	34.67	513.00	2.98	1847.12	5540.80
		0.67	501.21	1314.59	1815.79	1.45	0.05	-0.06	32.38	514.85	2.78	1845.45	5529.21
		0.78	438.75	1417.49	1856.24	1.45	0.05	-0.06	30.39	516.58	2.62	1844.20	5519.35
		0.89	387.92	1509.31	1897.23	1.45	0.04	-0.07	28.64	518.22	2.50	1843.28	5510.86
		1.00	345.84	1592.01	1937.85	1.44	0.04	-0.07	27.09	519.75	2.39	1842.58	5503.45
		0.00	1163.40	0.01	1163.41	1.09	0.11	0.01	57.98	502.00	505.55	1169.05	4963.65
		0.11	388.80	422.74	811.53	1.09	0.08	-0.02	49.45	504.64	1.85	1155.16	4912.84
		0.22	287.26	559.58	846.84	1.09	0.07	-0.04	44.42	506.86	1.58	1147.86	4883.75
		0.33	230.35	636.25	866.60	1.09	0.06	-0.05	40.52	508.99	1.48	1142.68	4861.71
Escherichia	Aminogly-	0.44	191.48	689.60	881.08	1.09	0.05	-0.06	37.34	511.04	1.42	1138.78	4844.04
coli	cosides	0.56	162.74	730.64	893 37	1.08	0.04	-0.06	34.67	513.00	1 38	1135 73	4829 41
		0.67	140 53	763.99	904 52	1.08	0.04	-0.07	32.38	514 84	1 35	1133 30	4817.06
		0.78	122.86	792.05	914 90	1.08	0.03	-0.08	30.39	516 58	1 32	1131 32	4806.47
		0.89	108.48	816.21	924 69	1.08	0.03	-0.08	28.64	518.22	1.30	1129.68	4797 27
		1.00	96.60	837.36	933.96	1.08	0.03	-0.08	27.09	519.74	1.28	1128.31	4789.19
		0.00	2646 73	0.03	2646 77	1.00	0.03	0.03	57.98	502.00	355.17	1629.11	5423.70
		0.11	887.43	1449.29	2336 72	1.23	0.09	-0.01	49.45	504.64	1 22	1617.25	5374.92
		0.22	657.35	1976.36	2633.72	1.21	0.07	-0.03	44 42	506.86	1.02	1611.25	5347 32
		0.33	528.02	2276.33	2804.35	1.24	0.06	-0.05	40.52	508.99	0.94	1607.22	5326.25
T h h i .	A	0.44	430.42	2480.58	2004.33	1.24	0.05	-0.05	37.34	511.04	0.94	1603.07	5300.23
Escherichia	Aminopeni-	0.44	439.42	2400.30	2010.59	1.23	0.05	-0.00	24.67	512.00	0.90	1601.30	5309.23
1011	CHIIIIS	0.50	222.05	2032.00	2075 59	1.23	0.03	-0.00	34.07	515.00	0.87	1500.30	5293.07
		0.07	322.93	2752.05	3075.58	1.23	0.04	-0.07	32.37	514.65	0.65	1599.30	5265.00
		0.78	282.47	2850.51	3132.98	1.23	0.04	-0.07	30.38	516.59	0.85	1597.58	52/2.73
		0.89	249.52	2932.60	3182.12	1.23	0.05	-0.08	28.64	518.22	0.82	1596.16	5263.73
		1.00	222.25	3002.84	3225.09	1.23	0.05	-0.08	27.09	519.75	0.81	1594.96	5255.83
		0.00	25.81	0.00	25.81	0.65	0.07	-0.04	57.98	502.00	905.07	-964.51	2830.09
		0.11	8.59	4.08	12.67	0.65	0.05	-0.05	49.44	504.64	4.24	-980.16	2///.48
		0.22	6.33	5.29	11.62	0.66	0.04	-0.07	44.41	506.87	3.70	-988.61	2/4/.23
	_	0.33	5.07	6.05	11.12	0.66	0.04	-0.07	40.51	509.00	3.44	-994.74	2/24.24
Escherichia	Car-	0.44	4.21	6.63	10.84	0.66	0.03	-0.08	37.33	511.06	3.27	-999.49	2/05./2
coli	bapenems	0.56	3.57	7.10	10.67	0.66	0.03	-0.08	34.66	513.01	3.14	-1003.31	2690.32
		0.67	3.08	7.51	10.58	0.66	0.02	-0.09	32.37	514.86	3.04	-1006.46	2677.25
		0.78	2.69	7.86	10.54	0.66	0.02	-0.09	30.38	516.60	2.95	-1009.11	2666.00
		0.89	2.37	8.16	10.53	0.66	0.02	-0.09	28.63	518.23	2.88	-1011.37	2656.17
		1.00	2.11	8.44	10.55	0.66	0.02	-0.10	27.08	519.76	2.82	-1013.32	2647.52
		0.00	1096.15	0.00	1096.15	0.93	0.10	-0.01	57.98	502.00	3248.34	1134.38	4928.97
Escherichia	Cephalo-	0.11	364.73	142.49	507.22	0.93	0.08	-0.03	49.45	504.64	5.16	1119.23	4876.90
coli	sporins	0.22	269.09	215.30	484.39	0.93	0.06	-0.04	44.41	506.86	3.86	1111.15	4847.02
		0.33	215.49	260.44	475.93	0.94	0.06	-0.05	40.52	508.99	3.40	1105.24	4824.25

		0.44	170.00	000.01	171.02	0.04	0.05	0.04	07.04	544.05	2.45	1100 17	1005 00
		0.44	178.90	292.94	4/1.83	0.94	0.05	-0.06	37.34	511.05	3.15	1100.67	4805.90
		0.56	151.87	318.32	470.19	0.94	0.04	-0.07	34.66	513.00	2.98	1097.02	4/90.68
		0.67	131.02	339.16	470.17	0.94	0.04	-0.07	32.37	514.85	2.86	1094.05	4777.80
		0.78	114.44	356.83	471.26	0.94	0.04	-0.07	30.38	516.59	2.76	1091.61	4766.73
		0.89	100.97	372.16	473.13	0.94	0.03	-0.08	28.63	518.22	2.69	1089.56	4757.12
		1.00	89.85	385.68	475.53	0.94	0.03	-0.08	27.08	519.75	2.62	1087.83	4748.68
		0.00	1619.80	0.02	1619.81	2.05	0.19	0.10	57.98	502.00	432.73	1354.36	5148.96
		0.11	545.77	1365.08	1910.85	2.03	0.14	0.05	49.45	504.64	0.80	1345.02	5102.70
		0.22	404.90	1876.47	2281.37	2.02	0.12	0.02	44.42	506.86	0.65	1340.04	5075.93
		0.33	325.61	2138.92	2464.53	2.01	0.11	0.00	40.52	508.99	0.61	1336.46	5055.49
Escherichia	Fluoroquin-	0.44	271.31	2306.92	2578.23	2.01	0.09	-0.01	37.34	511.04	0.59	1333.91	5039.16
coli	olones	0.56	231.09	2427.84	2658.93	2.00	0.08	-0.02	34.67	513.00	0.58	1332.09	5025.77
		0.67	199.96	2521.30	2721.26	2.00	0.07	-0.03	32.37	514.85	0.57	1330.81	5014.58
		0.78	175.15	2596.98	2772.14	2.00	0.07	-0.04	30.38	516.58	0.56	1329.93	5005.08
		0.89	154.95	2660.30	2815.25	1.99	0.06	-0.04	28.64	518.22	0.55	1329.35	4996.92
		1.00	138.22	2714.53	2852.75	1.99	0.06	-0.05	27.09	519.75	0.55	1328.98	4989.85
		0.00	4424.37	0.00	4424.37	1.77	0.17	0.08	57.98	502.00	9196.09	1917.09	5711.69
		0.11	1476.11	323.24	1799.35	1.77	0.13	0.04	49.45	504.64	9.18	1902.25	5659.93
		0.22	1091.96	576.51	1668.47	1.77	0.11	0.01	44.42	506.86	5.82	1895.66	5631.55
		0.33	877.44	780.83	1658.27	1.77	0.09	-0.01	40.52	508.99	4.57	1891.62	5610.66
Klebsiella	Aminogly-	0.44	731.05	954.78	1685.84	1.76	0.08	-0.02	37.34	511.04	3.89	1889.01	5594.27
pneumoniae	cosides	0.56	622.80	1106.72	1729.52	1.76	0.07	-0.03	34.67	513.00	3.46	1887.29	5580.98
*		0.67	539.06	1241.47	1780.53	1.75	0.06	-0.04	32.38	514.84	3.15	1886.16	5569.93
		0.78	472.32	1362.26	1834.58	1.75	0.06	-0.05	30.39	516.58	2.92	1885.44	5560.59
		0.89	417.96	1471.38	1889.34	1.74	0.05	-0.06	28.64	518.22	2.74	1885.01	5552.59
		1.00	372.93	1570.59	1943.51	1.74	0.05	-0.06	27.09	519.74	2.60	1884.77	5545.65
		0.00	721.63	0.01	721.64	2.34	0.21	0.12	57.98	502.00	272.75	900.68	4695.27
		0.11	241.13	362.49	603.62	2.34	0.17	0.07	49 44	504 64	1 34	887 24	4644 88
		0.22	178.49	449.17	627.66	2 33	0.14	0.04	44 41	506.87	1.27	881.20	4617.04
		0.33	143 58	499.19	642.78	2 32	0.12	0.02	40.51	509.00	1.17	877.94	4596.92
Klahsialla	Cor	0.44	119.80	537.10	656.90	2.32	0.10	0.00	37 33	511.06	1.17	876.24	4581 45
pneumoniae	bapenems	0.56	102.23	568.81	671.04	2.31	0.09	-0.01	34.66	513.01	1.10	875 51	4569.15
prominent	Superiento	0.67	88.64	596.52	685.16	2.30	0.08	-0.03	32 37	514.86	1.07	875.39	4559.11
		0.78	77.80	621.26	699.06	2.2)	0.07	-0.03	30.38	516.60	1.07	875.66	4550.77
		0.89	68.96	643.64	712.60	2.20	0.06	-0.04	28.63	518.23	1.07	876.19	4543.73
		1.00	61.63	664.06	725.60	2.27	0.06	-0.04	27.08	510.25	1.02	876.87	4537 71
		0.00	5212.15	0.00	5212.15	1.70	0.00	-0.05	57.08	502.00	8736.02	2007.52	5802.12
		0.00	3212.13	208.15	2022.00	1.79	0.17	0.08	37.98 40.45	502.00	0730.92	2007.52	5750.10
		0.11	1/34./4	296.13	2032.69	1.79	0.14	0.04	49.43	504.04	7.01	1992.33	5750.19
771.1 • 11		0.22	1285.01	505.77	1840.79	1.79	0.11	0.01	44.41	506.80	7.01	1985.82	5721.09
Klebstella	Cephalo-	0.35	1030.71	/88.01	1818.72	1.78	0.10	-0.01	40.52	508.99	5.34	1981.69	5700.70
pneumonide	sponus	0.44	838.30	981.72	1840.27	1./8	0.08	-0.02	37.34	511.05	4.40	1979.00	5684.25
		0.56	/31.28	1152.00	1883.28	1.//	0.07	-0.03	34.66	513.00	3.91	1977.21	56/0.86
		0.67	632.86	1303.59	1936.46	1.77	0.07	-0.04	32.37	514.85	3.54	19/6.02	5659.76
		0.78	554.45	1439.85	1994.30	1.77	0.06	-0.05	30.38	516.59	3.26	1975.26	5650.39

		0.89	490.60	1563.23	2053.83	1.76	0.05	-0.06	28.63	518.22	3.04	1974.79	5642.35
		1.00	437.71	1675.62	2113.33	1.76	0.05	-0.06	27.08	519.75	2.87	1974.54	5635.39
		0.00	4909.07	0.09	4909.15	1.22	0.12	0.02	57.98	502.00	252.24	1975.28	5769.88
		0.11	1645.76	3445.99	5091.75	1.22	0.09	-0.01	49.45	504.64	0.96	1963.12	5720.80
		0.22	1217.28	4412.49	5629.77	1.22	0.07	-0.03	44.42	506.86	0.84	1956.45	5692.34
		0.33	976.86	4906.11	5882.96	1.22	0.06	-0.05	40.52	508.99	0.81	1951.69	5670.72
Klebsiella	Fluoroquin-	0.44	812.50	5228.96	6041.47	1.22	0.05	-0.06	37.34	511.04	0.79	1948.15	5653.40
pneumoniae	olones	0.56	690.94	5466.92	6157.86	1.21	0.05	-0.06	34.67	513.00	0.78	1945.43	5639.11
		0.67	596.96	5654.64	6251.59	1.21	0.04	-0.07	32.37	514.85	0.77	1943.29	5627.05
		0.78	522.13	5809.20	6331.33	1.21	0.04	-0.07	30.38	516.58	0.76	1941.59	5616.74
		0.89	461.26	5940.19	6401.45	1.21	0.03	-0.08	28.64	518.22	0.75	1940.22	5607.79
		1.00	410.90	6053.52	6464.42	1.21	0.03	-0.08	27.09	519.75	0.75	1939.09	5599.96
		0.00	4689.84	0.02	4689.86	1.86	0.18	0.08	57.98	502.00	1257.81	1949.72	5744.32
		0.11	1565.49	619.81	2185.30	1.86	0.14	0.04	49.45	504.64	5.07	1935.18	5692.86
		0.22	1159.21	914.22	2073.44	1.85	0.11	0.01	44.42	506.86	3.89	1929.13	5665.02
		0.33	932.62	1154.54	2087.16	1.85	0.09	-0.01	40.52	508.99	3.28	1925.78	5644.81
Pseudomonas	Aminogly-	0.44	777.96	1364.74	2142.70	1.84	0.08	-0.03	37.34	511.04	2.89	1923.84	5629.10
aeruginosa	cosides	0.56	663.49	1551.72	2215.22	1.83	0.07	-0.04	34.67	513.00	2.61	1922.74	5616.42
		0.67	574.85	1719.37	2294.22	1.83	0.06	-0.05	32.38	514.84	2.41	1922.17	5605.93
		0.78	504.12	1870.54	2374.66	1.82	0.05	-0.06	30.39	516.58	2.25	1921.93	5597.08
		0.89	446.44	2007.52	2453.95	1.82	0.05	-0.06	28.64	518.22	2.13	1921.91	5589.50
		1.00	398.59	2132.18	2530.78	1.81	0.04	-0.07	27.09	519.74	2.03	1922.05	5582.92
		0.00	5672.48	0.08	5672.56	1.78	0.17	0.08	57.98	502.00	309.76	2055.32	5849.92
		0.11	1894.05	2590.51	4484.56	1.78	0.13	0.04	49.44	504.64	1.47	2041.48	5799.12
		0.22	1399.93	3233.29	4633.21	1.78	0.11	0.01	44.41	506.87	1.33	2034.61	5770.45
Pseudomonas		0.33	1124.01	3590.12	4714.13	1.78	0.10	-0.01	40.51	509.00	1.28	2030.27	5749.25
	Car-	0.44	935.94	3848.31	4784.25	1.77	0.08	-0.02	37.33	511.06	1.24	2027.43	5732.64
aeruginosa	bapenems	0.56	797.04	4056.81	4853.85	1.77	0.07	-0.03	34.66	513.01	1.21	2025.57	5719.20
		0.67	689.71	4234.49	4924.20	1.76	0.06	-0.04	32.37	514.86	1.18	2024.35	5708.07
		0.78	604.24	4390.45	4994.69	1.76	0.06	-0.05	30.38	516.60	1.16	2023.58	5698.69
		0.89	534.67	4529.80	5064.47	1.75	0.05	-0.06	28.63	518.23	1.14	2023.14	5690.68
		1.00	477.06	4655.79	5132.85	1.75	0.05	-0.06	27.08	519.76	1.12	2022.92	5683.75
		0.00	6794.82	0.10	6794.92	2.79	0.24	0.16	57.98	502.00	295.72	2157.34	5951.94
		0.11	2274.10	3098.83	5372.93	2.78	0.19	0.10	49.45	504.64	1.47	2144.18	5901.86
		0.22	1686.75	3901.33	5588.08	2.77	0.16	0.06	44.42	506.86	1.32	2139.06	5874.94
		0.33	1359.79	4408.43	5768.22	2.75	0.13	0.04	40.52	508.99	1.24	2136.86	5855.89
Pseudomonas	C G II	0.44	1136.96	4812.54	5949.50	2.74	0.11	0.01	37.34	511.04	1.19	2136.27	5841.52
aeruginosa	Certazidime	0.56	972.13	5160.34	6132.47	2.72	0.10	0.00	34.67	513.00	1.14	2136.61	5830.28
-		0.67	844.44	5469.43	6313.86	2.70	0.09	-0.02	32.37	514.85	1.10	2137.51	5821.26
		0.78	742.44	5748.53	6490.98	2.69	0.08	-0.03	30.38	516.59	1.06	2138.73	5813.87
		0.89	659.15	6002.90	6662.04	2.67	0.07	-0.04	28.63	518.22	1.03	2140.14	5807.71
		1.00	589.94	6236.13	6826.07	2.66	0.06	-0.05	27.08	519.75	1.00	2141.64	5802.51
Pseudomonas	Fluoroquin-	0.00	5647.23	0.01	5647.24	1.45	0.14	0.05	57.98	502.00	4123.77	2053.73	5848.32
aeruginosa	olones	0.11	1884.34	464.40	2348.74	1.45	0.11	0.01	49.45	504.64	8.15	2038.93	5796.61

		0.22	1393.47	817.99	2211 46	1.45	0.09	-0.01	44 42	506.86	5 23	2032 15	5768.04
		0.33	1118.93	1094 71	2213.64	1.15	0.08	-0.03	40.52	508.99	4 16	2027 74	5746.77
		0.44	931.45	1321.20	2252.65	1.15	0.07	-0.04	37.34	511.04	3 59	2024.66	5729.91
		0.56	792 79	1512 72	2305 51	1 44	0.06	-0.05	34.67	513.00	3 23	2022 43	5716.11
		0.67	685.56	1678.40	2363.97	1.44	0.05	-0.06	32.37	514.85	2.97	2020.80	5704 56
		0.78	600.15	1824 11	2424.26	1 44	0.04	-0.06	30.38	516 58	2.78	2019 58	5694 72
		0.89	530.62	1953.81	2484.43	1.44	0.04	-0.07	28.64	518.22	2.63	2018.67	5686.24
		1.00	473.06	2070.36	2543.42	1.44	0.04	-0.07	27.09	519.75	2.51	2017.98	5678.85
		0.00	4732.17	0.00	4732.17	1.80	0.18	0.08	56.98	483.00	5529.18	1889 50	5531 50
		0.11	1571.68	651.10	2222.78	1.80	0.14	0.04	48.52	485.65	4.89	1875.83	5481.49
		0.22	1160.11	1134.71	2294.82	1.80	0.11	0.01	43.56	487.86	3.17	1869.97	5454.34
		0.33	931.10	1475.32	2406.42	1.79	0.10	-0.01	39.73	489.97	2.59	1866.25	5434.19
Pseudomonas		0.44	775.10	1736.17	2511.27	1.79	0.08	-0.02	36.61	492.00	2.30	1863.74	5418.28
aeruginosa	Piperacillin	0.56	659.91	1947.30	2607.21	1.78	0.07	-0.03	33.98	493.92	2.11	1862.03	5405.32
0		0.67	570.90	2124.58	2695.48	1.78	0.06	-0.04	31.74	495.74	1.97	1860.87	5394.52
		0.78	500.04	2277.22	2777.26	1.77	0.06	-0.05	29.78	497.45	1.87	1860.10	5385.37
		0.89	442.37	2411.04	2853.41	1.77	0.05	-0.06	28.07	499.05	1.79	1859.61	5377.53
		1.00	394.62	2529.96	2924.58	1.76	0.05	-0.06	26.55	500.55	1.73	1859.32	5370.72
		0.00	4453.86	0.14	4454.00	1.79	0.17	0.08	56.98	483.00	142.14	1857.13	5499.13
		0.11	1484.65	4271.34	5755.99	1.78	0.14	0.04	48.52	485.65	0.70	1845.12	5450.77
		0.22	1093.75	5168.77	6262.52	1.78	0.12	0.01	43.56	487.87	0.65	1838.42	5422.80
		0.33	876.65	5597.49	6474.14	1.78	0.10	0.00	39.73	489.98	0.64	1833.95	5401.90
Streptococcus		0.44	729.06	5874.40	6603.46	1.77	0.09	-0.02	36.61	492.00	0.64	1830.87	5385.42
pneumoniae	Macrolides	0.56	620.25	6080.02	6700.26	1.77	0.08	-0.03	33.99	493.92	0.63	1828.71	5372.01
		0.67	536.28	6244.69	6780.97	1.77	0.07	-0.04	31.74	495.74	0.63	1827.20	5360.86
		0.78	469.50	6382.68	6852.18	1.76	0.06	-0.05	29.79	497.44	0.63	1826.14	5351.43
		0.89	415.20	6501.71	6916.91	1.76	0.06	-0.05	28.08	499.04	0.63	1825.43	5343.36
		1.00	370.27	6606.46	6976.73	1.76	0.05	-0.06	26.56	500.54	0.62	1824.95	5336.37
		0.00	4378.22	0.00	4378.23	1.31	0.13	0.03	56.98	483.00	4024.50	1848.31	5490.31
		0.11	1455.95	824.43	2280.39	1.31	0.10	-0.01	48.52	485.65	3.57	1835.03	5440.72
		0.22	1074.65	1359.61	2434.26	1.31	0.08	-0.03	43.57	487.86	2.45	1829.21	5413.63
		0.33	862.53	1715.76	2578.29	1.30	0.06	-0.04	39.74	489.97	2.06	1825.35	5393.35
Streptococcus	Deniallina	0.44	717.86	1981.58	2699.44	1.30	0.05	-0.06	36.62	491.99	1.86	1822.56	5377.16
pneumoniae	Perifcilinis	0.56	610.88	2192.71	2803.58	1.30	0.05	-0.06	34.00	493.91	1.73	1820.46	5363.81
		0.67	528.13	2366.92	2895.05	1.30	0.04	-0.07	31.75	495.72	1.64	1818.83	5352.54
		0.78	462.21	2514.42	2976.63	1.29	0.04	-0.08	29.80	497.43	1.57	1817.55	5342.89
		0.89	408.55	2641.67	3050.22	1.29	0.03	-0.08	28.09	499.03	1.51	1816.52	5334.50
		1.00	364.11	2753.02	3117.13	1.29	0.03	-0.08	26.57	500.53	1.47	1815.68	5327.14

Pathogen	Drug	Lambda	Growth in Antimicro- bial Con- sumption	Tempera- ture	Precipita- tion	Relative Humidity	Extremely Warm Conditions during the Day	Extremely Cold Conditions during the	Extremely Warm Conditions during the Night	Extremely Cold Conditions during the Night	Extremely Dry Conditions	Extremely Wet Conditions	Extremely Windy Days	Growth in GDP per Capita
		0.00	1 1 1	4 30	1.97	1.70	9.47	2 54	7.82	1.03	1.40	1 34	1 33	3.05
		0.00	0.86	1.42	1.17	1.70	1 39	1.00	1.36	1.55	0.98	0.94	0.95	1.30
		0.22	0.69	0.79	0.78	0.76	0.64	0.74	0.68	0.78	0.74	0.72	0.73	0.78
		0.33	0.57	0.53	0.78	0.70	0.04	0.58	0.00	0.78	0.74	0.58	0.58	0.78
Acinetobac-	Aminogly-	0.35	0.48	0.39	0.46	0.47	0.40	0.38	0.45	0.47	0.48	0.48	0.48	0.41
ter spp.	cosides	0.56	0.40	0.31	0.40	0.39	0.23	0.39	0.35	0.38	0.40	0.40	0.40	0.33
		0.67	0.35	0.25	0.30	0.33	0.19	0.33	0.20	0.32	0.34	0.35	0.35	0.28
		0.78	0.31	0.21	0.27	0.39	0.16	0.29	0.18	0.27	0.30	0.30	0.30	0.24
		0.89	0.27	0.18	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.20
		1.00	0.24	0.16	0.21	0.23	0.12	0.22	0.10	0.21	0.23	0.23	0.23	0.18
		0.00	1 16	4 28	1.95	1.71	9.36	2.53	7.73	1.90	1 38	1 33	1 33	2.95
		0.11	0.88	1.41	1.12	1.04	1.39	1.01	1.36	1.13	0.97	0.94	0.95	1.29
		0.22	0.70	0.79	0.78	0.76	0.64	0.74	0.68	0.78	0.74	0.72	0.73	0.78
		0.33	0.57	0.53	0.59	0.59	0.40	0.58	0.45	0.59	0.59	0.58	0.58	0.55
Acinetobac-	Car-	0.44	0.48	0.39	0.47	0.47	0.29	0.47	0.33	0.47	0.48	0.48	0.48	0.42
ter spp.	bapenems	0.56	0.41	0.31	0.38	0.39	0.23	0.39	0.26	0.38	0.40	0.40	0.40	0.33
**	ŕ	0.67	0.35	0.25	0.32	0.33	0.19	0.33	0.22	0.32	0.34	0.35	0.35	0.28
		0.78	0.31	0.21	0.27	0.29	0.16	0.29	0.18	0.27	0.30	0.30	0.30	0.24
		0.89	0.27	0.18	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.21
		1.00	0.24	0.16	0.21	0.22	0.12	0.22	0.14	0.21	0.23	0.23	0.23	0.18
		0.00	1.13	4.31	1.96	1.70	9.48	2.55	7.82	1.94	1.40	1.34	1.33	3.04
		0.11	0.87	1.42	1.12	1.04	1.39	1.01	1.36	1.13	0.98	0.94	0.95	1.30
		0.22	0.70	0.79	0.78	0.76	0.64	0.74	0.68	0.78	0.75	0.72	0.73	0.78
		0.33	0.57	0.53	0.59	0.59	0.40	0.58	0.45	0.59	0.59	0.58	0.58	0.54
Acinetobac-	Fluoro-	0.44	0.48	0.39	0.46	0.47	0.29	0.47	0.33	0.47	0.48	0.48	0.48	0.41
ter spp.	quinolones	0.56	0.41	0.31	0.38	0.39	0.23	0.39	0.26	0.38	0.40	0.40	0.40	0.33
		0.67	0.35	0.25	0.32	0.33	0.19	0.33	0.21	0.32	0.34	0.35	0.35	0.28
		0.78	0.31	0.21	0.27	0.29	0.16	0.29	0.18	0.27	0.30	0.30	0.30	0.24
		0.89	0.27	0.18	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.20
		1.00	0.24	0.16	0.21	0.22	0.12	0.22	0.14	0.21	0.23	0.23	0.23	0.18
		0.00	1.11	4.13	1.92	1.61	8.85	2.50	7.78	1.89	1.38	1.30	1.35	3.00
		0.11	0.86	1.41	1.11	1.02	1.39	0.99	1.36	1.12	0.98	0.94	0.96	1.30
Entone ocorres	Ami-	0.22	0.69	0.79	0.78	0.75	0.65	0.73	0.68	0.78	0.74	0.72	0.73	0.78
faecalis	nopenicil-	0.33	0.57	0.53	0.59	0.59	0.41	0.58	0.44	0.59	0.59	0.58	0.59	0.55
faecalis	lins	0.44	0.48	0.39	0.47	0.48	0.30	0.47	0.33	0.47	0.48	0.48	0.48	0.42
		0.56	0.41	0.31	0.38	0.40	0.24	0.39	0.26	0.38	0.40	0.41	0.40	0.33
		0.67	0.36	0.25	0.32	0.34	0.19	0.33	0.21	0.32	0.34	0.35	0.35	0.28

## Supplementary Annexure 10: Variance Inflation Factors for Confounders

1   0.78   0.73   0.71   0.72   0.74   0.75   0.															
1089   0.27   0.19   0.24   0.25   0.16   0.24   0.26   0.23   0.05   0.23   0.23   0.05   0.23   0.25   0.25   0.25   0.23   0.23   0.44   0.44   0.44   0.44   0.45   0.44   0.25   0.24   0.25 <th< td=""><td></td><td></td><td>0.78</td><td>0.31</td><td>0.21</td><td>0.28</td><td>0.29</td><td>0.16</td><td>0.29</td><td>0.18</td><td>0.27</td><td>0.30</td><td>0.30</td><td>0.30</td><td>0.24</td></th<>			0.78	0.31	0.21	0.28	0.29	0.16	0.29	0.18	0.27	0.30	0.30	0.30	0.24
1.00   0.24   0.16   0.21   0.21   0.23   0.33   0.30   0.35   0.53   0.50   0.51   0.53   0.57   0.53   0.57   0.53   0.57   0.53   0.57   0.53   0.57   0.53   0.57   0.53   0.57   0.53   0.57   0.53   0.57   0.53   0.57   0.53   0.57   0.53   0.57   0.53   0.57   0.53   0.57   0.53   0.57   0.53   0.57   0.53   0.57   0.53   0.57   0.53   0.57   0.53   0.52   0.51   0.53   0.53   0.53   0.52   0.51   0.52   0.51   0.53   0.53   0.52   0.51   0.52   0.51   0.53   0.53   0.53   0.52   0.51   0.52   0.51 <th< td=""><td></td><td></td><td>0.89</td><td>0.27</td><td>0.19</td><td>0.24</td><td>0.25</td><td>0.14</td><td>0.25</td><td>0.16</td><td>0.24</td><td>0.26</td><td>0.26</td><td>0.26</td><td>0.21</td></th<>			0.89	0.27	0.19	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.21
Entronework   0.00   1.10   4.11   1.91   1.61   8.87   2.90   7.81   1.90   1.20			1.00	0.24	0.16	0.21	0.22	0.13	0.22	0.14	0.21	0.23	0.23	0.23	0.18
net   net<			0.00	1.10	4.11	1.91	1.61	8.87	2.50	7.81	1.90	1.39	1.29	1.35	2.99
Listnessex   0.62   0.69   0.79   0.75   0.67   0.77   0.78   0.74   0.72   0.73   0.75     Listnessex   0.43   0.43   0.43   0.59   0.59   0.44   0.59   0.58   0.59     fiesses   0.44   0.43   0.43   0.43   0.44   0.49   0.39   0.25   0.38   0.40   0.44   0.39   0.48   0.48   0.48   0.42     0.67   0.36   0.21   0.22   0.31   0.21   0.28   0.29   0.14   0.35   0.35   0.35   0.28     0.78   0.31   0.21   0.22   0.14   0.22   0.16   0.22   0.30   0.30   0.30   0.30   0.30   0.30   0.31			0.11	0.86	1.41	1.11	1.02	1.39	0.99	1.36	1.12	0.98	0.93	0.96	1.30
Intermanan   number   num			0.22	0.69	0.79	0.78	0.75	0.65	0.73	0.67	0.78	0.74	0.72	0.73	0.78
Internance jscadii   Germanii   0.44   0.48   0.49   0.47   0.33   0.47   0.48   0.48   0.48   0.42     jscadii   Gin   0.65   0.44   0.33   0.36   0.40   0.44   0.49   0.33   0.21   0.32   0.34   0.43   0.35   0.35   0.23     0.67   0.36   0.47   0.31   0.21   0.32   0.34   0.42   0.35   0.35   0.24     0.89   0.27   0.19   0.24   0.25   0.14   0.25   0.16   0.24   0.26   0.23   0.23   0.24     0.10   0.24   0.16   0.21   0.22   0.13   0.22   0.14   0.21   0.23   0.23   0.24   0.23   0.24   0.23   0.23   0.24   0.23   0.24   0.23   0.24   0.23   0.24   0.23   0.24   0.23   0.24   0.23   0.24   0.24   0.25   0.23   0.23   0.24   0.24			0.33	0.57	0.53	0.59	0.59	0.41	0.58	0.44	0.59	0.59	0.58	0.59	0.55
jendli   cin   0.56   0.41   0.31   0.38   0.40   0.29   0.26   0.38   0.40   0.41   0.40   0.33     0.67   0.36   0.31   0.21   0.28   0.32   0.32   0.30   0.30   0.30   0.20   0.21   0.22   0.16   0.22   0.16   0.22   0.16   0.24   0.26   0.26   0.21   0.23   0.23   0.23   0.23   0.21   0.21   0.23   0.23   0.23   0.21   0.21   0.23   0.23   0.21   0.21   0.21   0.23   0.23   0.21   0.21   0.23   0.23   0.25   0.11   0.46   0.41   1.12   0.91   1.12   0.98   0.79   0.78   0.75   0.43   0.47   0.48   0.74   0.72   0.73   0.75   0.55   0.41   0.58   0.44   0.59   0.48   0.40   0.59   0.51   0.55   0.51   0.58   0.41   0.59   0.51   0	Enterococcus	Gentami-	0.44	0.48	0.39	0.47	0.48	0.30	0.47	0.33	0.47	0.48	0.48	0.48	0.42
Example is interval   0.67   0.36   0.25   0.32   0.34   0.19   0.33   0.21   0.32   0.33   0.22     0.89   0.77   0.19   0.24   0.25   0.14   0.25   0.16   0.24   0.26   0.26   0.26   0.21   0.23   0.14   0.21   0.23   0.23   0.23   0.23   0.23   0.24   0.25   0.16   0.21   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.24   0.23   0.24   0.23   0.24   0.23   0.24   0.23   0.23   0.24   0.23   0.24   0.23   0.24   0.23   0.24   0.23   0.24   0.23   0.24   0.25   0.25   0.25   0.25   0.24   0.23   0.21   0.23   0.21   0.23   0.23   0.24   0.33   0.24   0.33   0.24   0.33	faecalis	cin	0.56	0.41	0.31	0.38	0.40	0.24	0.39	0.26	0.38	0.40	0.41	0.40	0.33
			0.67	0.36	0.25	0.32	0.34	0.19	0.33	0.21	0.32	0.34	0.35	0.35	0.28
			0.78	0.31	0.21	0.28	0.29	0.16	0.29	0.18	0.27	0.30	0.30	0.30	0.24
inf   inf<			0.89	0.27	0.19	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.21
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $			1.00	0.24	0.16	0.21	0.22	0.13	0.22	0.14	0.21	0.23	0.23	0.23	0.18
Entrementary farcadia   Ami- openicial- invantary   0.11   0.86   1.41   1.11   1.02   1.39   0.99   1.36   1.12   0.98   0.94   0.96   1.30     Entrementary facadia   0.33   0.57   0.53   0.59   0.59   0.41   0.58   0.74   0.72   0.73   0.78     Main   0.44   0.48   0.59   0.51   0.53   0.59   0.51   0.53   0.59   0.51     Cin   0.56   0.44   0.48   0.39   0.47   0.33   0.47   0.48   0.48   0.44   0.48   0.44   0.48   0.44   0.48   0.44   0.48   0.44   0.44   0.48   0.44   0.44   0.44   0.42   0.44   0.25   0.16   0.24   0.26   0.24   0.26   0.24   0.24   0.25   0.16   0.24   0.26   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23 <th< td=""><td></td><td></td><td>0.00</td><td>1.10</td><td>4.11</td><td>1.92</td><td>1.61</td><td>8.85</td><td>2.50</td><td>7.79</td><td>1.88</td><td>1.38</td><td>1.29</td><td>1.36</td><td>2.97</td></th<>			0.00	1.10	4.11	1.92	1.61	8.85	2.50	7.79	1.88	1.38	1.29	1.36	2.97
Entenwares facadia   0.033 0.33   0.67 0.57   0.78 0.53   0.67 0.59   0.64 0.56   0.73 0.59   0.78 0.59   0.78 0.55   0.59 0.55     jecalis   0.44   0.48   0.33   0.57   0.53   0.59   0.58   0.44   0.48   0.49   0.44   0.48   0.40   0.44   0.44   0.44   0.44   0.44   0.44   0.44   0.44   0.44   0.44   0.44   0.44   0.40   0.33   0.21   0.32   0.34   0.30   0.30   0.30   0.30   0.30   0.30   0.30   0.32   0.14   0.25   0.16   0.24   0.26   0.26   0.26   0.26   0.26   0.26   0.23   0.23   0.23   0.23   0.18   1.30   1.30   1.30   1.30   1.30   1.30   1.30   1.30   1.30   0.33   0.47   0.48 <td< td=""><td></td><td></td><td>0.11</td><td>0.86</td><td>1.41</td><td>1.11</td><td>1.02</td><td>1.39</td><td>0.99</td><td>1.36</td><td>1.12</td><td>0.98</td><td>0.94</td><td>0.96</td><td>1.30</td></td<>			0.11	0.86	1.41	1.11	1.02	1.39	0.99	1.36	1.12	0.98	0.94	0.96	1.30
Entennovari facadii   Vancomy cin   0.33 0.43   0.57 0.44   0.58 0.59   0.44 0.48   0.58 0.30   0.47   0.33 0.47   0.48 0.33   0.47   0.48 0.48   0.48   0.48   0.48   0.48   0.48   0.48   0.48   0.48   0.48   0.44   0.44   0.48   0.44   0.43   0.22   0.14   0.22   0.31   0.22   0.24   0.26   0.22   0.14   0.22   0.16   0.24   0.26   0.26   0.26   0.26   0.22   0.14   0.22   0.14   0.21   0.22   0.14   0.21   0.22   0.14   0.21   0.22   0.13   0.30   0.31   0.30   0.31   0.31   0.32   0.31   0.30   0.3			0.22	0.69	0.79	0.78	0.75	0.65	0.73	0.68	0.78	0.74	0.72	0.73	0.78
Entensoura   Vancemy- in   0.44   0.48   0.43   0.30   0.47   0.33   0.47   0.48   0.48   0.44   0.48   0.44   0.48   0.48   0.42     jaculis   0.56   0.41   0.31   0.38   0.40   0.24   0.39   0.26   0.38   0.40   0.41   0.40   0.33     0.67   0.36   0.21   0.22   0.34   0.19   0.33   0.21   0.32   0.34   0.30   0.30   0.30   0.30   0.24   0.24   0.25   0.14   0.22   0.18   0.28   0.20   0.33   0.21   0.23   0.24   0.33   0.31   0.33   0.37   0.55   0.55   0.55   0.55		<b>N</b> 7	0.33	0.57	0.53	0.59	0.59	0.41	0.58	0.44	0.59	0.59	0.58	0.59	0.55
jacadi:   Chi   0.56   0.41   0.31   0.32   0.34   0.33   0.26   0.38   0.40   0.41   0.40   0.33     0.67   0.36   0.25   0.32   0.34   0.32   0.34   0.35   0.34   0.25   0.28   0.22   0.16   0.22   0.16   0.22   0.16   0.24   0.26   0.26   0.26   0.26   0.22   0.26   0.22   0.16   0.22   0.16   0.22   0.16   0.22   0.16   0.21   0.22   0.11   0.21   0.23   0.24   0.33   0.31   0.33   0.75   0.65   0.73   0.64   0.59   0.58   0.59   0.55	Enterococcus	vancomy-	0.44	0.48	0.39	0.47	0.48	0.30	0.47	0.33	0.47	0.48	0.48	0.48	0.42
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	faecalis	ciii	0.56	0.41	0.31	0.38	0.40	0.24	0.39	0.26	0.38	0.40	0.41	0.40	0.33
Arris facium   Arris 0,56   0.31 0.0   0.21 0.27   0.13 0.24   0.25 0.25   0.14 0.22   0.16 0.22   0.16 0.24   0.26 0.26   0.26 0.26   0.22 0.23   0.23 0.23   0.23   0.23 0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.23   0.24   0.26   0.58   0.44   0.44   0.44   0.44   0.44   0.44   0.44			0.67	0.36	0.25	0.32	0.34	0.19	0.33	0.21	0.32	0.34	0.35	0.34	0.28
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $			0.78	0.31	0.21	0.28	0.29	0.16	0.29	0.18	0.28	0.30	0.30	0.30	0.24
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $			0.89	0.27	0.19	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.21
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$			1.00	0.24	0.16	0.21	0.22	0.13	0.22	0.14	0.21	0.23	0.23	0.23	0.18
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $			0.00	1.11	4.13	1.92	1.61	8.85	2.50	7.78	1.89	1.38	1.30	1.35	3.00
$ \begin{array}{c} & \begin{array}{c} & \begin{array}{c} & \begin{array}{c} 0.22 \\ \\ Eintervoraceus \\ faccium \end{array} \end{array} \begin{array}{c} \begin{array}{c} 0.22 \\ 0.69 \end{array} & 0.69 \end{array} & 0.79 \\ 0.33 \end{array} & 0.57 \end{array} & 0.53 \end{array} & 0.59 \\ 0.57 \end{array} & 0.53 \end{array} & 0.59 \end{array} & 0.59 \\ 0.57 \end{array} & 0.53 \end{array} & 0.59 \end{array} & 0.59 \end{array} & 0.41 \\ 0.58 \end{array} & 0.44 \end{array} & 0.58 \end{array} & 0.74 \end{array} & 0.72 \end{array} & 0.73 \end{array} & 0.78 \\ 0.59 \end{array} & 0.59 $ & 0.59 \end{array} & 0.59  & 0.59 \end{array} & 0.59  & 0.59 \end{array} & 0.59  & 0.59  & 0.59  & 0.59  & 0.59  &			0.11	0.86	1.41	1.11	1.02	1.39	0.99	1.36	1.12	0.98	0.94	0.96	1.30
$ \begin{array}{c} Enterword and for the form of the $			0.22	0.69	0.79	0.78	0.75	0.65	0.73	0.68	0.78	0.74	0.72	0.73	0.78
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		Ami-	0.33	0.57	0.53	0.59	0.59	0.41	0.58	0.44	0.59	0.59	0.58	0.59	0.55
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Enterococcus	nopenicil-	0.44	0.48	0.39	0.47	0.48	0.30	0.47	0.33	0.47	0.48	0.48	0.48	0.42
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	faecium	lins	0.56	0.41	0.31	0.38	0.40	0.24	0.39	0.26	0.38	0.40	0.41	0.40	0.33
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$			0.67	0.36	0.25	0.32	0.34	0.19	0.33	0.21	0.32	0.34	0.35	0.35	0.28
Entervoccus   Gentami- cin   0.44   0.24   0.25   0.14   0.25   0.16   0.24   0.26   0.23 <th0.23< th="">   0.24   <th0.25< td="" th<=""><td></td><td></td><td>0.78</td><td>0.31</td><td>0.21</td><td>0.28</td><td>0.29</td><td>0.16</td><td>0.29</td><td>0.18</td><td>0.27</td><td>0.30</td><td>0.30</td><td>0.30</td><td>0.24</td></th0.25<></th0.23<>			0.78	0.31	0.21	0.28	0.29	0.16	0.29	0.18	0.27	0.30	0.30	0.30	0.24
Index   0.24   0.16   0.21   0.22   0.13   0.22   0.14   0.21   0.23   0.23   0.23   0.25   0.25   0.18     0.00   1.10   4.11   1.91   1.61   8.87   2.50   7.81   1.90   1.39   1.29   1.35   2.99     0.11   0.86   1.41   1.11   1.02   1.39   0.99   1.36   1.12   0.98   0.93   0.96   1.30     0.22   0.69   0.79   0.78   0.75   0.65   0.73   0.67   0.78   0.74   0.72   0.73   0.78     0.33   0.57   0.53   0.59   0.41   0.58   0.44   0.59   0.59   0.58   0.59   0.55     Enterococcus   Gentami-   0.44   0.48   0.39   0.47   0.33   0.47   0.48   0.48   0.48   0.48   0.48   0.44   0.48   0.48   0.44   0.44   0.40   0.33     faec			0.89	0.27	0.19	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.21
Enterococcus   Gentami- cin   0.44   0.41   1.91   1.61   0.67   2.30   7.61   1.90   1.39   1.29   1.33   2.99     0.11   0.86   1.41   1.11   1.02   1.39   0.99   1.36   1.12   0.98   0.93   0.96   1.30     0.22   0.69   0.79   0.78   0.75   0.65   0.73   0.67   0.78   0.74   0.72   0.73   0.78     0.33   0.57   0.53   0.59   0.59   0.41   0.58   0.44   0.59   0.59   0.58   0.59   0.55     Enterococcus   Gentami- Gentami-   0.44   0.48   0.39   0.47   0.48   0.44   0.48   0.48   0.44   0.48   0.44   0.44   0.48   0.39   0.26   0.38   0.40   0.41   0.40   0.33     0.67   0.36   0.25   0.32   0.34   0.19   0.33   0.21   0.32   0.34   0.35 <td< td=""><td></td><td></td><td>1.00</td><td>0.24</td><td>0.10</td><td>1.01</td><td>1.61</td><td>0.13</td><td>2.50</td><td>7.91</td><td>1.00</td><td>1.20</td><td>1.20</td><td>1.25</td><td>2.00</td></td<>			1.00	0.24	0.10	1.01	1.61	0.13	2.50	7.91	1.00	1.20	1.20	1.25	2.00
Enterococcus   Gentami- cin   0.44   0.48   0.39   0.47   0.48   0.30   0.47   0.33   0.57   0.53   0.59   0.59   0.67   0.78   0.74   0.72   0.73   0.78     0.33   0.57   0.53   0.59   0.59   0.41   0.58   0.44   0.59   0.59   0.58   0.59   0.55     Enterococcus   Gentami- cin   0.44   0.48   0.39   0.47   0.48   0.30   0.47   0.33   0.47   0.48   0.44   0.49   0.48   0.42     faecium   cin   0.56   0.41   0.31   0.38   0.40   0.24   0.39   0.26   0.38   0.40   0.41   0.40   0.33     0.67   0.36   0.25   0.32   0.34   0.19   0.33   0.21   0.32   0.34   0.35   0.35   0.28   0.29     0.78   0.31   0.21   0.28   0.29   0.16   0.29   0.18   0.			0.00	0.86	4.11	1.91	1.01	1.30	0.99	1.36	1.90	0.98	0.93	0.96	2.99
0.22 0.09 0.79 0.78 0.73 0.05 0.75 0.07 0.78 0.74 0.72 0.73 0.78   0.33 0.57 0.53 0.59 0.59 0.41 0.58 0.44 0.59 0.59 0.58 0.59 0.55   Enterococcus Gentami- 0.44 0.48 0.39 0.47 0.48 0.30 0.47 0.33 0.47 0.48 0.48 0.48 0.48 0.42   faecium cin 0.56 0.41 0.31 0.38 0.40 0.24 0.39 0.26 0.38 0.40 0.41 0.40 0.33   0.67 0.36 0.25 0.32 0.34 0.19 0.33 0.21 0.32 0.34 0.35 0.35 0.28   0.67 0.36 0.25 0.32 0.34 0.19 0.33 0.21 0.32 0.34 0.35 0.35 0.28   0.78 0.31 0.21 0.28 0.29 0.16 0.24 0.26 0.26 0.26 0.26 0.21 <td></td> <td></td> <td>0.22</td> <td>0.80</td> <td>0.70</td> <td>0.78</td> <td>0.75</td> <td>0.65</td> <td>0.99</td> <td>0.67</td> <td>0.78</td> <td>0.98</td> <td>0.93</td> <td>0.90</td> <td>0.78</td>			0.22	0.80	0.70	0.78	0.75	0.65	0.99	0.67	0.78	0.98	0.93	0.90	0.78
Enterococcus Gentami- 0.44 0.48 0.39 0.47 0.48 0.30 0.47 0.33 0.47 0.48 0.48 0.42   faecium cin 0.56 0.41 0.31 0.38 0.40 0.24 0.39 0.26 0.38 0.40 0.41 0.40 0.33   faecium cin 0.56 0.41 0.31 0.38 0.40 0.24 0.39 0.26 0.38 0.40 0.41 0.40 0.33   0.67 0.36 0.25 0.32 0.34 0.19 0.33 0.21 0.32 0.34 0.35 0.35 0.35 0.35   0.67 0.36 0.25 0.32 0.34 0.19 0.33 0.21 0.32 0.34 0.35 0.35 0.35 0.35 0.35 0.35   0.67 0.36 0.25 0.32 0.34 0.19 0.33 0.21 0.32 0.34 0.35 0.35 0.35 0.35 0.35 0.35 0.35 0.35 0.35 0.35 0.35 0.35			0.22	0.09	0.79	0.78	0.73	0.05	0.73	0.07	0.78	0.74	0.72	0.75	0.78
facium 6.44 6.46 6.55 6.47 6.35 6.47 6.46 6.46 6.46 6.46 6.42   facium cin 0.56 0.41 0.31 0.38 0.40 0.24 0.39 0.26 0.38 0.40 0.41 0.40 0.33   0.67 0.36 0.25 0.32 0.34 0.19 0.33 0.21 0.32 0.34 0.40 0.41 0.40 0.33   0.67 0.36 0.25 0.32 0.34 0.19 0.33 0.21 0.32 0.34 0.35 0.40 0.41 0.40 0.33   0.67 0.36 0.25 0.32 0.34 0.19 0.33 0.21 0.32 0.34 0.35 0.40 0.41 0.40 0.33   0.67 0.36 0.25 0.32 0.33 0.21 0.33 0.21 0.32 0.31 0.30 0.30 0.30 0.30 0.30 0.24   0.89 0.27 0.19 0.24 0.25 0.14 0.21 0.23 <t< td=""><td>Enterococcus</td><td>Gentami</td><td>0.44</td><td>0.48</td><td>0.39</td><td>0.47</td><td>0.48</td><td>0.30</td><td>0.38</td><td>0.33</td><td>0.47</td><td>0.48</td><td>0.38</td><td>0.48</td><td>0.42</td></t<>	Enterococcus	Gentami	0.44	0.48	0.39	0.47	0.48	0.30	0.38	0.33	0.47	0.48	0.38	0.48	0.42
0.67   0.36   0.25   0.32   0.34   0.19   0.33   0.21   0.32   0.34   0.35   0.35   0.28     0.67   0.36   0.25   0.32   0.34   0.19   0.33   0.21   0.32   0.34   0.35   0.35   0.28     0.78   0.31   0.21   0.28   0.29   0.16   0.29   0.18   0.27   0.30   0.30   0.30   0.24     0.89   0.27   0.19   0.24   0.25   0.14   0.25   0.16   0.24   0.26   0.26   0.26   0.26   0.21   0.21   0.22   0.13   0.22   0.14   0.21   0.23   0.23   0.23   0.23   0.18	faecium	cin	0.56	0.40	0.31	0.38	0.40	0.30	0.39	0.35	0.38	0.40	0.40	0.40	0.33
0.57 0.50 0.52 0.51 0.51 0.17 0.52 0.51 0.55	<i></i>		0.50	0.36	0.25	0.30	0.40	0.19	0.33	0.20	0.32	0.40	0.35	0.40	0.28
$\begin{array}{cccccccccccccccccccccccccccccccccccc$			0.78	0.31	0.21	0.28	0.29	0.16	0.29	0.18	0.27	0.30	0.30	0.30	0.24
1.00 0.24 0.16 0.21 0.22 0.13 0.22 0.14 0.21 0.23 0.23 0.23 0.18			0.89	0.27	0.19	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.21
			1.00	0.24	0.16	0.21	0.22	0.13	0.22	0.14	0.21	0.23	0.23	0.23	0.18

		0.00	1.10	4.11	1.92	1.61	8.85	2.50	7.79	1.88	1.38	1.29	1.36	2.97
		0.11	0.86	1.41	1.11	1.02	1.39	0.99	1.36	1.12	0.98	0.94	0.96	1.30
		0.22	0.69	0.79	0.78	0.75	0.65	0.73	0.68	0.78	0.74	0.72	0.73	0.78
		0.33	0.57	0.53	0.59	0.59	0.41	0.58	0.44	0.59	0.59	0.58	0.59	0.55
Enterococcus	Vancomy-	0.44	0.48	0.39	0.47	0.48	0.30	0.47	0.33	0.47	0.48	0.48	0.48	0.42
faecium	cin	0.56	0.41	0.31	0.38	0.40	0.24	0.39	0.26	0.38	0.40	0.41	0.40	0.33
		0.67	0.36	0.25	0.32	0.34	0.19	0.33	0.21	0.32	0.34	0.35	0.34	0.28
		0.78	0.31	0.21	0.28	0.29	0.16	0.29	0.18	0.28	0.30	0.30	0.30	0.24
		0.89	0.27	0.19	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.21
		1.00	0.24	0.16	0.21	0.22	0.13	0.22	0.14	0.21	0.23	0.23	0.23	0.18
		0.00	1.10	4.11	1.92	1.61	8.86	2.50	7.78	1.88	1.38	1.29	1.36	2.99
		0.11	0.86	1.41	1.11	1.02	1.39	0.99	1.36	1.12	0.98	0.93	0.96	1.30
		0.22	0.69	0.79	0.78	0.75	0.65	0.73	0.68	0.78	0.74	0.72	0.73	0.78
		0.33	0.57	0.53	0.59	0.59	0.41	0.58	0.44	0.59	0.59	0.58	0.59	0.55
Escherichia	Aminogly-	0.44	0.48	0.39	0.47	0.48	0.30	0.47	0.33	0.47	0.48	0.48	0.48	0.42
coli	cosides	0.56	0.41	0.31	0.38	0.40	0.24	0.39	0.26	0.38	0.40	0.41	0.40	0.33
		0.67	0.36	0.25	0.32	0.34	0.19	0.33	0.21	0.32	0.34	0.35	0.34	0.28
		0.78	0.31	0.21	0.28	0.29	0.16	0.29	0.18	0.28	0.30	0.30	0.30	0.24
		0.89	0.27	0.19	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.21
		1.00	0.24	0.16	0.21	0.22	0.13	0.22	0.14	0.21	0.23	0.23	0.23	0.18
		0.00	1.11	4.13	1.92	1.61	8.85	2.50	7.78	1.89	1.38	1.30	1.35	3.00
		0.11	0.86	1.41	1.11	1.02	1.39	0.99	1.36	1.12	0.98	0.94	0.96	1.30
		0.22	0.69	0.79	0.78	0.75	0.65	0.73	0.68	0.78	0.74	0.72	0.73	0.78
		0.33	0.57	0.53	0.59	0.59	0.41	0.58	0.44	0.59	0.59	0.58	0.59	0.55
Escherichia	Ami-	0.44	0.48	0.39	0.47	0.48	0.30	0.47	0.33	0.47	0.48	0.48	0.48	0.42
coli	nopenicil-	0.56	0.41	0.31	0.38	0.40	0.24	0.39	0.26	0.38	0.40	0.41	0.40	0.33
	mis	0.67	0.36	0.25	0.32	0.34	0.19	0.33	0.21	0.32	0.34	0.35	0.35	0.28
		0.78	0.31	0.21	0.28	0.29	0.16	0.29	0.18	0.27	0.30	0.30	0.30	0.24
		0.89	0.27	0.19	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.21
		1.00	0.24	0.16	0.21	0.22	0.13	0.22	0.14	0.21	0.23	0.23	0.23	0.18
		0.00	1.15	4.12	1.91	1.62	8.93	2.50	7.80	1.88	1.38	1.29	1.35	2.97
		0.11	0.88	1.40	1.11	1.02	1.39	0.99	1.36	1.12	0.98	0.93	0.96	1.30
		0.22	0.70	0.79	0.78	0.75	0.65	0.73	0.67	0.78	0.74	0.72	0.73	0.78
		0.33	0.57	0.53	0.59	0.59	0.41	0.58	0.44	0.59	0.59	0.58	0.59	0.55
Escherichia	Car-	0.44	0.48	0.39	0.47	0.47	0.30	0.47	0.33	0.47	0.48	0.48	0.48	0.42
coli	bapenems	0.56	0.41	0.31	0.38	0.39	0.23	0.39	0.26	0.38	0.40	0.41	0.40	0.33
		0.67	0.35	0.25	0.32	0.33	0.19	0.33	0.21	0.32	0.34	0.35	0.35	0.28
		0.78	0.31	0.21	0.28	0.29	0.16	0.29	0.18	0.27	0.30	0.30	0.30	0.24
		0.89	0.27	0.19	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.21
		1.00	0.24	0.16	0.21	0.22	0.13	0.22	0.14	0.21	0.23	0.23	0.23	0.18
		0.00	1.13	4.12	1.92	1.61	8.88	2.51	7.78	1.88	1.38	1.29	1.35	2.97
Escherichia	Cephalo-	0.11	0.87	1.41	1.11	1.02	1.39	0.99	1.36	1.12	0.98	0.93	0.96	1.30
coli	sporins	0.22	0.70	0.79	0.78	0.75	0.65	0.73	0.68	0.78	0.74	0.72	0.73	0.78
		0.33	0.57	0.53	0.59	0.59	0.41	0.58	0.44	0.59	0.59	0.58	0.59	0.55

		0.44	0.48	0.39	0.47	0.48	0.30	0.47	0.33	0.47	0.48	0.48	0.48	0.42
		0.56	0.41	0.31	0.38	0.40	0.23	0.39	0.26	0.38	0.40	0.41	0.40	0.33
		0.50	0.36	0.25	0.32	0.34	0.19	0.33	0.20	0.32	0.34	0.35	0.35	0.28
		0.78	0.30	0.21	0.28	0.29	0.15	0.29	0.18	0.27	0.30	0.30	0.30	0.20
		0.89	0.27	0.19	0.24	0.25	0.10	0.25	0.16	0.24	0.26	0.26	0.26	0.21
		1.00	0.24	0.16	0.21	0.22	0.13	0.22	0.14	0.21	0.23	0.23	0.23	0.18
		0.00	1 10	4.12	1.92	1 61	8.86	2.50	7 78	1.89	1 38	1.29	1 35	2.98
		0.11	0.86	1 41	1.11	1.02	1 39	0.99	1.36	1.02	0.98	0.94	0.96	1.30
		0.22	0.69	0.79	0.78	0.75	0.65	0.73	0.68	0.78	0.74	0.72	0.73	0.78
		0.33	0.57	0.53	0.70	0.75	0.05	0.79	0.00	0.70	0.74	0.58	0.79	0.55
Ecohomishia	Elucato	0.33	0.37	0.30	0.39	0.39	0.41	0.38	0.44	0.39	0.39	0.38	0.39	0.55
Escherichia	Fluoro-	0.44	0.46	0.39	0.47	0.46	0.30	0.47	0.33	0.47	0.48	0.40	0.48	0.42
1011	quinoiones	0.56	0.41	0.31	0.38	0.40	0.24	0.39	0.26	0.38	0.40	0.41	0.40	0.55
		0.67	0.56	0.25	0.32	0.54	0.19	0.55	0.21	0.32	0.54	0.55	0.55	0.28
		0.78	0.31	0.21	0.28	0.29	0.16	0.29	0.18	0.27	0.30	0.30	0.30	0.24
		0.89	0.27	0.19	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.21
		1.00	0.24	0.16	0.21	0.22	0.13	0.22	0.14	0.21	0.23	0.23	0.23	0.18
		0.00	1.10	4.11	1.92	1.61	8.86	2.50	7.78	1.88	1.38	1.29	1.36	2.99
		0.11	0.86	1.41	1.11	1.02	1.39	0.99	1.36	1.12	0.98	0.93	0.96	1.30
		0.22	0.69	0.79	0.78	0.75	0.65	0.73	0.68	0.78	0.74	0.72	0.73	0.78
		0.33	0.57	0.53	0.59	0.59	0.41	0.58	0.44	0.59	0.59	0.58	0.59	0.55
Klebsiella	Aminogly-	0.44	0.48	0.39	0.47	0.48	0.30	0.47	0.33	0.47	0.48	0.48	0.48	0.42
pneumoniae	cosides	0.56	0.41	0.31	0.38	0.40	0.24	0.39	0.26	0.38	0.40	0.41	0.40	0.33
		0.67	0.36	0.25	0.32	0.34	0.19	0.33	0.21	0.32	0.34	0.35	0.34	0.28
		0.78	0.31	0.21	0.28	0.29	0.16	0.29	0.18	0.28	0.30	0.30	0.30	0.24
		0.89	0.27	0.19	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.21
		1.00	0.24	0.16	0.21	0.22	0.13	0.22	0.14	0.21	0.23	0.23	0.23	0.18
		0.00	1.15	4.12	1.91	1.62	8.93	2.50	7.80	1.88	1.38	1.29	1.35	2.97
		0.11	0.88	1.40	1.11	1.02	1.39	0.99	1.36	1.12	0.98	0.93	0.96	1.30
		0.22	0.70	0.79	0.78	0.75	0.65	0.73	0.67	0.78	0.74	0.72	0.73	0.78
		0.33	0.57	0.53	0.59	0.59	0.41	0.58	0.44	0.59	0.59	0.58	0.59	0.55
Klebsiella	Car-	0.44	0.48	0.39	0.47	0.47	0.30	0.47	0.33	0.47	0.48	0.48	0.48	0.42
pneumoniae	bapenems	0.56	0.41	0.31	0.38	0.39	0.23	0.39	0.26	0.38	0.40	0.41	0.40	0.33
		0.67	0.35	0.25	0.32	0.33	0.19	0.33	0.21	0.32	0.34	0.35	0.35	0.28
		0.78	0.31	0.21	0.28	0.29	0.16	0.29	0.18	0.27	0.30	0.30	0.30	0.24
		0.89	0.27	0.19	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.21
		1.00	0.24	0.16	0.21	0.22	0.13	0.22	0.14	0.21	0.23	0.23	0.23	0.18
		0.00	1.13	4.12	1.92	1.61	8.88	2.51	7.78	1.88	1.38	1.29	1.35	2.97
		0.11	0.87	1.41	1.11	1.02	1.39	0.99	1.36	1.12	0.98	0.93	0.96	1.30
VIII	Carbala	0.22	0.70	0.79	0.78	0.75	0.65	0.73	0.68	0.78	0.74	0.72	0.73	0.78
NICOSICILA	Cepnaio-	0.33	0.57	0.53	0.59	0.59	0.41	0.58	0.44	0.59	0.59	0.58	0.59	0.55
preumoniae	sporms	0.44	0.48	0.39	0.47	0.48	0.30	0.47	0.33	0.47	0.48	0.48	0.48	0.42
		0.56	0.41	0.31	0.38	0.40	0.23	0.39	0.26	0.38	0.40	0.41	0.40	0.33
		0.67	0.36	0.25	0.32	0.34	0.19	0.33	0.21	0.32	0.34	0.35	0.35	0.28

		0.78	0.31	0.21	0.28	0.29	0.16	0.29	0.18	0.27	0.30	0.30	0.30	0.24
		0.89	0.27	0.19	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.21
		1.00	0.24	0.16	0.21	0.22	0.13	0.22	0.14	0.21	0.23	0.23	0.23	0.18
		0.00	1.10	4.12	1.92	1.61	8.86	2.50	7.78	1.89	1.38	1.29	1.35	2.98
		0.11	0.86	1.41	1.11	1.02	1.39	0.99	1.36	1.12	0.98	0.94	0.96	1.30
		0.22	0.69	0.79	0.78	0.75	0.65	0.73	0.68	0.78	0.74	0.72	0.73	0.78
		0.33	0.57	0.53	0.59	0.59	0.41	0.58	0.44	0.59	0.59	0.58	0.59	0.55
Klebsiella	Fluoro-	0.44	0.48	0.39	0.47	0.48	0.30	0.47	0.33	0.47	0.48	0.48	0.48	0.42
pneumoniae	quinolones	0.56	0.41	0.31	0.38	0.40	0.24	0.39	0.26	0.38	0.40	0.41	0.40	0.33
		0.67	0.36	0.25	0.32	0.34	0.19	0.33	0.21	0.32	0.34	0.35	0.35	0.28
		0.78	0.31	0.21	0.28	0.29	0.16	0.29	0.18	0.27	0.30	0.30	0.30	0.24
		0.89	0.27	0.19	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.21
		1.00	0.24	0.16	0.21	0.22	0.13	0.22	0.14	0.21	0.23	0.23	0.23	0.18
		0.00	1.10	4.11	1.92	1.61	8.86	2.50	7.78	1.88	1.38	1.29	1.36	2.99
		0.11	0.86	1.41	1.11	1.02	1.39	0.99	1.36	1.12	0.98	0.93	0.96	1.30
		0.22	0.69	0.79	0.78	0.75	0.65	0.73	0.68	0.78	0.74	0.72	0.73	0.78
		0.33	0.57	0.53	0.59	0.59	0.41	0.58	0.44	0.59	0.59	0.58	0.59	0.55
Pseudomonas	Aminogly-	0.44	0.48	0.39	0.47	0.48	0.30	0.47	0.33	0.47	0.48	0.48	0.48	0.42
aeruginosa	cosides	0.56	0.41	0.31	0.38	0.40	0.24	0.39	0.26	0.38	0.40	0.41	0.40	0.33
		0.67	0.36	0.25	0.32	0.34	0.19	0.33	0.21	0.32	0.34	0.35	0.34	0.28
		0.78	0.31	0.21	0.28	0.29	0.16	0.29	0.18	0.28	0.30	0.30	0.30	0.24
		0.89	0.27	0.19	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.21
		1.00	0.24	0.16	0.21	0.22	0.13	0.22	0.14	0.21	0.23	0.23	0.23	0.18
		0.00	1.15	4.12	1.91	1.62	8.93	2.50	7.80	1.88	1.38	1.29	1.35	2.97
		0.11	0.88	1.40	1.11	1.02	1.39	0.99	1.36	1.12	0.98	0.93	0.96	1.30
		0.22	0.70	0.79	0.78	0.75	0.65	0.73	0.67	0.78	0.74	0.72	0.73	0.78
		0.33	0.57	0.53	0.59	0.59	0.41	0.58	0.44	0.59	0.59	0.58	0.59	0.55
Pseudomonas	Car-	0.44	0.48	0.39	0.47	0.47	0.30	0.47	0.33	0.47	0.48	0.48	0.48	0.42
aeruginosa	bapenems	0.56	0.41	0.31	0.38	0.39	0.23	0.39	0.26	0.38	0.40	0.41	0.40	0.33
		0.67	0.35	0.25	0.32	0.33	0.19	0.33	0.21	0.32	0.34	0.35	0.35	0.28
		0.78	0.31	0.21	0.28	0.29	0.16	0.29	0.18	0.27	0.30	0.30	0.30	0.24
		0.89	0.27	0.19	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.21
		1.00	0.24	0.16	0.21	0.22	0.13	0.22	0.14	0.21	0.23	0.23	0.23	0.18
		0.00	1.11	4.11	1.92	1.61	8.86	2.50	7.78	1.88	1.39	1.30	1.35	2.97
		0.11	0.86	1.40	1.11	1.02	1.39	0.99	1.36	1.12	0.98	0.94	0.96	1.30
		0.22	0.69	0.79	0.78	0.75	0.65	0.73	0.68	0.78	0.74	0.72	0.73	0.78
		0.33	0.57	0.53	0.59	0.59	0.41	0.58	0.44	0.59	0.59	0.58	0.59	0.55
Pseudomonas	Ceftazidim	0.44	0.48	0.39	0.47	0.48	0.30	0.47	0.33	0.47	0.48	0.48	0.48	0.42
aeruginosa	e	0.56	0.41	0.31	0.38	0.40	0.24	0.39	0.26	0.38	0.40	0.41	0.40	0.33
		0.67	0.36	0.25	0.32	0.34	0.19	0.33	0.21	0.32	0.34	0.35	0.35	0.28
		0.78	0.31	0.21	0.28	0.29	0.16	0.29	0.18	0.27	0.30	0.30	0.30	0.24
		0.89	0.27	0.19	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.21
		1.00	0.24	0.16	0.21	0.22	0.13	0.22	0.14	0.21	0.23	0.23	0.23	0.18
		0.00	1.10	4.12	1.92	1.61	8.86	2.50	7.78	1.89	1.38	1.29	1.35	2.98

		0.11	0.86	1.41	1.11	1.02	1.39	0.99	1.36	1.12	0.98	0.94	0.96	1.30
		0.22	0.69	0.79	0.78	0.75	0.65	0.73	0.68	0.78	0.74	0.72	0.73	0.78
		0.33	0.57	0.53	0.59	0.59	0.41	0.58	0.44	0.59	0.59	0.58	0.59	0.55
D I	171	0.44	0.48	0.39	0.47	0.48	0.30	0.47	0.33	0.47	0.48	0.48	0.48	0.42
Pseudomonas	Fluoro-	0.56	0.41	0.31	0.38	0.40	0.24	0.39	0.26	0.38	0.40	0.41	0.40	0.33
aeruginosa	quinoiones	0.67	0.36	0.25	0.32	0.34	0.19	0.33	0.21	0.32	0.34	0.35	0.35	0.28
		0.78	0.31	0.21	0.28	0.29	0.16	0.29	0.18	0.27	0.30	0.30	0.30	0.24
		0.89	0.27	0.19	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.21
		1.00	0.24	0.16	0.21	0.22	0.13	0.22	0.14	0.21	0.23	0.23	0.23	0.18
		0.00	1.13	4.29	1.95	1.64	9.55	2.51	7.83	1.90	1.42	1.32	1.35	2.95
		0.11	0.87	1.42	1.12	1.03	1.39	1.00	1.35	1.13	0.99	0.93	0.96	1.29
		0.22	0.70	0.79	0.78	0.76	0.64	0.74	0.68	0.78	0.75	0.72	0.73	0.78
		0.33	0.57	0.53	0.59	0.59	0.40	0.58	0.45	0.59	0.59	0.58	0.59	0.55
Pseudomonas	D'	0.44	0.48	0.39	0.47	0.48	0.29	0.47	0.33	0.47	0.48	0.48	0.48	0.42
aeruginosa	Piperacillin	0.56	0.41	0.31	0.38	0.39	0.23	0.39	0.26	0.38	0.40	0.40	0.40	0.33
		0.67	0.35	0.25	0.32	0.33	0.19	0.33	0.22	0.32	0.34	0.35	0.35	0.28
		0.78	0.31	0.21	0.27	0.29	0.16	0.29	0.18	0.27	0.29	0.30	0.30	0.24
		0.89	0.27	0.18	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.21
		1.00	0.24	0.16	0.21	0.22	0.12	0.22	0.14	0.21	0.23	0.23	0.23	0.18
		0.00	1.15	4.48	1.93	1.64	8.97	2.52	7.87	1.91	1.39	1.30	1.38	3.03
		0.11	0.88	1.41	1.11	1.03	1.39	0.99	1.36	1.13	0.98	0.94	0.97	1.30
		0.22	0.70	0.78	0.78	0.75	0.65	0.73	0.67	0.79	0.74	0.73	0.74	0.78
		0.33	0.57	0.52	0.59	0.59	0.41	0.58	0.44	0.59	0.59	0.58	0.59	0.54
Streptococcus	Macrolidos	0.44	0.48	0.38	0.47	0.47	0.30	0.47	0.32	0.47	0.48	0.48	0.48	0.41
pneumoniae	Macrondes	0.56	0.41	0.30	0.38	0.39	0.23	0.39	0.26	0.38	0.40	0.40	0.40	0.33
		0.67	0.35	0.25	0.32	0.33	0.19	0.33	0.21	0.32	0.34	0.35	0.34	0.28
		0.78	0.31	0.21	0.28	0.29	0.16	0.29	0.18	0.27	0.30	0.30	0.30	0.24
		0.89	0.27	0.18	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.20
		1.00	0.24	0.16	0.21	0.22	0.13	0.22	0.14	0.21	0.23	0.23	0.23	0.18
		0.00	1.11	4.50	1.93	1.64	8.98	2.51	7.87	1.90	1.39	1.30	1.38	3.04
		0.11	0.86	1.41	1.11	1.03	1.39	0.99	1.36	1.13	0.97	0.94	0.97	1.30
		0.22	0.69	0.78	0.78	0.75	0.65	0.73	0.67	0.79	0.74	0.73	0.74	0.78
		0.33	0.57	0.52	0.59	0.59	0.41	0.58	0.44	0.59	0.59	0.58	0.59	0.54
Streptococcus	Dominilling	0.44	0.48	0.38	0.47	0.47	0.30	0.47	0.32	0.47	0.48	0.48	0.48	0.41
pneumoniae	Perifcilinis	0.56	0.41	0.30	0.38	0.39	0.23	0.39	0.26	0.38	0.40	0.40	0.40	0.33
		0.67	0.36	0.25	0.32	0.33	0.19	0.33	0.21	0.32	0.34	0.35	0.34	0.28
		0.78	0.31	0.21	0.28	0.29	0.16	0.29	0.18	0.27	0.30	0.30	0.30	0.24
		0.89	0.27	0.18	0.24	0.25	0.14	0.25	0.16	0.24	0.26	0.26	0.26	0.20
		1.00	0.24	0.16	0.21	0.22	0.13	0.22	0.14	0.21	0.23	0.23	0.23	0.18

# Supplementary Annexure 11: Narratives of the Shared Socioeconomic Pathways

SSP	Narrative
SSP1	Sustainability – Taking the Green Road: Low challenges to mitigation and adaptation The world shifts gradually, but pervasively, toward a more sustainable path, emphasizing more inclusive development that respects perceived environmental boundaries. Management of the global commons slowly improves; educational and health investments accelerate the demographic transition, and the emphasis on economic growth shifts toward a broader emphasis on human well-being. Driven by an increasing commit- ment to achieving development goals, inequality is reduced across and within countries. Consumption is oriented toward low material growth and lower resource and energy intensity.
SSP2	<b>Middle of the Road: Medium challenges to mitigation and adaptation</b> The world follows a path where social, economic, and technological trends do not shift markedly from historical patterns. Development and income growth proceed unevenly, with some countries making rela- tively good progress while others fall short of expectations. Global and national institutions work toward but make slow progress in achieving sustainable development goals. Environmental systems experience deg- radation, although there are some improvements, and overall, the intensity of resource and energy use de- clines. Global population growth is moderate and levels off in the second half of the century. Income ine- quality persists or improves slowly, and challenges to reducing vulnerability to societal and environmental changes remain.
SSP3	<b>Regional Rivalry – A Rocky Road: High challenges to mitigation and adaptation</b> A resurgent nationalism, concerns about competitiveness and security, and regional conflicts push countries to increasingly focus on domestic or, at most, regional issues. Policies shift over time to become increasingly oriented toward national and regional security issues. Countries focus on achieving energy and food security goals within their regions at the expense of broader-based development. Investments in education and technological development decline. Economic development is slow, consumption is material-intensive, and inequalities persist or worsen over time. Population growth is low in industrialized and high in developing countries. A low international priority for addressing environmental concerns leads to substantial environmental degradation in some regions.
SSP4	Inequality – A Road Divided: Low challenges to mitigation, high challenges to adaptation Highly unequal investments in human capital, combined with increasing disparities in economic opportunity and political power, lead to increasing inequalities and stratification both across and within countries. Over time, a gap widens between an internationally connected society contributing to knowledge- and capital- intensive sectors of the global economy and a fragmented collection of lower-income, poorly educated so- cieties working in a labor-intensive, low-tech economy. Social cohesion degrades, and conflict and unrest become increasingly common. Technology development is high in the high-tech economy and sectors. The globally connected energy sector diversifies, with investments in both carbon-intensive fuels like coal and unconventional oil and low-carbon energy sources. Environmental policies focus on local issues around middle and high-income areas.
SSP5	Fossil-fueled Development – Taking the Highway High challenges to mitigation, low challenges to adaptation This world places increasing faith in competitive markets, innovation, and participatory societies to produce rapid technological progress and development of human capital as the path to sustainable development. Global markets are increasingly integrated. There are also substantial investments in health, education, and institutions to enhance human and social capital. At the same time, the push for economic and social devel- opment is coupled with the exploitation of abundant fossil fuel resources and the adoption of resource and energy-intensive lifestyles worldwide. All these factors lead to the rapid growth of the global economy while the global population peaks and declines in the 21st century. Local environmental problems like air pollution are successfully managed. If necessary, there is faith in effectively addressing social and ecological systems, including geo-engineering.

Source: Riahi et al. (2017).

#### Supplementary Annexure 12: Projected Climate Indicators

The <u>online dashboard</u> presents the projected climate indicators under SSPs. The projected climate indicators have been derived by applying the methodology presented in Section 3.2 to the projected climate variables (Mean, Maximum, and Minimum Temperature, Precipitation, Relative Humidity, and Wind Speed) obtained from the Geophysical Fluid Dynamics Laboratory Earth System Model, as reported by the Intersectoral Impact Model Intercomparison Project (Potsdam Institute for Climate Impact Research 2022). A detailed discussion about the global variation of the same climate indicators is available from Fernando (2023).

As observed in the <u>online dashboard</u>, the mean temperature remains almost constant throughout the period under SSP 1-2.6. However, under SSP 2-4.5, Southern Europe experiences an increasing trend. Across both scenarios, Northern and Eastern Europe experience the highest temperature increment from the 1961-90 baseline. The temperature experienced across all the regions increases from SSP 1-2.6 to SSP 2-4.5. In contrast to temperature, precipitation generally decreases across the SSPs amidst global warming. Northern and Eastern Europe experience minimal precipitation reductions. Southern Europe experiences the lowest precipitation among all the regions. Relative humidity changes are minimal across SSPs.

As the <u>online dashboard</u> presents, extremely warm conditions, both day and night, increase across the regions as warming increases. The magnitude of the changes notably increases for those during the night. While the growth of extremely warm conditions stabilizes during the day as warming increases, the opposite happens during the night, where the trends under SSP 1-2.6 are more stable than SSP 2-4.5. Southern Europe and Western Asia appear to experience the most potent effects under both SSPs. Given the non-linearities of global warming, changes in extremely cold conditions are different across scenarios and regions. For example, although the extremely cold conditions during the night reduce in Eastern Europe under SSP 2-4.5, compared to SSP 1-2.6, those conditions during the day do not reduce as much under SSP 2-4.5, compared to SSP 1-2.6.

In general, extremely dry, wet, and windy conditions increase across SSPs amidst warming, as illustrated in the <u>online dashboard</u>. The changes in extremely dry conditions are minimal across some regions, while Southern Europe experiences a stable yet higher deviation in extremely dry conditions under SSP 2-4.5 compared to SSP 1-2.6. The magnitude of changes in extremely wet conditions increases with warming. Western and Northern Europe experience the highest changes in extremely wet conditions under SSP 1-2.6 and SSP 2-4.5, respectively. Extremely windy conditions increase across all regions, with Northern Europe experiencing growth across both SSPs.