

Data-Driven Stewardship Intelligence for Antimicrobial Resistance in India

by

Jasmine Kaur

(PhD21208)

Under the Supervision of

Prof. Tavpritesh Sethi
IIIT-Delhi
&
Dr. Harpreet Singh
ICMR-Delhi

Department of Computational Biology

Indraprastha Institute of Information Technology

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Jasmine Kaur

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Certificate

This is to certify that the thesis titled "**Data-Driven Stewardship Intelligence for Antimicrobial Resistance in India**" being submitted by **Jasmine Kaur** to the **Indraprastha Institute of Information Technology, Delhi**, for the award of the degree of **Doctor of Philosophy**, is an original research work carried out by her under my supervision. In my opinion, the thesis has reached the standards, fulfilling the requirements of the regulations relating to the degree.

The results contained in this thesis have not been submitted in part or in whole to any other university or institute for the award of any degree/diploma.





Prof. Tavpritesh Sethi

Professor, Computational Biology

Founding Head,

Center of Excellence in Healthcare

IIIT Delhi, 110020

Dr. Harpreet Singh

Scientist G

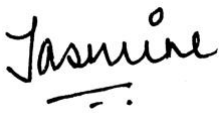
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Declaration

I acknowledge that I am fully responsible for the entire content of my thesis, including any sections assisted by online tools, including Artificial Intelligence-based tools. I accept full accountability for any violations of ethical standards in publications arising from the use of such tools.

Month, Year: July, 2026



Student Name: Jasmine Kaur

Roll Number: PhD21208





Advisor Name: Dr Tavpritesh Sethi, Dr Harpreet Singh

Indraprastha Institute of Information Technology Delhi

New Delhi 110020

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Abstract

Antimicrobial resistance (AMR) is one of the most urgent public health threats of the present century. Antimicrobial stewardship and surveillance are integral pillars of the response to AMR. However, connecting these pillars requires interpretable evidence on resistance levels, temporal change and local context. This thesis develops analytical and translational approaches to turn routine surveillance data into evidence for stewardship prioritisation.The first objective is to characterise longitudinal and geographical patterns of AMR in India using multicentric IAMRSN data from bloodstream and urinary tract infections. Resistance trends varied across organisms, antibiotics and regions. Imipenem resistance increased by an estimated 0.22 percentage points per month in *Escherichia coli* bloodstream isolates and 0.37 percentage points per month in *Pseudomonas aeruginosa* urinary isolates. Bayesian network modelling identified conditional associations with state-level Sustainable Development Goal indicators, without establishing causality.Building on these patterns, the second objective moved beyond retrospective description towards examining temporal lead-lag relationships using cross-correlation. Cefotaxime resistance in *E. coli* bloodstream isolates showed a leading temporal association with imipenem and meropenem resistance at approximately 9–10 months. These findings identify candidate surveillance indicators whose robustness and prospective predictive performance require further evaluation.

The third objective is to develop an interpretable trajectory-based scorecard *AMROrbit* for AMR monitoring. *AMROrbit* jointly captures resistance burden and temporal momentum by estimating both baseline resistance and directional change, enabling countries, hospitals, or pathogen–drug combinations to be classified into interpretable stewardship trajectories. Applied to 5,920 country–organism–antibiotic–specimen trajectories, we observed 17.7% were spiralling-out in comparison to only 13.4% as spiralling-in. *AMROrbit* has been implemented as a web-based tool to analyse

susceptibility testing data. It is currently being evaluated with clinical partners at AIIMS New Delhi and Max Hospital, with planned scale-up across multiple AIIMS in collaboration with CDAC. This objective extends AMR surveillance from trend estimation to prioritisation, allowing decision-makers to identify where resistance is not only high, but also worsening.

The fourth objective defined a translational pathway through *AMRSense* for generating and triangulating contextual baseline evidence from community records, awareness assessments, prescriptions, antibiotic-use data and laboratory surveillance. Completed contributions included the conceptual architecture, application prototypes, awareness materials, a Delphi-validated KAP instrument, and development and pilot testing of the community data-collection workflow. KAP data collection is ongoing, while wider deployment and evaluation of effects on antibiotic-use practices and resistance remain future work. AMRaura is a proposed multidimensional integration framework whose development and prospective validation fall outside the completed work reported in this thesis.

Together, these objectives address a central actionability gap in AMR surveillance. The thesis argues that a major barrier to effective AMR stewardship is not only the absence of data, but the limited conversion of existing and emerging data streams into dynamic, interpretable, and actionable intelligence. The thesis connects resistance trend analysis, candidate temporal indicators and trajectory-based prioritisation with a pathway for contextual surveillance, providing an empirical and methodological foundation for more informed stewardship.

Keywords: *Antimicrobial resistance, AMR stewardship, IAMRSN, lead–lag analysis, AWaRe, AMROrbit, phase-space scorecard, digital health, trajectory-based monitoring, India*

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- *AMROrbit* Scorecard: A Dynamic Phase Space Model for Strategic Monitoring and Actionable Insights on Global AMR Trajectories. Jasmine Kaur, Tavpritesh Sethi. [**Vivli Innovation award, 2024**] https://amr.vivli.org/data-challenge/2024-finalist-and-award-winning-solutions/
- *AMRSense*: Empowering Communities with a Proactive One Health Ecosystem. Tavpritesh Sethi, Jasmine Kaur, Tikesh Bisen, Harpreet Singh, Nikhil Doegar [**Second Prize Trinity Challenge on AMR, 2024**]

List of Publications

Publications and Preprints

- **Kaur J**, Singh H, Sethi T. Emerging trends in antimicrobial resistance in bloodstream infections: a multicentric longitudinal study in India, 2017–2022. ***The Lancet Regional Health – Southeast Asia***. 2024;26:100412. doi:10.1016/j.lansea.2024.100412
- **Kaur J**, Nagori A, Veeraraghavan B, Ohri V, Lodha R, ICMR-AMR Surveillance Network collaborators, Walia K, Singh H, Sethi T. 5-Year Trends and Associations of Antimicrobial Resistance in Urinary Tract Infections in India (2017-2021): A Multi-Centric, Retrospective, Longitudinal Analysis. **Preprint** available at SSRN: http://dx.doi.org/10.2139/ssrn.4316853
- **Kaur J**, Abraham TN, Pendyala R, Vairamuthu M, Gupta A, Sethi T. *AMROrbit:* a trajectory-based scorecard for antimicrobial stewardship using routine susceptibility testing data, *JAC-Antimicrobial Resistance*, Volume 8, Issue 4, August 2026, dlag116, https://doi.org/10.1093/jacamr/dlag116
- Rana S, **Kaur J**, Gudi N, Chandramohan KN, Mutreja A, Ahmad R, Shannawaz M, Chaudhry U, Sethi T, Singh H. Development and Evaluation of an Antimicrobial Resistance Knowledge, Attitude and Practice Instrument for Accredited Social Health Activists in Karnataka, India. (**Submitted**)

Other Publications and Preprints

- **Kaur J**, Singh H, Sethi T. The AMR surveillance actionability gap: from laboratory reporting to stewardship intelligence. (**Submitted**)
- Sethi T, **Kaur J**, Roychoudhury C, et al. Transforming urban primary health care through digitalization: the Sanjeevani Clinic experience in Madhya Pradesh. *medRxiv*. 2026. doi:10.64898/2026.01.13.26343577

International Conference Acceptances

- *AMROrbit* Scorecard: A Dynamic Phase Space Model for Strategic Monitoring and Actionable Insights on Global AMR Trajectories. **Jasmine Kaur**, Tavpritesh Sethi. [AMR Conference, Basel, Switzerland, 2025]
- AMR Surveillance with the *AMROrbit* Scorecard: Actionable Insights from a Multi-country model for ESKAPE pathogens and *E. coli*. **Jasmine Kaur**, Tavpritesh Sethi, Noel Abraham Tiju, Rishi Pendyala, Muthuraj Vairamuthu, Aryan Gupta [ESCMID 2025, Vienna, Austria]
- Dynamic Modelling of Global Antimicrobial Resistance Trajectories: Insights for Policy and Sustainable Development. **Jasmine Kaur**, Tavpritesh Sethi, Noel Abraham Tiju, Rishi Pendyala, Muthuraj Vairamuthu, Aryan Gupta [ASM Microbe 2025]
- *AMRSense*: A People-Centric, AI-Enabled Scorecard for Antimicrobial Resistance Stewardship and Surveillance in Karnataka, India. Tavpritesh Sethi, Tikesh Bisen, **Jasmine Kaur**, Nachiket Gudi, Nikhil Doegar, Gaurav Agarwal, Harpreet Singh, Chandramohan KN [PMAC 2026]
- Beyond Hospital Surveillance: Insights from Antibiotic Sales, Prescriptions, and Resistance Using a Large-Scale Digital Pharmacy Platform in India. **Jasmine Kaur**, Vineet Madan, Nikhil Doegar, Gaurav Agarwal, Tavpritesh Sethi [ASM Microbe 2026]

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Abbreviations

AIC Akaike information criterion

AMK Amikacin

AMR Antimicrobial Resistance

AMP Ampicillin

AMSP Antimicrobial Stewardship Program

ASHA Accredited Social Health Activist

AST Antimicrobial Susceptibility Testing

ATLAS Antimicrobial Testing Leadership and Surveillance

AWaRe Access, Watch, and Reserve (classification)

BIC Bayesian information criterion

BNs Bayesian Networks

BPPL Bacterial Priority Pathogens List

BSI Bloodstream Infection

CA-BSI Community-Acquired Bloodstream Infection

CAI Community-Acquired Infection

CA-UTI Community-Acquired Urinary Tract Infection

CAZ Ceftazidime

CDC Centers for Disease Control and Prevention

CFZ Cefazolin

CIP Ciprofloxacin

CLSI Clinical and Laboratory Standards Institute

COVID19 Coronavirus Disease 2019

CST Colistin

DDs Disc-diffusion zone diameter

DDD Defined Daily Dose

DOT Days of Therapy

EQAS External Quality Assurance Systems

ESKAPE *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter spp.*

ETP Ertapenem

ESBL Extended-spectrum β-lactamase

EUCAST European Committee on Antimicrobial Susceptibility Testing

FEP Cefepime

FOS Fosfomycin

GAP Global Action Plan

GEN Gentamicin

GLASS Global Antimicrobial Resistance and Use Surveillance System

GRAM Global Research on Antimicrobial Resistance

HA-BSI Hospital-Acquired Bloodstream Infection

HAI Hospital-Acquired Infection

HA-UTI Hospital-Acquired Urinary Tract Infection

HLG High-level Gentamicin

ICMR Indian Council of Medical Research

IAMRSN Indian Council of Medical Research Antimicrobial Resistance Surveillance Network

ICU Intensive Care Unit

IPM Imipenem

ISS Imaginary Sample Size

LMICs Low- and middle-income countries

LVX Levofloxacin

LZD Linezolid

MDR Multi-drug Resistance

MEM Meropenem

MIC Minimum Inhibitory Concentration

MRSA Methicillin-resistant Staphylococcus aureus

MSSA Methicillin-susceptible Staphylococcus aureus

NAP National Action Plan

NCs Nodal Centers

NIT Nitrofurantoin

OPD Outpatient Department

PTZ Piperacillin-tazobactam

SDG Sustainable Development Goal

SENTRY Surveillance and Epidemiology of Resistance Trends Antimicrobial Surveillance Program

SOPs Standard Operating Procedures

TAX Cefotaxime

TEC Teicoplanin

TMP-SMZ Trimethoprim-sulfamethoxazole

TOB Tobramycin

UTI Urinary Tract Infection

UTs Union Territories

VAN Vancomycin

WHO World Health Organization

Chapter 1: Introduction

1.1 Introduction to AMR

1.1.1 What is AMR?

AMR occurs when bacteria, viruses, fungi and parasites no longer respond to antimicrobial medicines, making infections harder to treat and increasing the risk of severe illness, spread and death (World Health Organization, 2025). AMR occurs across all pathogens, amongst which bacterial AMR has the highest burden (Laxminarayan et al., 2013; Prestinaci et al., 2015)

AMR is a fundamental biological and evolutionary process. Microorganisms have existed in ecological environments for billions of years, where naturally occurring antimicrobial compounds are produced by other microbes. As a defensive response to these compounds, the neighbouring organisms have developed mechanisms to protect themselves. Studies examining ancient DNA and environmental microbial communities have demonstrated that genes encoding resistance mechanisms such as β-lactamases and efflux pumps were present even before the clinical introduction of antibiotics (Bush & Bradford, 2016; D'Costa et al., 2011; Wright, 2007). However, the extensive and often inappropriate use of antimicrobials has created conditions that strongly favour the survival and spread of resistant organisms. When we consume antibiotics, the resistant organisms survive while the susceptible microorganisms are killed, thus increasing the resistant population over successive cycles (Andersson & Hughes, 2010; Davies & Davies, 2010). Moreover, the spread of resistance across geographical and ecological boundaries is also contributed by factors such as travel, food supply chains and environmental contamination (Davies

& Davies, 2010; Martínez, 2008). Thus, the existence of AMR is not the challenge but the unprecedented speed and scale at which it is emerging across healthcare, community, and environmental settings.

1.1.2 Resistance Evolution Across Classes

Exposure to a single antibiotic can select for bacterial populations that already carry resistance determinants, or favour the expansion of variants that acquire such determinants through mutation or horizontal gene transfer. When these determinants confer resistance to multiple agents, selection by one antibiotic may therefore reduce susceptibility to more than one antibiotic class. This can be explained by two related mechanisms:

a) Co-resistance: The term refers to situations where multiple resistance genes are co-located on a single mobile genetic element. When these elements move between bacteria, selection by one antibiotic can also maintain resistance to others on the same unit (Gillings, 2014; Partridge et al., 2018).

b) Cross-resistance: It occurs when a single resistance mechanism reduces susceptibility to multiple antimicrobial agents, usually because the antibiotics share similar targets or structures. Mutations affecting antibiotic target sites or regulatory changes that increase the activity of multidrug efflux pumps can produce this effect (Blair et al., 2015; Nishino et al., 2021)

1.2 Scale and Consequences of the AMR Crisis

1.2.1 Global Burden of AMR

As per recent estimates by the GRAM project, approximately 4.95 million deaths were found to be associated with bacterial AMR, with 1.27 million deaths directly attributable to AMR (Murray et al., 2022). Projections suggest that the global burden of AMR may continue to increase if current trends in antibiotic use, infection prevention, and surveillance remain unchanged (Naghavi et al., 2024). A major proportion of the deaths was contributed by only six bacterial pathogens *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Acinetobacter baumannii*, *Streptococcus pneumoniae*, and *Pseudomonas aeruginosa* (Murray et al., 2022).

The burden of AMR is disproportionately high in Low-and-middle-income group countries (LMICs) because of higher disease burdens, over-the-counter sales of antibiotics, and limited diagnostic infrastructure (Sulis et al., 2022). India is one of the worst affected due to a strained healthcare infrastructure amidst a high infectious disease burden and unregulated use of antibiotics (Manesh & Varghese, 2021). Annual reports from the Indian Council of Medical Research AMR surveillance network reveal high resistance rates to third-generation cephalosporin resistance in *Escherichia coli* bloodstream isolates and carbapenems in *Klebsiella pneumoniae (*ICMR, 2025)

1.2.2 Impact of AMR on the Economy

The impact of AMR is observable beyond clinical treatment failure. Drug-resistant infections were estimated to have an increase in approximately US$6,000 to US$30,000 costs per patient, alongside longer admissions and worse clinical outcomes for drug-resistant infections (Cosgrove & Carmeli, 2003).

As resistant infections become more common, the effects penetrate across households, hospitals, labour markets, and national economies. A modelling study by the World Bank suggests that unchecked AMR could reduce annual global gross domestic product by 1.1% in a low-impact

scenario and by 3.8% in a high-impact scenario by 2050 (O'Neill, 2014; World Bank Group, 2017). The same report projected that, under severe resistance conditions, low-income countries could incur GDP losses exceeding 5% by 2050. Additional global health expenditure attributable to AMR could range from US$330 billion to US$1.2 trillion by 2050, depending on the severity of the resistance scenario modelled.

1.2.3 AMR and the Sustainable Development Goals

The Sustainable Development Goals (SDGs) (Figure 1.1) represent a universal call to action to achieve sustainable development by 2030, with an emphasis on balancing social progress, economic growth, and environmental sustainability. It has a set of 17 goals aimed at addressing major global challenges, including poverty, inequality, health, environmental degradation, and economic development (United Nations General Assembly, 2015; World Health Organization, 2021b).

AMR can be understood as an emergent outcome of a complex adaptive system involving microorganisms, patients, healthcare providers, medicine suppliers, institutions and their wider environment. In such systems, agents interact and adapt, and their responses can alter the conditions influencing subsequent behaviour (Plsek and Greenhalgh, 2001). In the AMR context, microbial adaptation and changes in prescribing, medicine access and care-seeking can generate feedback between antibiotic exposure and resistance. Gautham et al. (2021) illustrate the importance of examining antibiotic provision within interconnected provider, community, regulatory and pharmaceutical systems. This perspective provides a conceptual basis for

interpreting resistance alongside wider development conditions. It does not imply that an individual SDG indicator has an isolated or directly estimable causal effect on AMR.



Figure 1.1: Sustainable Development Goals (SDGs). The 17 interconnected global goals adopted under the 2030 Agenda for Sustainable Development (Source: United Nations General Assembly, 2015; United Nations Sustainable Development Goals website: https://www.un.org/sustainabledevelopment/sustainable-development-goals/).

However, within the SDG framework, AMR is increasingly acknowledged as a cross-cutting threat that undermines progress on multiple goals simultaneously (Tayler, 2021). AMR most directly relates to SDG 3, which seeks to ensure good health and well-being for all. Indirectly, SDG 1 (No Poverty), SDG 6 (Clean Water and Sanitation), and SDG 8 (Decent Work and Economic Growth) may be affected as resistant infections increase healthcare costs and reduce workforce participation through prolonged illness and premature mortality. The release of resistant organisms into the environment, through untreated wastewater, pharmaceutical discharge, and agricultural runoff, can amplify AMR transmission cycles (Berendonk et al., 2015; Singer et al., 2016). Recognising the

growing burden of resistant infections, in 2020, the United Nations introduced Indicator 3.d.2, defined as the "proportion of bloodstream infections due to selected antimicrobial-resistant organisms" (World Health Organization, 2021b). This indicator will be used to monitor the resistance percentage of bloodstream infections due to selected antimicrobial-resistant organisms, specifically MRSA, among patients with *S. aureus* bloodstream infection and *E. coli* resistant to third-generation cephalosporins among patients whose blood sample are taken and tested.

1.3 WHO Priority Pathogens and Critical Antibiotic Classes

1.3.1 WHO Priority Pathogens

The burden of AMR is disproportionately concentrated in a limited set of microorganism–antibiotic combinations that account for the majority of severe infections and therapeutic failures. To identify bacterial pathogens that require urgent attention, the World Health Organization introduced the Bacterial Priority Pathogens List (BPPL) in 2017 (Tacconelli et al., 2018).

As per the BPPL (Figure 1.2), the microorganisms were classified into three priority groups using multiple criteria such as resistance prevalence, associated mortality, transmissibility, healthcare burden, and the availability of effective therapeutic options:

(a) Critical priority include carbapenem-resistant Gram-negative organisms such as Acinetobacter baumannii and Enterobacterales

(b) High priority include organisms such as methicillin-resistant Staphylococcus aureus and fluoroquinolone-resistant Salmonella; and

(c) Medium priority with pathogens where resistance remains a concern, but with relatively greater availability of treatment options.

The list was subsequently updated in 2024 to incorporate the latest epidemiological evidence and emerging resistance threats (Sati et al., 2025).

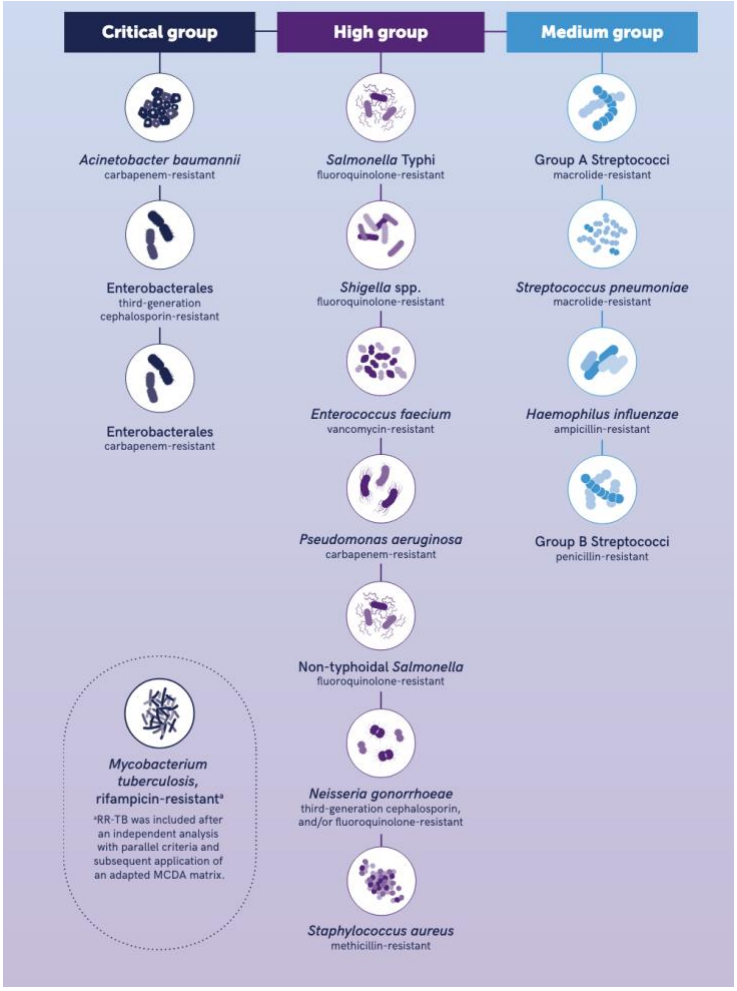


Figure 1.2: The 2024 WHO Bacterial Priority Pathogens List. Microorganisms are grouped into Critical, High, and Medium priority tiers, highlighting key microorganisms–antibiotic combinations of global clinical importance. (Source: https://www.who.int/publications/i/item/9789240093461)

1.3.2 Antibiotic AWaRe classification

The AWaRe framework, introduced by WHO, classifies antibiotics into three categories: Access, Watch, and Reserve (World Health Organization, 2019; World Health Organization, 2023).

1. Widely available and affordable antibiotics recommended as first- or second-line therapy for common infections are included in the Access group. Some examples include antibiotics such as amoxicillin and ampicillin.
2. The Watch group has antibiotics like third-generation cephalosporins, fluoroquinolones, and carbapenems, which are essential but have a higher resistance potential. Since resistance to these antibiotics can rapidly compromise treatment options, their use should be carefully monitored within stewardship programs.
3. The Reserve category contains antibiotics such as colistin and tigecycline, which are last resort antimicrobials intended for treatment of infections caused by multidrug-resistant organisms.

As per the WHO recommendations, at least 70% of national antibiotic consumption should originate from the Access category, with the aim of limiting excessive exposure to Watch and Reserve antibiotics and thereby reducing selective pressure for resistance (Zanichelli et al., 2023). The BPPL and AWaRe frameworks provide complementary perspectives on the AMR landscape. The BPPL identifies the pathogens that pose the greatest clinical threat, while AWaRe categorises the antibiotic classes whose use must be carefully managed.

The organisms and antibiotic classes examined in subsequent chapters are therefore not considered in isolation, but correspond to microorganism–antibiotic combinations included in BPPL and AWaRe.

1.4 Global efforts

Over the past decade, the increased recognition of AMR as a global crisis has prompted substantial policy recognition. As an effort to address the issue, many international and national agencies have proposed strategic frameworks to strengthen surveillance and promote rational antibiotic use.

1.4.1 WHO Global Action Plan

In 2015, the World Health Organisation introduced the Global Action Plan on AMR with a key focus on improving awareness, strengthening surveillance and research, reducing infection rates, optimising antimicrobial use, and ensuring sustainable investment in diagnostics and treatments (World Health Organization, 2015).

1.4.2 National Action Plan

Following the recommendations of the GAP, by 2024, around 170 countries had developed national action plans. Amongst them, roughly two-thirds reported some level of implementation of the NAP. Around 90–100 countries have contributed data to WHO's GLASS platform, suggesting progress in surveillance capacity (World Health Organization, 2025).

India's first National Action Plan was launched in 2017, structured around six priorities including awareness, surveillance, infection prevention, rational antibiotic use, research, and governance (Ministry of Health and Family Welfare, 2017; Ranjalkar & Chandy, 2019). The launch of NAP marked a shift in the positioning of AMR within national policy and supported the expansion of AMR surveillance. However, as implementation progressed, differences across states became

more apparent, and progress was contingent on laboratory capacity, funding, and health system infrastructure. Sustained efforts were required to build capacity beyond the human health sector, particularly within a One Health framework.

These experiences appear to have informed the updated National Action Plan (NAP 2.0, 2025–2029), which places greater emphasis on One Health integration, strengthening surveillance systems, laboratory expansion, and monitoring antibiotic use in the country. The NAP-AMR 2.0 addresses gaps in the first NAP through stronger inter-sectoral coordination, laboratory capacity, infection control, private-sector engagement, timelines and budgeted stakeholder plans. NAP 2.0 also explicitly mentions digital integration and data management, suggesting a shift toward more interoperable systems (Ministry of Health and Family Welfare, Government of India, 2025).

1.5 AMR Surveillance and Stewardship: from measurement to action

Surveillance and Stewardship are considered as two foundational pillars in the public health response to AMR, which, when combined, build the foundational link between identification of resistance and its response. Surveillance is used to generate evidence on the occurrence, distribution, and temporal change of resistance, and stewardship is designed to use this information to optimise antibiotic use in clinical settings

Surveillance is done through routinely generated antimicrobial susceptibility testing (AST) reports interpreted using standard breakpoints such as CLSI or EUCAST. Clinical specimens are collected from patients in whom infection is suspected, organisms are identified in the laboratory, and susceptibility results are generated for selected antibiotics. Laboratories produce isolate-level

results, which are then aggregated into resistance proportions for specific microorganism–antibiotic–specimen combinations. These summaries form the basis of cumulative antibiograms, institutional reports, national surveillance outputs, and global AMR monitoring systems. However, a resistance proportion is not a direct measure of the true prevalence of resistance in the population. It is a conditional estimate derived when the number of resistant isolates are divided by the number of tested isolates, after a sequence of clinical, laboratory, and analytical filters. Both the numerator and denominator are shaped by who seeks care, who is sampled, which specimens are collected, which antibiotics are tested, how repeat isolates are handled, which interpretive breakpoints are applied, and how the data are aggregated. A reported increase in resistance may therefore reflect a real change in resistance biology, but it may also reflect changes in testing behaviour, patient case-mix, referral patterns, laboratory methods, or preprocessing choices.

This interpretive issue is particularly important because cultures are not requested randomly. They are more likely to be ordered for patients with severe infections, treatment failure, recurrent infection, hospitalisation, tertiary-care referral, or prior antibiotic exposure. Routine laboratory data can therefore over-represent difficult-to-treat infections compared with the broader population of infections. Conversely, limited diagnostic access, low blood-culture utilisation, and antibiotic use before sampling may lead to under-ascertainment of infections. Differences in reported resistance across hospitals, regions, or time periods may therefore reflect differences in diagnostic behaviour and healthcare access, not only differences in the underlying circulation of resistant organisms.

Stewardship programmes aim to ensure that antibiotics are used only when indicated, and that the selected agent, dose, route, and duration are appropriate for the clinical syndrome and patient context. In well-resourced settings, stewardship teams bring together microbiologists, infectious

disease specialists, pharmacists, clinicians, infection-control teams, and data analysts to support rational antibiotic use (Dyar et al., 2017). Frameworks such as AWaRe provide a programme-level approach to monitoring and optimising antibiotic use, particularly by encouraging greater use of Access antibiotics and limiting unnecessary exposure to Watch and Reserve antibiotics (Hsia et al., 2019). However, patient-level antibiotic decisions still require integration of clinical severity, likely source of infection, local susceptibility patterns, prior microbiology, allergy history, renal function, and microbiological confirmation where available.

Although AMR surveillance is meant to support action, its translation into practice remains incomplete. Surveillance outputs are often retrospective whereas clinical and stewardship decisions are made prospectively, often under uncertainty and before culture confirmation. Surveillance therefore, contributes strongly to understanding resistance, but less consistently to acting on it in a timely manner. This limitation is reinforced by the form in which AMR results are usually reported as resistance proportions or trends, often with limited integration of prescribing, consumption, clinical, or denominator data.

The key challenge for stewardship intelligence is therefore not the availability of data, but the absence of analytical approaches that can convert surveillance outputs into signals that are timely, interpretable, and action-oriented. This unresolved gap provides the conceptual motivation for the work presented in the following chapters.

Chapter 2: Background and Related Work

2.1 Classification of AMR Surveillance Systems

AMR surveillance systems can be classified based on the data generation process, the scale at which surveillance operates, and the purpose the data serve. These dimensions are not mutually exclusive, and each surveillance system is positioned across all three, shaping both the nature of the data and its interpretability (Holt et al., 2025; Lim, Ashley, Hamers, Turner, Kesteman, Akech, Corso, Mayxay, Okeke, Limmathurotsakul, & van Doorn, 2021).

2.1.1. Mode of Data Collection: Active and Passive Surveillance

Most AMR surveillance today relies on routine clinical workflows where cultures are obtained based on physician judgment and processed within existing laboratory systems known as passive surveillance (Ashley et al., 2019; Lim, Ashley, Hamers, Turner, Kesteman, Akech, Corso, Mayxay, Okeke, Limmathurotsakul, & van Doorn, 2021). Large-scale platforms such as the Global Antimicrobial Resistance and Use Surveillance System and national programmes, including the Indian Council of Medical Research AMR network, are built on this model (Seale et al., 2017; Walia et al., 2019). Its primary advantage is feasibility, i.e. data are continuously generated without additional sampling infrastructure or funding. However, the data reflect clinical decision-making as much as underlying epidemiology. This introduces an inherent bias as patients who are more severely ill, have failed prior treatment, or are admitted to tertiary care settings are more likely to be sampled (Ashley et al., 2019; van Leth & Schultsz, 2023). Even when the underlying prevalence of resistance is comparable, differences in culture utilisation and specimen-submission practices can substantially shift observed resistance proportions across settings. Passive surveillance should

therefore be interpreted as a signal from tested populations rather than a direct estimate of resistance in the population at risk. (van Leth & Schultsz, 2023).

Active surveillance is based on predefined sampling criteria, such as systematic screening of specific cohorts or sentinel populations (Lim et al., 2021). It is less common in AMR due to cost and operational constraints, but provides more representative estimates when implemented (Lim et al., 2021). These approaches are generally used in focused epidemiological studies, outbreak investigations, or validation exercises.

In real-world settings, the majority of systems are based on passive surveillance as they are scalable and self-sustaining, while active designs are used selectively where unbiased prevalence estimation becomes critical. The present thesis, therefore, treats routine surveillance data not as a direct measure of population prevalence but as a structured source of signals that can be analysed for temporal change, geographical heterogeneity, and stewardship relevance.

2.1.2. Organisational Scope: Global, Regional, and National Systems

Surveillance systems also differ in the scale at which coordination occurs, and this has implications for both comparability and use.

At the global level, systems such as the Global Antimicrobial Resistance and Use Surveillance System aim to standardise reporting across countries. Data are typically aggregated at the national level and reported as proportions of resistant isolates by organism, antibiotic, and specimen source. The expansion of GLASS has been substantial. The 2025 WHO Global Antibiotic Resistance Surveillance Report drew on more than 23 million bacteriologically confirmed infections, with data reported by 104 countries in 2023 and 110 countries during 2016–2023 (World Health Organization, 2025).

Regional surveillance systems operate across groups of countries and generally build on national surveillance structures already in place. They generally introduce sufficient standardisation through harmonised reporting formats, shared surveillance protocols, and coordination of laboratory methods. Examples include the Central Asian and European Surveillance of Antimicrobial Resistance (WHO Regional Office for Europe, 2019; WHO Regional Office for Europe, 2023) and the European Antimicrobial Resistance Surveillance Network (ECDC, 2017).

National surveillance systems operationalise AMR data collection within specific governance, laboratory, and healthcare contexts. They are responsible for generating primary data through networks of hospitals and laboratories, and for translating surveillance outputs into national policy and stewardship actions. Examples include surveillance programmes such as Japan Nosocomial Infections Surveillance (Kajihara et al., 2021). In India, surveillance is organised through multiple overlapping networks rather than a single unified system. The National Centre for Disease Control coordinates the national programme on AMR containment, aggregating data from tertiary-care hospitals, many of which use WHONET for data management. The Healthcare-associated Infection (HAI) Surveillance Network, led by AIIMS in collaboration with CDC and ICMR, focuses specifically on HAIs and uses an in-house developed reporting platform for data management (Mathur et al., 2022). The Indian Council of Medical Research AMR (IAMRSN) network, established in 2013, spans more than 20 tertiary care centres and selected private laboratories, supported by in-house data systems and standardised protocols for surveillance, infection control, and antimicrobial use (ICMR, 2025; Kaur et al., 2019; Kaur et al., 2021; Walia et al., 2019).

These differences shape how surveillance is actually used and how we interpret the analysis presented in this thesis. At the global level, the priority is comparability across countries, which

usually means working with highly standardised and aggregated data. This allows broad patterns to be tracked, but finer local variation is often lost. At the regional level, the priority is standardizing methods across countries within a geography, so the data becomes more internally consistent. At the national level, more granular data is being collected, which is also used to inform treatment guidelines, policy decisions, and, in many settings, routine stewardship.

2.1.3. Intended Use: Public Health, Clinical, and Research Surveillance

The surveillance systems can also be differentiated by their intended use, which includes how data are collected and what can be inferred from it.

Public health surveillance is designed for burden estimation, monitoring trends, and supporting policy development. Many systems, such as the Global Antimicrobial Resistance and Use Surveillance System, rely on standardised, often aggregated reporting to enable comparison across countries. However, these are based on limited details on clinical parameters. The resistance is typically expressed as proportions among tested isolates without a clear population denominator, which makes direct burden estimation difficult and may require additional modelling, as in the Global Burden of Disease analyses (Zeng et al., 2021).

Clinical surveillance is implemented within hospitals wherein data are used to guide empiric therapy and infection control. In this the timeline and contextual relevance are important. The data reflect specific patient populations and testing practices, which makes them useful for local stewardship but less suited for comparisons across settings (Kajihara et al., 2021; Lim, Ashley, Hamers, Turner, Kesteman, Akech, Corso, Mayxay, Okeke, Limmathurotsakul, & van Doorn, 2021).

In research and market-driven surveillance, surveillance is structured around standardised protocols, often with centralised testing. Their sampling is shaped by study design and therapeutic

priorities rather than population representativeness, which limits their use for estimating burden. Examples include programmes such as the Pfizer Antimicrobial Testing Leadership and Surveillance and the SENTRY Antimicrobial Surveillance. The resulting datasets are detailed frequently, including MIC distributions and isolate-level metadata and are well suited for studying resistance mechanisms or tracking emerging threats (Diekema et al., 2019; Fuhrmeister & Jones, 2019).

2.2 AMR Data Landscape

AMR surveillance systems determine how resistance is reported, but what can actually be analysed depends on the underlying data. AMR is not observed through a single measurable process. Instead, it becomes visible through a set of data streams that arise at different points in care and microbial ecology. AST data capture resistance patterns only after organisms have been cultured and tested. Microbiological data are derived from culture, and AST is performed on clinical isolates. The clinical records provide the patient characteristics and outcomes. The antibiotic use and prescription data reflect the selective pressures acting on these organisms. In some settings, the genomic and environmental datasets add further detail by describing resistance mechanisms and potential reservoirs (Baker et al., 2023; Jauneikaite et al., 2023).

2.2.1 Microbiological Data

The microbiology data include details on the isolated organism, specimen tested and antibiotic-specific results reported either as categorical interpretations or quantitative measures such as DDs or MICs (ECDC, 2017; Lim et al., 2021). These data are derived from antimicrobial susceptibility testing on cultured isolates and thus represent a selected subset rather than the population at risk (Ashley et al., 2019; Lim et al., 2021). Moreover, the culture process is not uniform and is

influenced by clinical judgement, severity of illness, and access to diagnostics. Once tested, the interpretation of resistance, susceptibility or intermediate from raw values is also influenced by the breakpoint definitions. Standards such as CLSI or EUCAST may shift resistance classifications even when the underlying biology remains unchanged.

2.2.2 Clinical Data

Clinical data includes patient characteristics such as preliminary diagnosis, age, gender, admission timelines, care setting, comorbidities, etc. These data provide the background patient context for interpreting the microbiological findings and are generated through routine care alongside the microbiology data. However, in many settings, clinical information is still recorded on paper or in fragmented digital systems, and thus, the data completeness and quality vary widely depending on the collection and storage mechanisms. Also, due to a lack of standardization these datasets suffer from inconsistency in the encoding of information, hampering integration with microbiology data. Privacy concerns are also substantial, especially when datasets include temporal and location-specific information, limiting data sharing and large-scale integration.

2.2.3 Antibiotic Consumption and Prescription Data

Data pertaining to the consumption and distribution of antibiotics are captured in hospitals through standardised reporting of Defined Daily Dose (DDD) or Days of Therapy (DOT) in aggregated form across wards, institutions, or time periods. DDD is useful for standardised comparisons of aggregate consumption, whereas DOT is often more clinically interpretable in hospital settings because it counts days of antimicrobial exposure. These metrics are WHO based standards and thus support comparisons across settings more easily than many other AMR-related data streams. However, since this data is aggregated, patient-level variations are mostly lost.

Patient level context can be derived from the prescription data which includes details on the prescribed drug, dose, duration, route, and sometimes the recorded indication. This makes them more useful for examining prescribing behaviour and for asking whether antibiotic exposure is likely to be appropriate, excessive, or poorly aligned with need. Since there is no standard format, the structure of prescription data depends heavily on local record systems, documentation habits, and the degree of digitisation. Even within the same health system, fields may be incomplete, coded differently, or not captured at all, which makes harmonisation difficult.

2.2.4 Genomic Data

Genomic data is generated to understand AMR in terms of underlying biological mechanisms, evolution, and spread of resistance. Data are generated using techniques such as whole-genome sequencing, targeted sequencing, metagenomics, plasmid analysis, and gene-focused assays and can be used to identify acquired resistance genes, chromosomal mutations, mobile genetic elements, and clonal relatedness between isolates. Genomic datasets are high-dimensional, technically demanding, and less standardised than routine laboratory records. The results are sensitive to differences in sequencing quality, assembly methods, reference databases, and interpretation pipelines. These data are commonly used to investigate outbreaks and transmission dynamics, and additional contextualization with phenotypic, clinical, and epidemiological information is useful.

2.2.5 One Health Data

The emergence and spread of resistance is interconnected amongst human, animal and environmental sectors. For instance, the antibiotic use in healthcare and livestock, the movement of organisms through food and direct contact, and the release of residues and resistant bacteria into wastewater or runoff all contribute to this wider ecology. Therefore, surveillance restricted to

clinical isolates cannot fully capture the broader ecological processes that drive the emergence, persistence and spread of resistance. However, for clinical stewardship, routine human microbiology data remain a critical operational data source. The relevant data are generated from several streams, including clinical microbiology laboratories, veterinary surveillance, farm and antimicrobial use records, food-chain sampling, and environmental surveillance. Combined analysis can highlight reservoirs, possible cross-sector linkages, and patterns that would be difficult to see from clinical data alone.

The main limitation in the AMR data landscape is not the availability of data, but the lack of linkage between data streams. Microbiology results are often available, but clinical context, antibiotic exposure, outcomes, genomic information, and environmental data are either missing or not interoperable. This restricts causal interpretation and limits the ability to move directly from a resistance proportion to a specific intervention. At the same time, AST data remain the most consistently available source across many surveillance systems. Therefore, a practical analytical framework must be able to extract meaningful information from AST data alone, while remaining compatible with richer clinical, prescribing, genomic, or One Health data when these become available.

2.3 Analytical Approaches to Modelling AMR

Analytical approaches for modelling AMR have evolved from descriptive epidemiology and cumulative antibiograms toward more complex statistical, temporal and machine-learning frameworks. The choice of method is shaped by the research question, but also by the structure and limitations of AMR data: whether the data are isolate-level or aggregated, whether denominators are available, whether observations are cross-sectional or longitudinal, whether patient-level metadata can be linked, and whether antimicrobial use, prescribing or consumption

data are available. Since AMR surveillance data are not generated from a uniform population sampling frame, it is shaped by who is tested, where specimens are collected, which antibiotics are included in AST panels, how repeat isolates are handled, and how laboratories apply interpretive standards. Thus, the choice of method depends on the problem statement as well as on the structure, granularity, and limitations of AMR data (World Health Organization, 2022; Murray et al., 2022; Poku et al., 2023)

2.3.1 Descriptive analysis

Descriptive analysis remains the foundation of routine AMR surveillance. AST results are commonly summarised as proportions of resistant organisms within a specific specimen-antibiotic combination, often stratified by geography, hospital, ward, age, sex, infection origin or time period (Seale et al., 2017; World Health Organization, 2021a, 2022). Although frequently used for antibiogram generation, empirical treatment guidance, stewardship review and public-health reporting, these results are affected by selective culturing, duplicate isolates, changes in diagnostic access, local testing practices, evolving breakpoints, and shifts in hospital case-mix. Thus, descriptive AMR surveillance is increasingly complemented by statistical models that can estimate uncertainty, quantify temporal change and account for clustering across institutions, regions or countries.

2.3.2 Regression-based approaches

Regression-based approaches are an extension of descriptive surveillance and include linear, logistic, binomial, Poisson, and mixed-effects models to estimate trends, compare resistance across groups, adjust for covariates and account for hierarchical data structures such as isolates nested

within hospitals, regions or countries. Hernandez et al. used regression-based methods to estimate resistance trends across multiple centres in London, illustrating how such models can move surveillance beyond static antibiogram summaries toward quantified temporal change (Hernandez et al., 2021). At a broader scale, regression-based and hierarchical modelling frameworks have also supported AMR burden estimation (Murray et al., 2022; Naghavi et al., 2024). These burden frameworks show how AMR data can be integrated with statistical inference to quantify population-level health impact. This thesis builds on trend estimation, but places greater emphasis on translating those estimates into interpretable resistance trajectories.

2.3.3 Time series and lag-based approaches

Time-series approaches become especially relevant when the question concerns change over time rather than the overall prevalence of resistance. Segmented regression and interrupted time-series models are often used to evaluate changes associated with stewardship interventions, infection-control policies, formulary restrictions, diagnostic changes, national action plans or pandemic-related disruptions. These models can estimate baseline trends, immediate level changes and post-intervention slope changes, making them useful when a defined intervention or policy shift is present (Poku et al., 2023). Dynamic regression and related time-series models extend this approach by linking antimicrobial consumption with resistance, estimating lagged associations and, where sufficiently granular longitudinal data exist, generating short-term forecasts. In a systematic review of hospital-based dynamic regression studies, Laffont-Lozes et al. identified 28 studies and reported that antimicrobial consumption explained 19–96% of AMR variation in multivariable dynamic regression models, with lag times commonly between two and four months (Laffont-Lozes et al., 2023). These approaches can be useful for generating early-warning

hypotheses, but their interpretation requires caution because temporal precedence and correlation do not establish causality. In this thesis, lead–lag analysis is therefore used cautiously, as a way to identify possible indicator antibiotics and temporal warning signals rather than to claim direct causal pathways.

2.3.4 Machine Learning approaches

Machine learning approaches are commonly used in AMR to predict resistance phenotypes, treatment susceptibility, or risk of resistant infection, with the long-term aim of supporting clinical decision-making. These models may use clinical predictors such as demographics, comorbidities, prior healthcare exposure and antimicrobial exposure; some also incorporate whole-genome sequencing data to predict phenotypic resistance (Kim et al., 2022; Sakagianni et al., 2023; Sakagianni et al., 2024; Wang et al., 2022). Large isolate-level surveillance datasets such as Pfizer ATLAS have expanded AMR modelling by enabling analyses of MIC distributions, pathogen–antibiotic resistance trajectories, antibiotic relationship networks, geospatial dashboards, and machine-learning-based resistance prediction (Agboeze et al., 2024; Allel et al., 2026; Catalán et al., 2022; Opiyo et al., 2025; Rajendran et al., 2026; Shaw, 2020; Valavarasu et al., 2025). Since AMR patterns are strongly shaped by local ecology, prescribing practice, laboratory workflow, and data completeness, these models, although useful, have limited generalisability (Kherabi et al., 2024; Ardila et al., 2025). Also, most of the available literature remains focused on model development, with less attention to external validation, prescribing impact, or clinical outcomes (Kim et al., 2022; Kherabi et al., 2024; Ardila et al., 2025). For the purpose of this thesis, these limitations support the use of interpretable surveillance-oriented methods rather than purely predictive models.

2.3.5 Emerging multimodal and federated approaches

Newer analytical approaches are increasingly being explored to move AMR surveillance beyond organism–antibiotic summaries and retrospective reporting. A major direction is multimodal integration, reflecting the fact that resistance is not generated by microbiology alone. Resistance phenotypes observed in AST data are shaped by antimicrobial exposure, prescribing behaviour, patient risk profiles, pathogen transmission, genomic mechanisms, infection-control practices, and wider health-system context. Consequently, recent work has begun to examine how AST data can be analysed together with prescribing records, antimicrobial consumption data, genomic information, electronic health record variables, and contextual indicators within joint analytical frameworks (Kherabi et al., 2024; Sakagianni et al., 2023, 2024). Integrative analysis enables looking beyond descriptive patterns to understand the conditions under which resistance emerges, spreads, and becomes clinically consequential.

AMR data are often fragmented across laboratories, hospitals, pharmacies, and public-health systems, with substantial heterogeneity in testing practices, coding standards, patient populations, and data governance arrangements. To address these, federated learning approaches have been proposed for developing shared models across institutions while keeping raw data local, an attractive feature in settings where patient-level microbiology and prescribing records cannot be easily centralised (Kherabi et al., 2024). However, federated modelling does not by itself solve problems of data quality, laboratory comparability, missingness, representativeness, or model calibration across sites. Its value for AMR surveillance will depend on harmonised definitions, robust external validation, transparent governance, and careful assessment of whether model performance is preserved across hospitals, geographies, and patient groups.

Generative models represent another emerging direction in AMR-related AI, but their more established use at present is closer to antimicrobial discovery, molecular design, and resistance-mechanism exploration than to routine surveillance or stewardship analytics (Arnold et al., 2025; Kherabi et al., 2024).

Large language models and vision-language models are also being explored for AMR-adjacent health-data workflows, particularly where relevant information is embedded in unstructured text, scanned prescriptions, laboratory reports or clinical documents. Published evidence on prescription-digitalisation work involves the use of machine-learning pipelines combining OCR, layout-aware segmentation, medical ontologies, semantic embeddings and catalogue matching to convert prescription images into structured medication information (Sharma M et al., 2023). However, recent systems have explored LLM- and multimodal-model-based workflows for prescription extraction and pharmacy operations (Ghazal et al., 2025; Jagatap et al., 2025). LLMs have also been evaluated for adjacent knowledge-intensive tasks such as medication-direction standardisation and evidence synthesis, including systems such as MEDIC and TrialMind (Pais et al., 2024; Wang et al., 2025). These developments suggest that multimodal AI may help convert unstructured clinical and prescription artefacts into analysable data, but their direct role in routine AMR surveillance has not been explored much. Moreover, prescription extraction and clinical text interpretation are safety-critical tasks and thus require catalogue grounding, audit trails, domain constraints, human verification and independent validation. For surveillance-oriented applications, these tools are therefore best viewed as complementary data-capture and synthesis technologies rather than substitutes for epidemiologically grounded, interpretable AMR analytics (Kherabi et al., 2024; Poku et al., 2023; Laffont-Lozes et al., 2023).

2.4 Research Objectives and Structure of the Thesis

The existing AMR surveillance and analytical approaches provide essential estimates of resistance, temporal trends and, in some settings, predictions. However, the literature reviewed above highlights a continuing need to translate these outputs into interpretable information for surveillance and stewardship within the constraints of routinely collected data. Aggregate resistance estimates can conceal the differences across organisms, antibiotics, infection syndromes, geographies, patient groups and healthcare settings, requiring examination of temporal patterns alongside contextual variation. Although literature evidence for lead-lag relations between antibiotic resistance and antibiotic consumption is available, the potential surveillance value of lead–lag relationships between resistance to different antibiotics requires investigation. Also, interpreting resistance burden alongside its direction and rate of change could further support surveillance prioritisation. Moreover, most data exists in silos and connecting these laboratory-derived findings with prescribing, antibiotic use and community context presents an additional challenge because these data arise from different populations and systems.

Together, these gaps motivate the overall aim of this thesis todevelopdata-driven approaches that can transform routinely generated antimicrobial susceptibility testing data into interpretable and actionable intelligence for AMR surveillance and stewardship. This aim is addressed through four linked research objectives described in Figure 2.1.

- To characterise longitudinal and contextual variation in AMR across organisms, antibiotics, infection syndromes, age groups, healthcare settings, and geographical regions using multicentric AMR surveillance data from India.
- To examine temporal lead-lag relationships in AMR and identify candidate indicator antibiotics that may support hypothesis generation and more focused surveillance.

- To develop an interpretable trajectory-based scorecard that combines resistance burden and rate of change to differentiate persistent, improving, and deteriorating AMR trajectories.
- To define a translational pathway for operationalising AMR intelligence by integrating analytical outputs with community-level data, awareness, prescription, antibiotic-use, and hospital-based surveillance components through *AMRSense*.

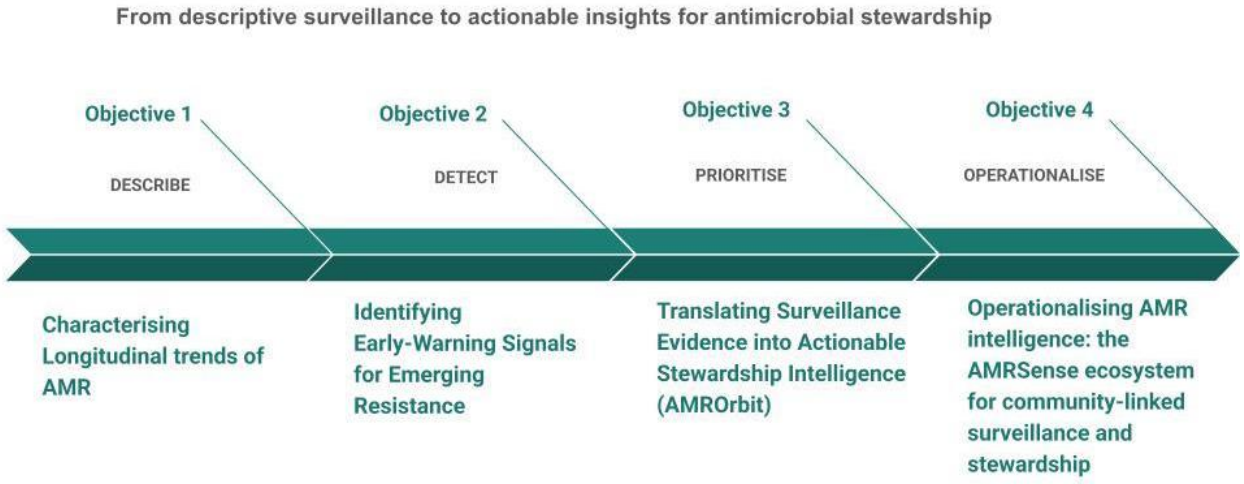


Figure 2.1 outlines the overall structure of the thesis. The objectives are organised as a progression from descriptive understanding to actionable insights for AMR Surveillance and Stewardship.

Objective	Chapter	Primary evidence/output
Characterise AMR variation	Chapter 3	Multicentre BSI and UTI analyses
Examine temporal signals	Chapter 4	Lead–lag and indicator-antibiotic analysis
Prioritise AMR trajectories	Chapter 5	*AMROrbit* scorecard and software
Operationalise intelligence	Chapter 6	*AMRSense* design and early implementation

Chapter 3: Characterising Longitudinal Spatio-temporal Trends in AMR and their Health Systems Context

This chapter summarises two syndrome-specific studies of AMR in BSIs and UTIs conducted using multicentric data from the ICMR Antimicrobial Resistance Surveillance Network using a broadly shared analytical framework. To avoid repetition and enable comparison across infection syndromes, the common data-processing and statistical methods are presented together, followed by BSI- and UTI-specific results. The lead–lag analyses reported within the two studies are reorganised separately in Chapter 4 because they address a distinct temporal research question. This chapter draws on Kaur et al. (2024) and Kaur et al. (2023).

3.1 Introduction

AMR represents an urgent health crisis with a global burden of 1.27 million deaths (95% UI 0.91–1.71 million) directly attributable to AMR and nearly 4.95 million deaths associated with resistant infections in 2019 (Murray et al., 2022). The largest share of this mortality burden was borne by invasive infections with bloodstream infections (BSIs) as one of the leading contributors, responsible for approximately 0.83 million AMR-attributable deaths. In comparison, urinary tract infections (UTIs) accounted for 0.96 million AMR-associated deaths and an estimated 0.26 million AMR-attributable deaths, largely driven by resistant *Escherichia coli* and *Klebsiella pneumoniae* (Rudd et al., 2020, Murray et al., 2022).

The most recent Lancet 2024 modelling study projects that if unchecked, annual AMR-attributable deaths could rise to 1.91 million by 2050, with total AMR-associated deaths increasing to 8.22 million annually (Naghavi et al., 2024). The burden will be disproportionately borne by low-and-

middle-income countries (LMICs), where high infectious disease burden, widespread antibiotic exposure, and constrained health systems amplify vulnerability (Lewnard et al., 2024).

AMR not only poses a significant threat to human health but also affects animal health and agriculture, thus undermining progress towards achieving several SDGs, particularly those related to health (SDG 3), hunger and agriculture (SDG 2), clean water (SDG 6), and economic growth (SDG 8). Economic analyses suggest profound downstream impacts of AMR on poverty, healthcare costs, and productivity. Within the SDG monitoring framework, indicator 3.d.2 includes two AMR-specific measures (i) the proportion of bloodstream infections due to *Escherichia coli* resistant to third-generation cephalosporins and (ii) the proportion due to methicillin-resistant Staphylococcus aureus. However, this inclusion has yet to be matched by a large empirical literature examining how resistance patterns relate to SDG-linked conditions, particularly at sub-national levels. The expected relationship between SDG and AMR is not self-evident. Higher levels of development may be associated with greater antibiotic consumption, wider healthcare access, and more frequent contact with formal medical systems, all of which can increase antimicrobial exposure and, in turn, selective pressure for resistance. On the contrary, better-developed settings may also have stronger public health infrastructure, improved infection prevention, greater diagnostic capacity, more appropriate prescribing, and more timely clinical management, which could act in the opposite direction and help limit the emergence or spread of resistance. Therefore, to understand the relationship, it is necessary to examine the empirical pattern directly.

Globally, India is amongst the high-burden countries due to high baseline rates of infectious diseases, substantial antibiotic consumption across human and animal sectors, and marked heterogeneity in healthcare access. The major contributors are bloodstream infections (sepsis) and

urinary tract infections, both with high mortality and morbidity rates. Multicentric data from 35 Indian ICUs have reported 56% sepsis cases, with nearly 45% of infections being attributable to multidrug-resistant organisms (Hammond et al., 2022). Single-centre studies have documented increasing carbapenem resistance in UTIs between 2011 and 2017, while more recent multicentric ICU-based studies report carbapenem resistance rates as high as 76% among Gram-negative hospital-acquired UTIs (Ravishankar et al., 2021; Mathur et al., 2022). However, much of the published literature from India remains single-centre, pathogen-specific, or cross-sectional in design. Such studies, while informative, limit the ability to characterise longitudinal resistance trajectories, detect early shifts in antimicrobial susceptibility, or quantify spatio-temporal heterogeneity at a national scale. In particular, there is limited systematic analysis of resistance trends in both BSIs and UTIs using standardised longitudinal surveillance data.

To address this gap, this chapter leverages longitudinal data from the Indian Council of Medical Research Antimicrobial Resistance Surveillance Network (IAMRSN), operational since 2013. The surveillance network comprises selected tertiary care centers across India, chosen to ensure representative geographic and population coverage. Since 2016, all sites have adopted standardised operating protocols, digital reporting systems, and antimicrobial susceptibility interpretation aligned with Clinical and Laboratory Standards Institute (CLSI) guidelines. Quantitative antimicrobial susceptibility testing data, including minimum inhibitory concentrations (MICs) or zone diameters, are centrally reported and subjected to quality assurance through designated nodal centers. Using this harmonised, multi-centric dataset, this chapter presents analytical frameworks to quantify resistance trends in BSI and UTIs across India and provide data-driven evidence for the association between AMR and SDGs.

3.2 Methods

3.2.1 Data Sources

AMR Data: Retrospective data from the IAMRSN were analysed from 2017 to 2022. IAMRSN, established in 2013, consists of nodal centers (NCs) dedicated to specific pathogen groups critical for AMR monitoring: Enterobacteriaceae, Gram-negative non-fermenters, Typhoidal salmonella, Diarrhoeagenic bacteria, Gram-positive organisms (including *Staphylococci* and *Enterococci*), and Fungal pathogens. Standardised data collection started with four NCs and has since expanded to 21 centers (Figure 3.1), incorporating additional regional centers across India. The sites under the IAMRSN are selected based on criteria such as population size and sample volume (Walia et al., 2019). AST data collection was standardized using the standard operating procedures (SOPs) based on Clinical Laboratory Standards Institute (CLSI) guidelines. These SOPs, which are periodically updated, not only aim to standardize practices across the network's tertiary care hospitals but also enhance the quality and reliability of AMR data collected. The initial identification of microorganisms up to species level was performed through standard tests like biochemical tests, proteomics, VITEK-2, MALDI-TOF, 16s rRNA sequencing, and Whole-genome sequencing. After this, antimicrobial susceptibility testing of the isolates was performed according to the ICMR SOPs. Standardized quantitative data (MICs or zone diameters) are submitted to the ICMR database (Kaur et al., 2019, 2021), and interpreted (Resistant/Susceptible/Intermediate) using CLSI guidelines for each microorganism-antibiotic combination for the respective years. The SOPs with further details are available on the ICMR website (*AMRSN*) and are regularly updated as per the feedback from the sites, as well as the latest CLSI guidelines. A comprehensive validation and quality assurance framework is implemented to

ensure the highest data quality standards within the IAMRSN. This framework encompasses internal and external quality controls designed to validate the data generated by the network's laboratories for each pathogenic group. The data are validated through a script with a defined set of rules overseen by the Nodal Centers (NCs). The participating laboratories engage in routine internal and external quality control measures. Additionally, the IAMRSN laboratories are integrated into the National EQAS, conducted by collaborating centers of the Indian Association of Medical Microbiologists. The National EQAS provides an additional layer of quality control, ensuring that laboratories across the country, irrespective of their location within the IAMRSN, adhere to uniform bacterial identification and AST standards. While the diversity and national coverage of sites ensured a wide-ranging representation of isolates, the standardized SOPs and data allowed analytical modelling carried out in this study.

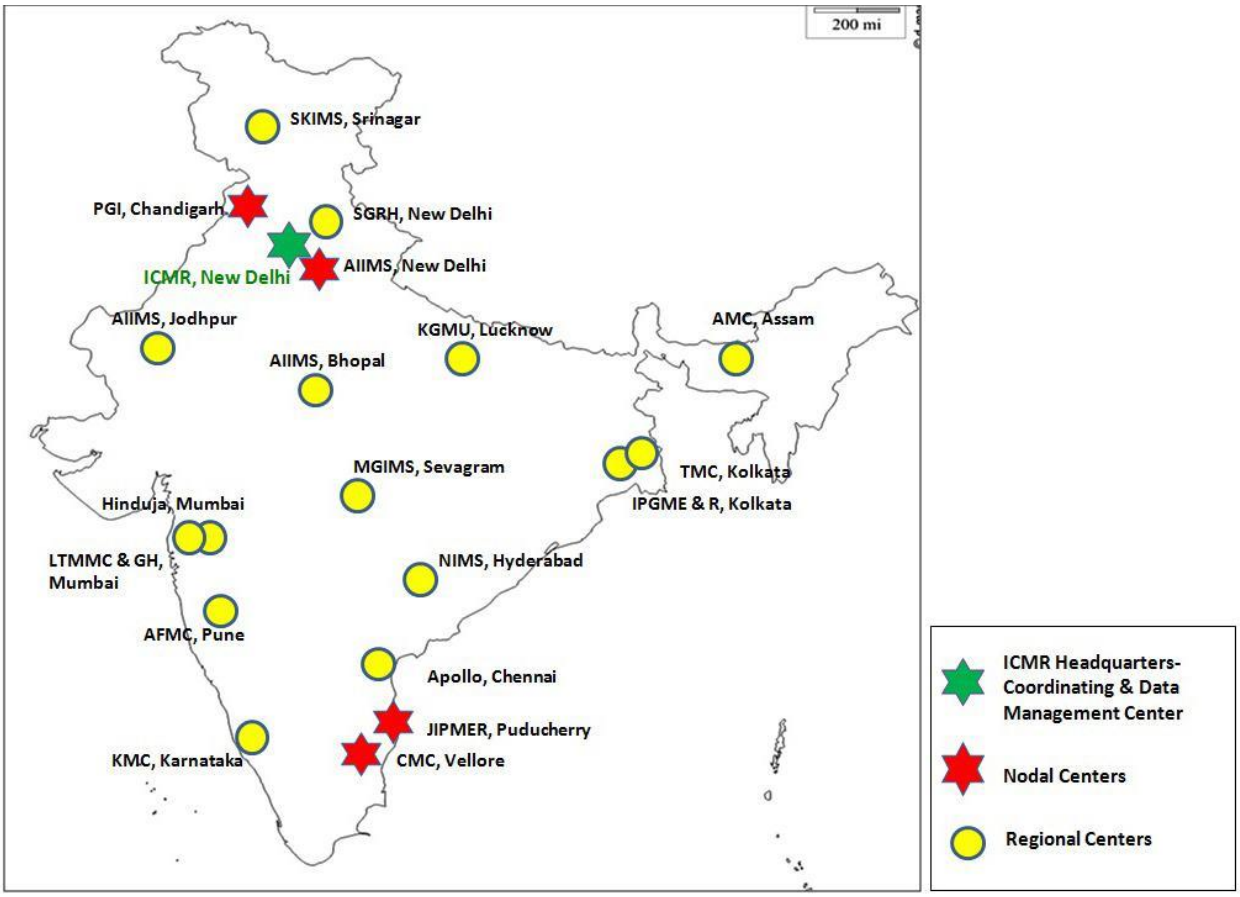


Figure 3.1. Geographic distribution of the Indian Council of Medical Research–Antimicrobial Resistance Surveillance Network (IAMRSN) across India. The map illustrates the national architecture of the IAMRSN, highlighting the ICMR Headquarters in New Delhi as the central coordinating and data management hub (green star), designated nodal centres responsible for reference testing and protocol harmonization (red stars), and participating regional centres contributing routine antimicrobial resistance surveillance data (yellow circles).

Source: AMRSN website: https://iamrsn.icmr.org.in/index.php/amrsn/amrsn.

SDG Data: The Sustainable Development Goals (SDGs) are a universal set of 17 interconnected goals established by the United Nations in 2015 as part of the 2030 Agenda for Sustainable Development. These goals were designed to be a "blueprint to achieve a better and more sustainable future for all" by addressing global challenges, including those related to poverty,

inequality, climate change, environmental degradation, peace, and justice. Each goal encompasses specific targets to be achieved over a 15-year period, encouraging countries to undertake efforts to end all forms of poverty, fight inequalities, and tackle climate change while ensuring that no one is left behind. NITI Aayog is overseeing the implementation of these goals in India. The data pertaining to the SDG ranking of states was taken from the SDG India Baseline Report 2018 (Niti Aayog, 2018), which assessed 62 priority indicators across 13 SDGs. Indicator values were normalised to a 0–100 scale, accounting for whether higher or lower values represented better performance. 100 indicated achievement of the specified target. Each goal score was calculated as the arithmetic mean of its normalised indicator scores, with equal weighting. Missing indicator values were excluded from the calculation rather than treated as zero. States and Union Territories were classified as Aspirants (0–49), Performers (50–64), Front Runners (65–99), or Achievers (100). The overall composite index averaged the goal scores. This study used the goal-specific performance categories as contextual variables in the Bayesian network analysis, excluding measures without variation in the study data.

3.2.2 Study Design

The study utilized retrospective data from the ICMR AMR Surveillance Network (IAMRSN), established in 2013 based on the following inclusion/exclusion criteria:

UTI: For the UTIs, the inclusion criteria for isolates were (i) identification of *Escherichia coli*, *Klebsiella (Klebsiella pneumoniae, Klebsiella oxytoca and Klebsiella species)*, *Pseudomonas aeruginosa*, or *Enterococcus (Enterococcus faecalis, Enterococcus faecium and Enterococcus species)* in the isolate, (ii) sample collection between 2017 and 2021 and (iii) completeness of state and district information for the patient.

BSI: For the BSIs, the inclusion criteria for the isolates were (i) identification of the following organisms in the isolate (*Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Klebsiella species*, *Acinetobacter baumannii*, *Acinetobacter calcoaceticus*, *Acinetobacter baumannii-calcoaceticu complex, Acinetobacter species*, *Staphylococcus aureus*, *Coagulase-negative Staphylococci* (CoNS), *Staphylococcus species*, *Pseudomonas aeruginosa*, *Enterococcus faecalis*, *Enterococcus faecium*, and *Enterococcus species*), (ii) sample collection between 2017 to 2022 and (iii) availability of state and district information for the isolate.

We used univariate and multivariate time-series modelling to investigate cluster-robust trends of AMR in India and contextualised our findings within the framework of state-level Sustainable Development Goals (SDGs) using a data-driven Bayesian network model. This work focused on analysing monthly-aggregated data and did not attempt to re-identify patients.

3.2.3 Descriptive Analysis

Isolation rates

The isolation percentage of an organism was calculated as:

$$Total\ isolation\ rate\ (Organism\ 1)\ = \frac{Count\ of\ isolates\ for\ organism\ 1\ (nO1)}{Count\ of\ total\ positive\ cultures\ (N)}\ *\ 100$$

$$Sample-wise\ isolation\ rate\ (Org1\ in\ sample\ 1)\ = \frac{Count\ of\ isolates\ for\ O1s1}{Count\ of\ total\ positive\ cultures\ for\ S1} * 100$$

$$Gender-wise\ isolation\ rate\ (Org\ 1\ in\ Gender\ 1)\ = \frac{Count\ of\ isolates\ O1g1}{Count\ of\ total\ positive\ cultures\ g1} * 100$$

$$Zone-wise\ isolation\ rate\ (Org\ 1\ in\ Zone\ 1)\ = \frac{Count\ of\ isolates\ O1z1}{Count\ of\ total\ positive\ cultures\ z1} * 100$$

Resistance rates

The rate of antimicrobial resistance (AMR) was calculated as:

$$AMR\ rate\ (R\%)\ = \frac{R\ count}{(R + I + S)\ count}$$

$$AMR\ rate\ (S\%)\ = \frac{S\ count}{(R + I + S)\ count}$$

where "R" represents the count of resistant isolates, "I" represents the count of intermediate isolates and "S" represents the count of susceptible isolates.

AMR rates in terms of R% have been used for the study.

Multi-drug Resistance (MDR) rate

An isolate was labelled multi-drug resistant if it showed resistance to 3 or more antibiotic classes (Cephems, Beta-lactam inhibitor, Carbapenems, Lipopeptides, Aminoglycosides, Quinolones/Fluoroquinolones, Folate Pathway Antagonists, Fosfomycins, Nitrofurans, Penicillins, Glycopeptides, Lipoglycopeptides, Oxazolidinones). Our bespoke code for calculating MDR rate is available on GitHub as "mdr.py" and uses the following equation:

$$MDR\ Rate\ = \frac{Count\ of\ MDR\ isolates\ for\ organism}{Count\ of\ total\ positive\ cultures\ for\ organism}\ *\ 100$$

Time series interpolation: Minimal pre-processing of the time series was done to avoid statistical artefacts. Time series with overall missing values for resistance rates of more than 20% were discarded. Time series that satisfied the criteria of less than five consecutive missing values were linearly interpolated.

Age stratified analysis: For age-wise analysis, age groups were considered as (i) Neonate- Less than 29 days, (ii) Pediatric- 29 days to 18 years, (iii) Reproductive- greater than 18 to 49 years, (iv) Middle- greater than 49 to 70 years, (v) Elderly- greater than 70 years. The Pediatric group was categorized into: Infants (29 days to less than equal to 1 year), Toddlers (1- less than equal to 3 years), Pre-schoolers (greater than 3- less than equal to 6 years), Middle childhood (greater than 6- less than 13 years) and Teenagers (13-17 years).

3.2.4 National Trends of Resistance

Monthly AMR rates for each antibiotic and organism were aggregated to generate univariate and multivariate time series. Robust confidence intervals (95%) were calculated using Bias-Corrected and Accelerated (BCa) bootstrapping with a rolling window of 3 months for plotting the yearly trends for every microorganism-antibiotic combination. The linear component of the time series was extracted using time series decomposition based on moving averages with a frequency of 12 (for monthly data). National estimates for resistance percentage were derived utilizing a linear regression model, with the dependent variable being resistance percentage and the independent variables being time, hospital, and their interaction effects. To mitigate potential biases introduced by clustering of data within hospitals and by heteroskedasticity and autocorrelation in temporal patterns, cluster-robust estimates of significance and standard errors were calculated. Further, the intercepts and slopes of each hospital were studied with respect to the national slope and intercept to generate an AMR Scorecard for the hospitals to monitor their resistance. To identify the linear relationship between two slopes and intercepts (continuous variables) obtained from the linear model for each hospital, Pearson's correlation coefficient (Benesty et al., 2009) was calculated for each drug-bug combination. Data were further stratified based on gender, zones, age groups, and community and hospital-acquired infections and analyzed separately using a simple linear

regression modelling approach to mitigate potential biases arising from different AMR rates in these subsets.

3.2.5 Geographical Patterns of AMR

The states were stratified into zones to assess the geographical distribution of AMR. The resistance rates for each zone and antibiotic combination were plotted using unsupervised hierarchical clustering utilising the complete method and Euclidean distance as the distance calculation function. This was visualised using a heatmap visualisation in R.

3.2.6 Modelling probabilistic associations between antimicrobial resistance and SDG indicators

Bayesian Networks (BNs) are directed acyclic graphs that model a set of variables and their conditional dependencies via directed edges. Each node in the graph represents a variable, while the edges indicate the conditional dependencies between these variables. This framework allows for both probabilistic reasoning and causal inference, offering insights into the structure and relationships within complex datasets. BNs are particularly useful for understanding the generative process behind the data, enabling predictions and inferences about the behaviour of interconnected systems. Their transparent and interpretable nature and the capacity to incorporate expert knowledge directly into the model structure make them an excellent tool for areas requiring careful reasoning about data, such as healthcare. This analysis employed BNs to model estimated conditional probabilities of resistance given specified categories of the included variables. These queries describe statistical associations and do not estimate intervention effects.

The conceptual premise was that AMR is situated within a broader development context extending beyond health services. Established discussions link AMR with poverty, food and agricultural

systems, water and sanitation, and economic development (World Health Organization et al., 2021). The analysis therefore examined whether state-level SDG measures showed conditional associations with observed resistance patterns. All available SDG measures with sufficient variation were considered as candidate contextual variables in an exploratory Bayesian network analysis. No uniform direction of association was assumed, and inclusion did not imply that every goal had a direct causal relationship with AMR.

UTI: For the UTI analysis, continuous variables were first discretised using k-means clustering to simplify the model without losing critical information. The discrete BN was then learned from the data, with the structure of conditional dependencies optimised using the hill climbing algorithm using the Bayesian information criterion (BIC) as scoring function and an imaginary sample size (ISS) of 7 in the wiseR package (Sethi & Maheshwari, 2018). Organism-specific models were constructed containing antibiotics specific to the organism. To strengthen the model's reliability, 301 BN instances were generated through bootstrapping, and a consensus network was derived using ensemble averaging and majority voting. The network model was queried to infer a node's change in conditional probabilities upon fixing a connected node using the Exact Inference algorithm implemented in WiseR. This robust BN model allowed for precise inference on how changes in one variable could influence the probability of outcomes related to antibiotic resistance, providing actionable insights for policy and practice.

Specifically, the covariates used in the models for both studies of *E. coli* were:

Covariate	**Definition**
identification_method	Method used for the identification of organism
collection_date	Date of sample collection
year	Year of sample collection
hospital_department	Hospital Department
hosp_location_type	Location within the hospital (OPD/Ward/ICU)

infection_type	Type of infection (Community/Hospital-acquired)
gender	Gender of the patient
Amikacin	AST result
Cefotaxime	AST result
Ciprofloxacin	AST result
Ertapenem	AST result
Imipenem	AST result
Meropenem	AST result
Nitrofurantoin	AST result
Piperacillin-tazobactam	AST result
Trimethoprim-sulfamethoxazole	AST result
covid	If the patient was affected by COVID19 or not (0/1)
SDG1	SDG1 reflects No Poverty. This contained the ranking of states based on their SDG1 achievement (classified as Aspirants, Performer, Front runners, Achiever)
SDG2	SDG2 reflects Zero Hunger. This contained the ranking of states based on their SDG2 achievement (classified as Aspirants, Performer, Front runners, Achiever)
SDG3	SDG3 reflects Good Health and Well-being. This contained the ranking of states based on their SDG3 achievement (classified as Aspirants, Performer, Front runners, Achiever)
SDG4	SDG4 reflects Quality Education. This contained the ranking of states based on their SDG4 achievement (classified as Aspirants, Performer, Front runners, Achiever)
SDG5	SDG5 reflects Gender Equality. This contained the ranking of states based on their SDG5 achievement (classified as Aspirants, Performer, Front runners, Achiever)
SDG6	SDG6 reflects Clean Water and Sanitation. This contained the ranking of states based on their SDG6 achievement (classified as Aspirants, Performer, Front runners, Achiever)
SDG7	SDG7 reflects Affordable and Clean Energy. This contained the ranking of states based on their SDG7 achievement (classified as Aspirants, Performer, Front runners, Achiever)
SDG8	SDG8 reflects Decent Work and Economic Growth. This contained the ranking of states based on their SDG8 achievement (classified as Aspirants, Performer, Front runners, Achiever)
SDG9	SDG9 reflects Industry, Innovation, and Infrastructure. This contained the ranking of states based on their SDG9 achievement (classified as Aspirants, Performer, Front runners, Achiever)
SDG10	SDG10 reflects Reduced Inequalities. This contained the ranking of states based on their SDG10 achievement (classified as Aspirants, Performer, Front runners, Achiever)
SDG11	SDG11 reflects Sustainable Cities and Communities. This contained the ranking of states based on their SDG2 achievement (classified as Aspirants, Performer, Front runners, Achiever)
SDG12	SDG12 reflects Responsible Consumption and Production. This contained the ranking of states based on their SDG2 achievement (classified as Aspirants, Performer, Front runners, Achiever)

SDG13	SDG13 reflects Climate Action. This contained the ranking of states based on their SDG2 achievement (classified as Aspirants, Performer, Front runners, Achiever)
SDG14	SDG14 reflects Life Below Water. This contained the ranking of states based on their SDG2 achievement (classified as Aspirants, Performer, Front runners, Achiever)
SDG15	SDG15 reflects Life on Land. This contained the ranking of states based on their SDG2 achievement (classified as Aspirants, Performer, Front runners, Achiever)
SDG16	SDG16 reflects Peace, Justice, and Strong Institutions. This contained the ranking of states based on their SDG2 achievement (classified as Aspirants, Performer, Front runners, Achiever)
SDG17	SDG17 reflects Partnerships for the Goals. This contained the ranking of states based on their SDG2 achievement (classified as Aspirants, Performer, Front runners, Achiever)

The SDG column contained the ranking for each state classified (Achievers- 100; Front Runner- 65 to 99; Performer- 50 to 64; Aspirant- 0 to 49) based on their specific goal achievement. The SDGs showing no variation in our data were removed before model development.

BSI: For the BSI analysis, continuous variables were discretized using k-means clustering, a machine learning algorithm that partitions n observations into k clusters, where each observation belongs to the cluster with the nearest mean. Since it is cumbersome to incorporate all possible confounding factors in pairwise associations, a probabilistic graphical model that decomposed the joint probability into conditional dependencies in a Bayesian network structure was learned from the data using the hill climbing algorithm and Akaike scoring criterion implemented in the wiseR package (Scutari, 2010; Sethi & Maheshwari, 2018). AIC was used to select the simplest model that balances the goodness of fit and model complexity to adequately explain the data trends. For robust inference, 301 BN instances were learned using bootstrapping to obtain a consensus network using ensemble-averaging and majority-voting criteria. The network model was queried for inferring the change in conditional probabilities of a node upon fixing a connected node using the Exact Inference algorithm implemented in wiseR.

3.2.7 Patient Consent and Ethics Approval

This study has been approved by the Ethics Committee of the Indraprastha Institute of Information Technology, Delhi (IIITD-IRB/ER/11/2022/2). This study utilized the routinely collected IAMRSN data. Access to anonymized IAMRSN data was provided by ICMR. Each hospital in the IAMRSN obtained its own ethics approvals for the collection of the surveillance data.

3.3 RESULTS

3.3.1 BSI

Primary Analysis

The IAMRSN database contained 511,224 isolates collected from January 1, 2017, to December 31, 2022. A total of 100,908 isolates were associated with bloodstream infections (from both peripheral and central catheters), of which 81,265 met the specified inclusion and exclusion criteria across 21 centers in 14 states/UTs. The available patient records were analysed separately for 8,786 CA-BSI and 12,079 HA-BSI. Due to inconsistencies in the reported date of birth, age groups could be assigned to 78,183 records.

Descriptive analysis (Tables 3.1 & 3.2) revealed geographical variations. *E. coli* BSIs were found to be more prevalent in isolates from Southern India, while *Staphylococcus* was more common in the North. *Acinetobacter* showed higher prevalence in the Central and North East zones. In contrast, *Klebsiella*, *P. aeruginosa*, and *Enterococcus* showed a more uniform distribution across the regions. A high rate of Multidrug resistance was observed in *Klebsiella*, *Acinetobacter*, and *Staphylococcus* isolates.

Table 3.1 - Distribution of bloodstream infection isolates by gender and geographical zone, with multidrug-resistance rates

		E. coli **(%)**	***Klebsiella*** **(%)**	***Acinetobacter*** **(%)**	***Staphylococcus*** **(%)**	***P. aeruginosa*** **(%)**	***Enterococcus*** **(%)**
Total	Total Isolates	16570/81265 (20.39%)	16486/81265 (20.29%)	11934/81265 (14.69%)	23717/81265 (29.18%)	5755/81265 (7.08%)	6803/81265 (8.37%)
Gender	Males (50376; 61.98%)	9211/50376 (18.28%)	10581/50376 (21.0%)	7611/50376 (15.11%)	15078/50376 (29.93%)	3639/50376 (7.22%)	4256/50376 (8.45%)
	Females (30867; 37.98%)	7353/30867 (23.82%)	5902/30867 (19.12%)	4320/30867 (14.0%)	8632/30867 (27.97%)	2116/30867 (6.86%)	2544/30867 (8.24%)
	Transgender (22; 0.03%)	6/22 (27.27%)	3/22 (13.64%)	3/22 (13.64%)	7/22 (31.82%)	0/22 (0.0%)	3/22 (13.64%)
Zone*	North Zone (28430; 34.98%)	3615/28430 (12.72%)	5711/28430 (20.09%)	4355/28430 (15.32%)	10744/28430 (37.79%)	1645/28430 (5.79%)	2360/28430 (8.3%)
	South Zone (27137; 33.39%)	7742/27137 (28.53%)	5303/27137 (19.54%)	3396/27137 (12.51%)	6130/27137 (22.59%)	2048/27137 (7.55%)	2518/27137 (9.28%)
	East Zone (8529; 10.49%)	2011/8529 (23.58%)	1880/8529 (22.04%)	1066/8529 (12.5%)	2139/8529 (25.08%)	741/8529 (8.69%)	692/8529 (8.11%)
	West Zone (12406; 15.26%)	2492/12406 (20.09%)	2701/12406 (21.77%)	2054/12406 (16.56%)	3336/12406 (26.89%)	1059/12406 (8.54%)	764/12406 (6.16%)
	Central Zone (1850; 2.27%)	304/1850 (16.43%)	387/1850 (20.92%)	418/1850 (22.59%)	431/1850 (23.3%)	117/1850 (6.32%)	193/1850 (10.43%)
	North-east Zone (2913; 3.58%)	406/2913 (13.94%)	504/2913 (17.3%)	645/2913 (22.14%)	937/2913 (32.17%)	145/2913 (4.98%)	276/2913 (9.47%)
MDR (%)	Isolates resistant to 3 or more antibiotic classes	3938/16570 (23.77%)	9915/16486 (60.14%)	9062/11934 (75.94%)	12133/23717 (51.16%)	1698/5755 (29.50%)	813/6803 (11.95%)

*North zone includes Himachal Pradesh, Punjab, Uttarakhand, Uttar Pradesh, Haryana, Ladakh, Chandigarh, Delhi, Jammu and Kashmir; South zone includes Andhra Pradesh, Karnataka, Kerala, Telangana, Tamil Nadu, Andaman and Nicobar, Lakshadweep, Puducherry; East zone includes Bihar, Odisha, Jharkhand, West Bengal; West zone includes Rajasthan, Gujarat, Goa, Maharashtra, Dadra and Nagar Haveli, Daman and Diu; Central zone includes Madhya Pradesh, Chhattisgarh; North-east zone includes Assam, Sikkim, Nagaland, Meghalaya, Manipur, Mizoram, Tripura, Arunachal Pradesh

Table 3.2 - Overall antibiotic resistance patterns across the study period

	E. coli **(%)**	***Klebsiella*** **(%)**	***Acinetobacter*** **(%)**	***Staphylococcus*** **(%)**	***P. aeruginosa*** **(%)**	***Enterococcus*** **(%)**
Amikacin	2898/16464 (17.6)	8799/16356 (53.8)	7529/10764 (69.95)	NA	1728/5696 (30.34)	NA
Cefepime	NA	NA	8990/11455 (78.48)	NA	NA	NA
Cefotaxime	11096/14048 (78.99)	10770/13592 (79.24)	NA	NA	NA	NA
Cefoxitin	NA	NA	NA	12765/19843 (64.33)	NA	NA
Ceftazidime	NA	NA	8963/11191 (80.09)	NA	1881/5568 (33.78)	NA
Ciprofloxacin	11581/15230 (76.04)	10312/15116 (68.22)	NA	11483/19336 (59.39)	1800/4942 (36.42)	NA
Clindamycin	NA	NA	NA	9722/23090 (42.1)	NA	NA
Colistin	NA	NA	180/4446 (4.05)	NA	NA	NA
Ertapenem	3016/12119 (24.89)	7224/11850 (60.96)	NA	NA	NA	NA
Erythromycin	NA	NA	NA	15054/22523 (66.84)	NA	NA
Imipenem	3200/13248 (24.15)	7766/14637 (53.06)	8600/11510 (74.72)	NA	1757/5093 (34.5)	NA
Levofloxacin	NA	NA	6592/10135 (65.04)	NA	NA	NA
Linezolid	NA	NA	NA	291/21918 (1.33)	NA	500/6471 (7.73)
Meropenem	3484/15735 (22.14)	9024/15327 (58.88)	8340/11629 (71.72)	NA	1733/5524 (31.37)	NA

Minocycline	NA	NA	2900/9656 (30.03)	NA	NA	NA
Piperacillin-tazobactam	5647/16205 (34.85)	10439/16169 (64.56)	8601/11646 (73.85)	NA	1282/5536 (23.16)	NA
Teicoplanin	NA	NA	NA	NA	NA	1044/6293 (16.59)
Tetracycline	NA	NA	NA	2994/16822 (17.8)	NA	NA
Trimethoprim-sulfamethoxazole	NA	NA	NA	7931/19223 (41.26)	NA	NA
Vancomycin	NA	NA	NA	118/13290 (0.89)	NA	1262/6475 (19.49)
Ampicillin	NA	NA	NA	NA	NA	3829/5822 (65.77)
Gentamicin HL	NA	NA	NA	NA	NA	3001/5200 (57.71)

NA Not applicable to gram-positive or gram-negative organisms

The study observed high resistance to Cephalosporins and Fluoroquinolones in *E. coli* and *Klebsiella* isolates, with additional resistance to Carbapenems observed in the latter. *Acinetobacter* isolates exhibited significant resistance to all tested antibiotics except for Minocycline. *Staphylococcus* isolates demonstrated high resistance levels to Cefoxitin, Ciprofloxacin, and Erythromycin. *P. aeruginosa* isolates exhibited uniform resistance across all tested antimicrobials. *Enterococcus* demonstrated high resistance to Ampicillin and High-level Gentamicin, while its resistance to Linezolid was comparatively low.

National Trends of Resistance

The modelling of monthly resistance rates for each pathogen revealed significant linear trends for each drug-bug combination. These trends were observed to be broadly consistent across diverse categories such as age groups, geographical regions, infection types, and genders (Table 3.3). Detailed descriptions of these trends follow.

E. coli

A significant increasing national monthly trend in resistance was identified for multiple drugs: Imipenem at 0.22% ($p<10^{-19}$), Piperacillin-Tazobactam at 0.22% ($p<10^{-16}$), Ciprofloxacin at 0.18% ($p<10^{-8}$), Meropenem at 0.15% ($p<10^{-7}$), Ertapenem at 0.09% ($p<10^{-8}$) and Amikacin at 0.06% ($p<10^{-31}$). In contrast, a significant decreasing trend in resistance was observed for Cefotaxime at 0.17% ($p<10^{-16}$) (Figure 3.2).

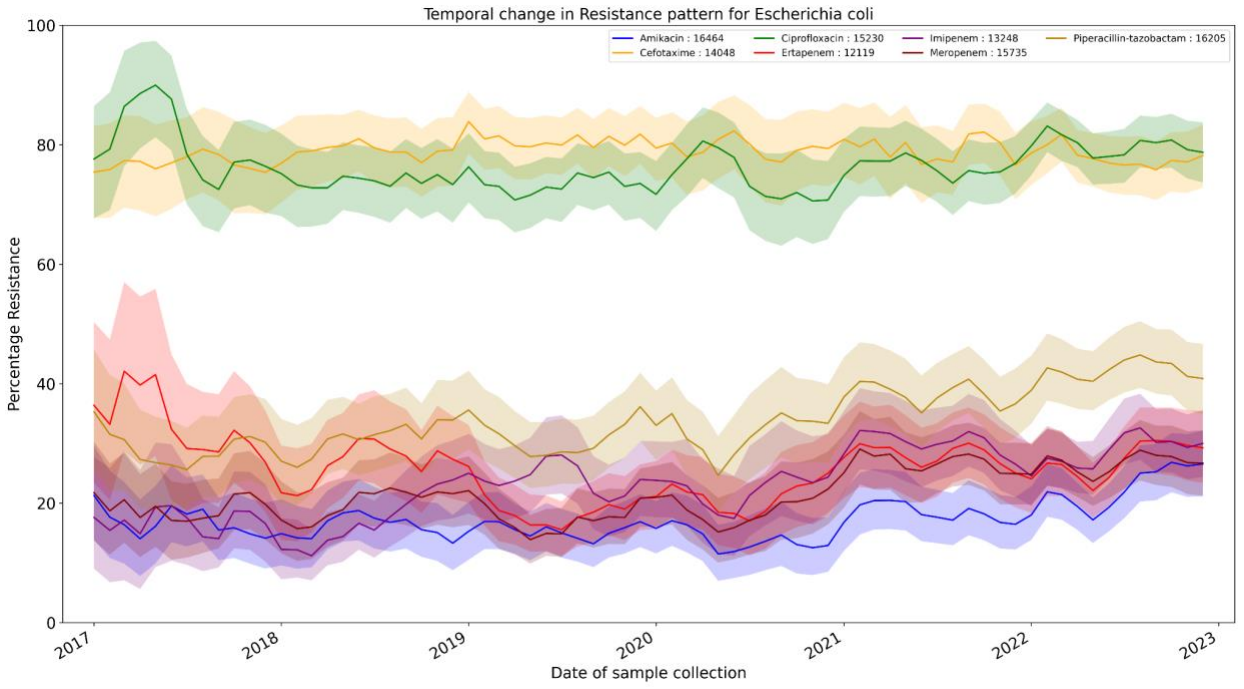


Figure 3.2- This figure shows monthly aggregated antibiotic resistance trends in *E. coli* BSIs from 2017 to 2022. The average rates are represented by lines with shaded areas indicating 95% confidence intervals generated by bootstrapping.

Klebsiella

A significant increasing national monthly trend in resistance was identified for multiple drugs: Imipenem at 0.24% ($p<0.001$), Piperacillin-Tazobactam at 0.17% ($p<0.0001$) and Meropenem at 0.17% ($p<0.01$). In contrast, a significant decrease in resistance was observed for Cefotaxime at 0.25% ($p<10-16$), Ertapenem at 0.09% ($p<10-16$), and Amikacin at 0.04% ($p<0.05$) (Figure 3.3).

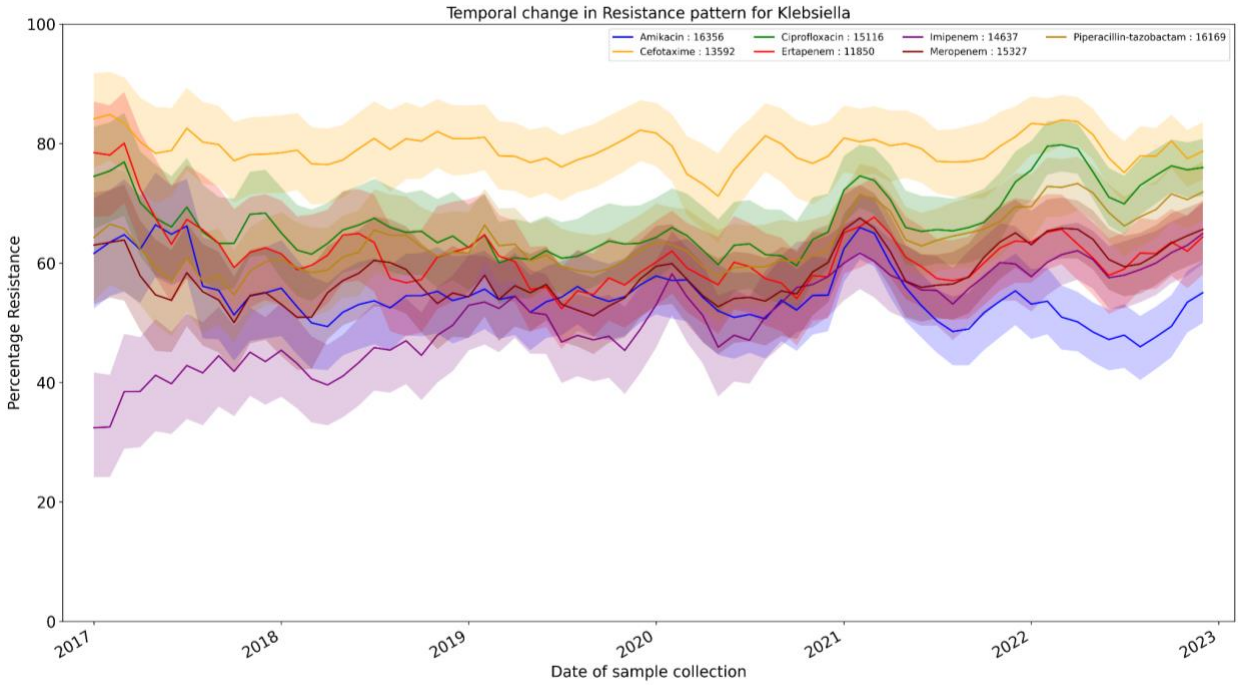


Figure 3.3- This figure shows monthly aggregated antibiotic resistance trends in *Klebsiella* BSIs from 2017 to 2022. The average rates are represented by lines with shaded areas indicating 95% confidence intervals generated by bootstrapping.

Acinetobacter

A significant increasing national monthly trend in resistance was identified for multiple drugs: Meropenem at 0.43% ($p<10^{-16}$), Imipenem at 0.21% ($p<10^{-16}$), Piperacillin-Tazobactam at 0.17% ($p<10^{-16}$), Cefepime at 0.13% ($p<10^{-16}$) and Ceftazidime at 0.08% ($p<10^{-16}$). In contrast, a significant decreasing trend in resistance was observed for Minocycline at 0.16% ($p<0.0001$) and Levofloxacin at 0.04% ($p<0.05$) (Figure 3.4).

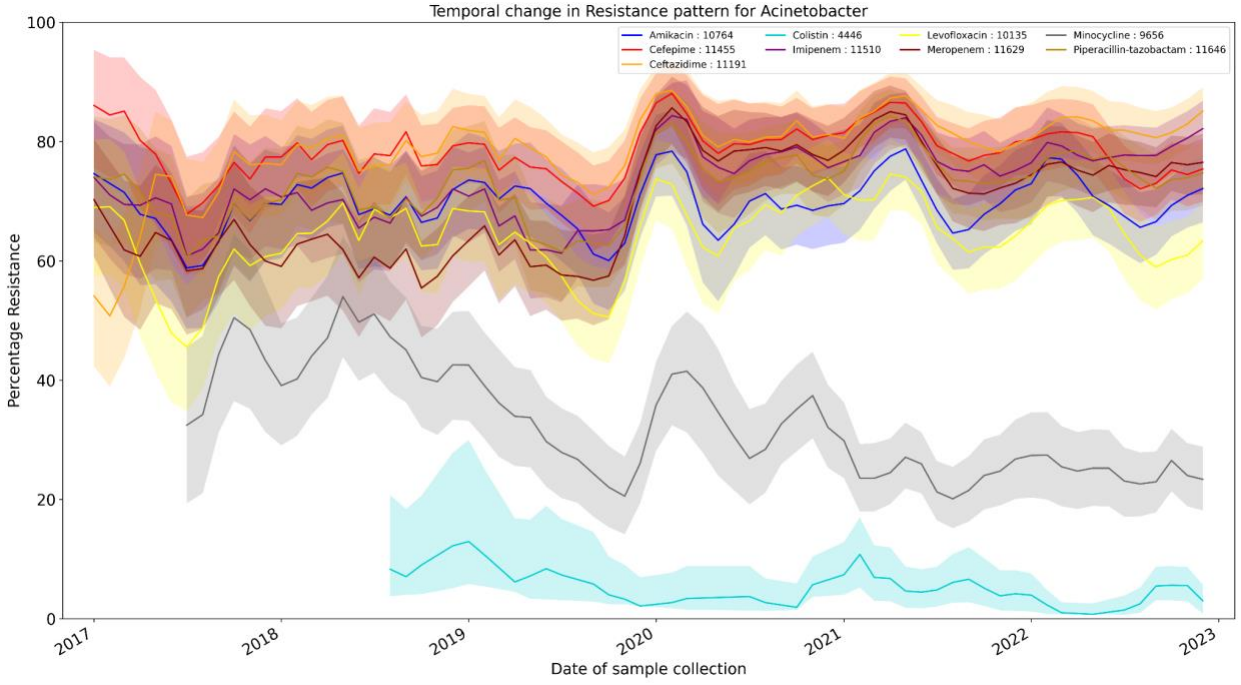


Figure 3.4- This figure shows monthly aggregated trends of antibiotic resistances in *Acinetobacter* BSIs from 2017 to 2022. The average rates are represented by lines with shaded areas indicating 95% confidence intervals generated by bootstrapping.

P. aeruginosa

A significant increasing national monthly trend in resistance was identified for multiple drugs: Meropenem at 0.18% ($p<10^{-16}$), Ceftazidime at 0.13% ($p<0.0001$), Piperacillin-Tazobactam at 0.09% ($p<10^{-16}$) and Cefepime at 0.08% ($p<10^{-16}$). In contrast, a significant decreasing trend in resistance was observed for Gentamicin at 0.06% ($p<10^{-16}$) (Figure 3.5).

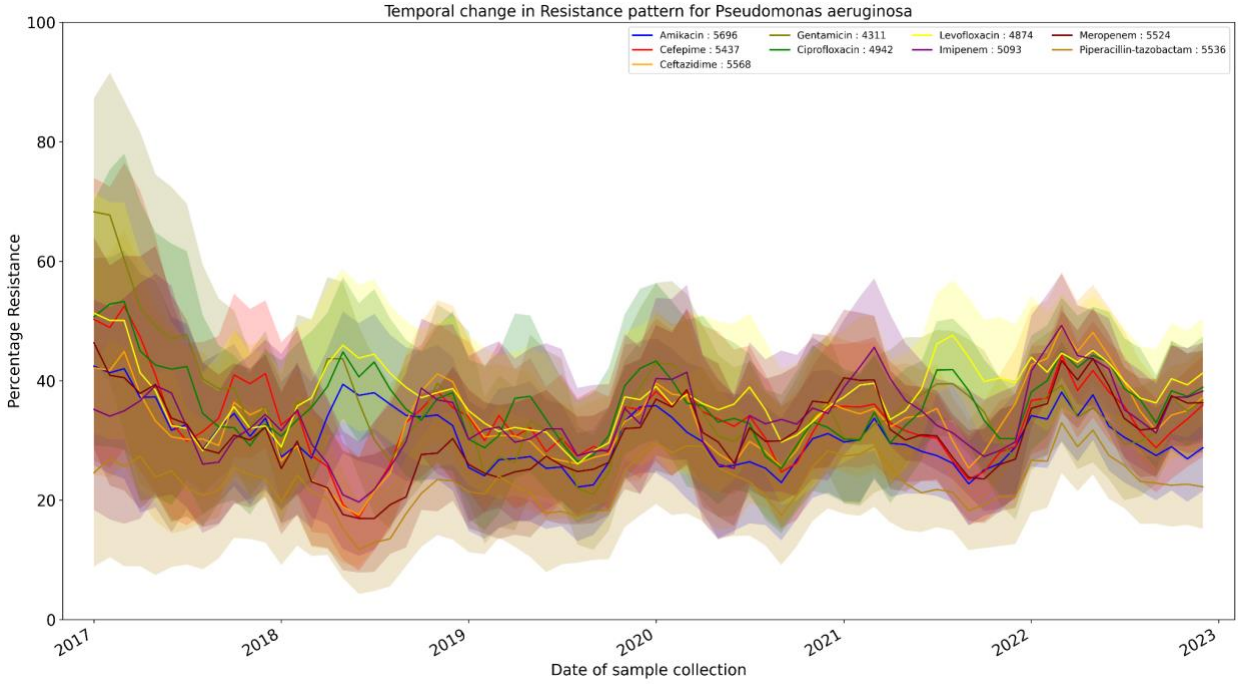


Figure 3.5- This figure shows monthly aggregated trends of antibiotic resistances in *Pseudomonas aeruginosa* BSIs from 2017 to 2022. The average rates are represented by lines with shaded areas indicating 95% confidence intervals generated by bootstrapping.

Staphylococcus

A significant increasing national monthly trend in resistance was identified for multiple drugs: Erythromycin at 0.33% ($p<10^{-16}$), Ciprofloxacin at 0.29% ($p<10^{-16}$), Tetracycline at 0.23% ($p<10^{-16}$) and Clindamycin at 0.15% ($p<0.0001$). In contrast, a significant decreasing trend in resistance was observed for Linezolid at 0.03% ($p<10^{-16}$) and Cefoxitin at 0.073% ($p<0.01$) (Figure 3.6).

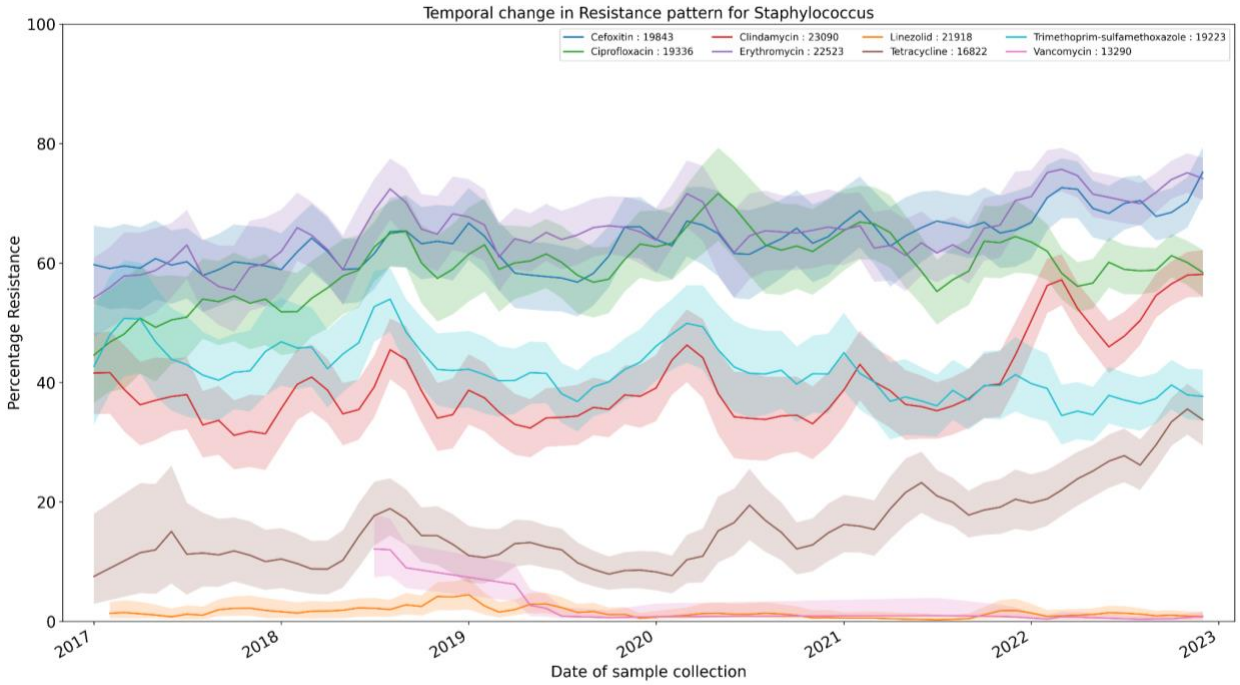


Figure 3.6- This figure shows monthly aggregated trends of antibiotic resistances in *Staphylococcus* BSIs from 2017 to 2022. The average rates are represented by lines with shaded areas indicating 95% confidence intervals generated by bootstrapping.

Enterococcus

A significant increase in national monthly resistance trends was identified for multiple drugs: Linezolid at 0.19% ($p<0.0001$) and Ampicillin at 0.10% ($p<0.001$). In contrast, a significant decreasing trend in resistance was observed for Gentamicin HL at 0.18% ($p<0.001$) (Figure 3.7).

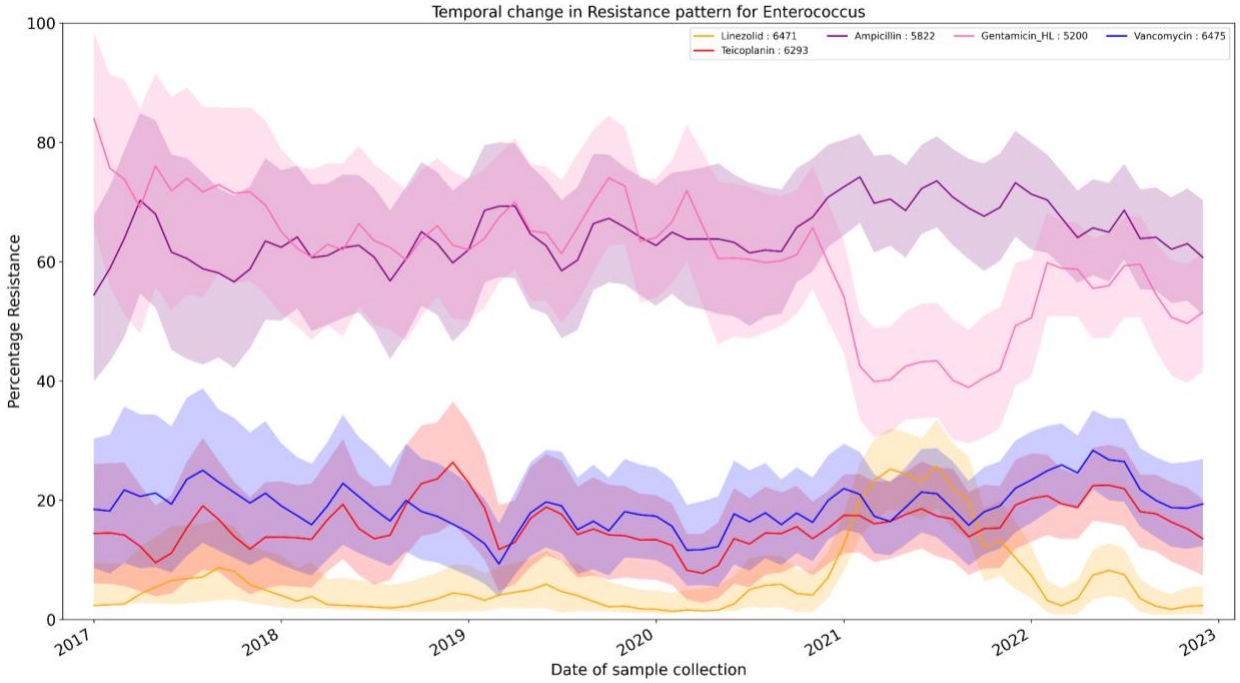


Figure 3.7- This figure shows monthly aggregated trends of antibiotic resistance in *Enterococcus* BSIs from 2017 to 2022. The average rates are represented by lines with shaded areas indicating 95% confidence intervals generated by bootstrapping.

Table 3.3- National monthly trends in antibiotic resistance among bloodstream isolates, 2017-2022

(a) Gram-negative organisms

Antibiotic	*E. coli*	*Klebsiella*	*P. aeruginosa*	*Acinetobacter*
Amikacin	+0.06 ($p=2.4\times10^{-32}$)	-0.04 (p=0.019)	-0.05 (p=0.101)	+0.001 (p=0.986)
Cefotaxime	-0.17 ($p<2.2\times10^{-16}$)	-0.25 ($p=5.9\times10^{-26}$)	-	-
Ciprofloxacin	+0.18 ($p=5.82\times10^{-9}$)	+0.08 (p=0.562)	+0.00075 (p=0.988)	-
Ertapenem	+0.09 ($p=7.78\times10^{-9}$)	-0.09 ($p<2.2\times10^{-16}$)	-	-
Imipenem	+0.22 ($p=2.13\times10^{-20}$)	+0.24 ($p=3\times10^{-4}$)	+0.11 (p=0.106)	+0.21 ($p<2.2\times10^{-16}$)
Meropenem	+0.15 ($p=1.35\times10^{-8}$)	+0.17 (p=0.003)	+0.18 ($p<2.2\times10^{-16}$)	+0.43 ($p<2.2\times10^{-16}$)
Piperacillin-tazobactam	+0.22 ($p=9.2\times10^{-21}$)	+0.17 ($p=9.6\times10^{-5}$)	+0.09 ($p<2.2\times10^{-16}$)	+0.17 ($p<2.2\times10^{-16}$)

(b) Gram-positive organisms

Antibiotic	*Staphylococcus*	*Enterococcus*
Ampicillin	-	+0.10 (p=0.0008)
Cefoxitin	-0.073 (p=0.002)	-
Ciprofloxacin	+0.29 ($p<2.2\times10^{-16}$)	-
Clindamycin	+0.15 ($p=9.02\times10^{-5}$)	-
Erythromycin	+0.33 ($p<2.2\times10^{-16}$)	-
Gentamicin HL	-	-0.18 (p=0.0007)
Linezolid	-0.03 ($p<2.2\times10^{-16}$)	+0.19 ($p=2.96\times10^{-5}$)
Teicoplanin	-	+0.002 (p=0.93)
Tetracycline	+0.23 ($p<2.2\times10^{-16}$)	-
TMP-SMX	-0.06 (p=0.48)	-
Vancomycin	-	+0.03 (p=0.561)

Local Patterns of AMR and Sustainable Development Goals

In our analysis, 91.4% of the patients were tested within their zone of residence, and 70.8% were tested within their state of residence.

E. coli

For single-drug resistance, antibiotic classes formed two distinct clusters of resistance. The Central and North zones showed very high resistance to all antibiotics. The South zone generally had the lowest antibiotic resistance, except for Cefotaxime and Ciprofloxacin. In MDR isolates, the Central and North-east zones showed higher resistance to all antibiotics except Amikacin in the former and Ciprofloxacin in the latter. The East zone had lower resistance except for Ciprofloxacin and Ertapenem (Figure 3.8).

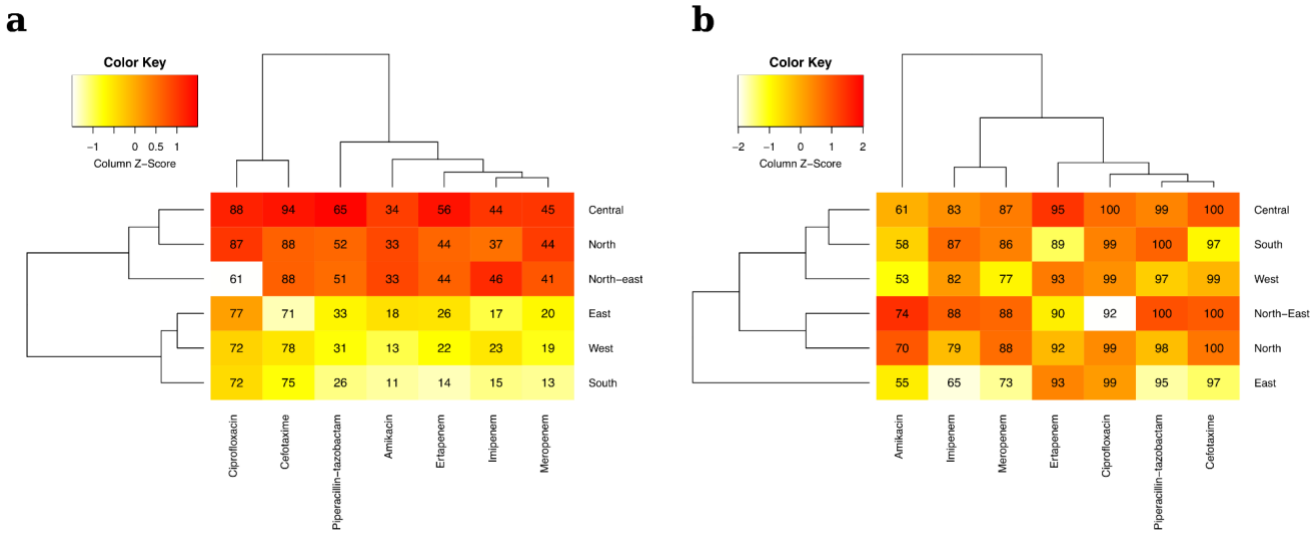


Figure 3.8- Geographical distribution of resistance for *E. coli* from bloodstream infections:a) all samples b) multi-drug-resistant samples. Numbers within the boxes represent the proportion of resistance for each antibiotic in the corresponding zone. Boxes are color-coded as per the deviation from column Z score.

Klebsiella

For single-drug resistance (Figure 3.9), the North and Central zones show high antibiotic resistance. The South zone had generally low resistance. The Central and East zones had a high resistance to Colistin, whereas the Central and West zones had a high resistance to Fosfomycin. In MDR isolates, the East zone showed lower resistance excepting Ciprofloxacin and Ertapenem.

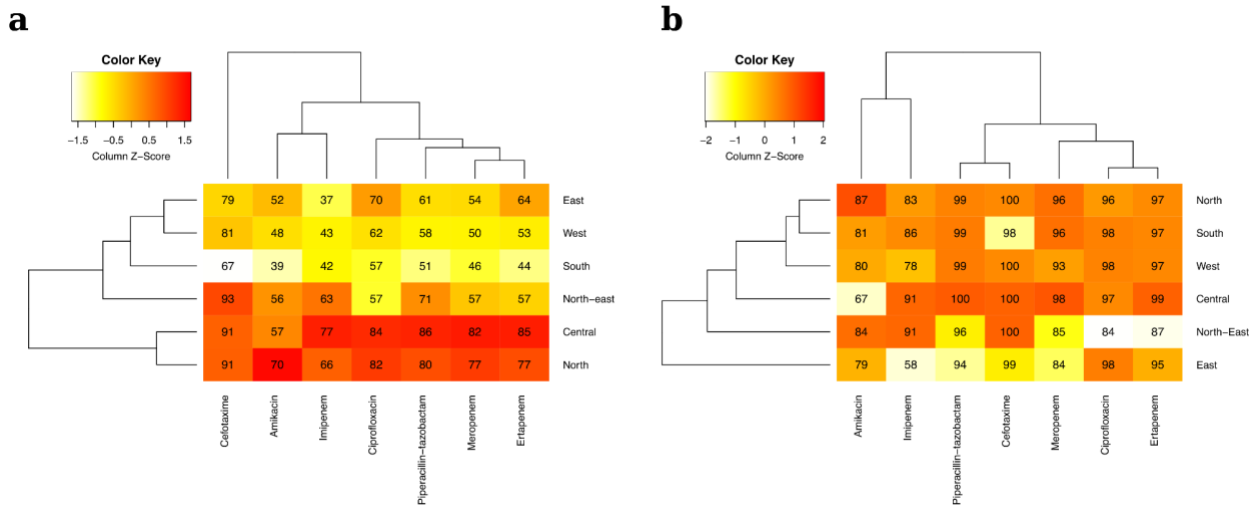


Figure 3.9- Geographical distribution of resistance in *Klebsiella* BSI a) all samples b) multi-drug resistant samples. Numbers within the boxes represent the proportion of resistance for each antibiotic in the corresponding zone. Boxes are color coded as per the deviation from column Z score.

Acinetobacter

For single drug resistance (Figure 3.10), the North zone showed high resistance to all antibiotics except Colistin. The northeast zone generally had the lowest resistance of all antibiotics except levofloxacin. In MDR isolates, the resistance level in North, South, Central and West zones is mostly high. The East zone had lower resistance except for Levofloxacin, Colistin and Ceftazidime. Increasing resistance rates for Imipenem, Meropenem and Piperacillin-tazobactam were observed for the North, South, East, West and Central zones.

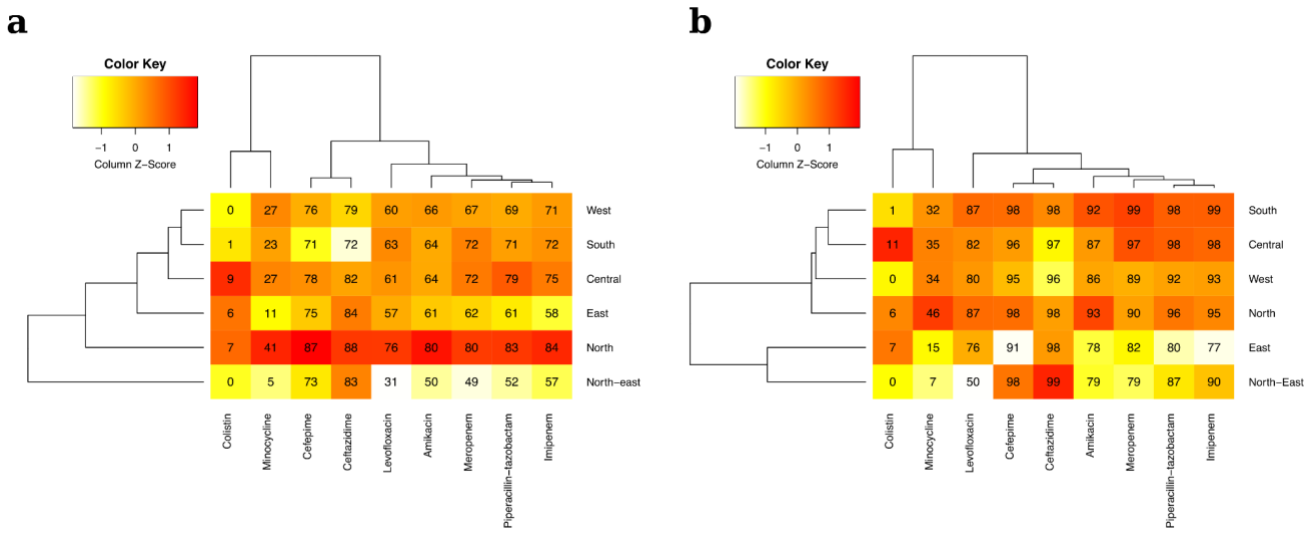


Figure 3.10- Geographical distribution of resistance in *Acinetobacter* BSI a) all samples b) multi-drug resistant samples. Numbers within the boxes represent the proportion of resistance for each antibiotic in the corresponding zone. Boxes are color coded as per the deviation from column Z score.

P. aeruginosa

The North zone had high resistance, whereas the East and South zones had low resistance for all antibiotics (Figure 3.11a). In MDR isolates, the North-east zone had low resistance to most antibiotics (Figure 3.11b).

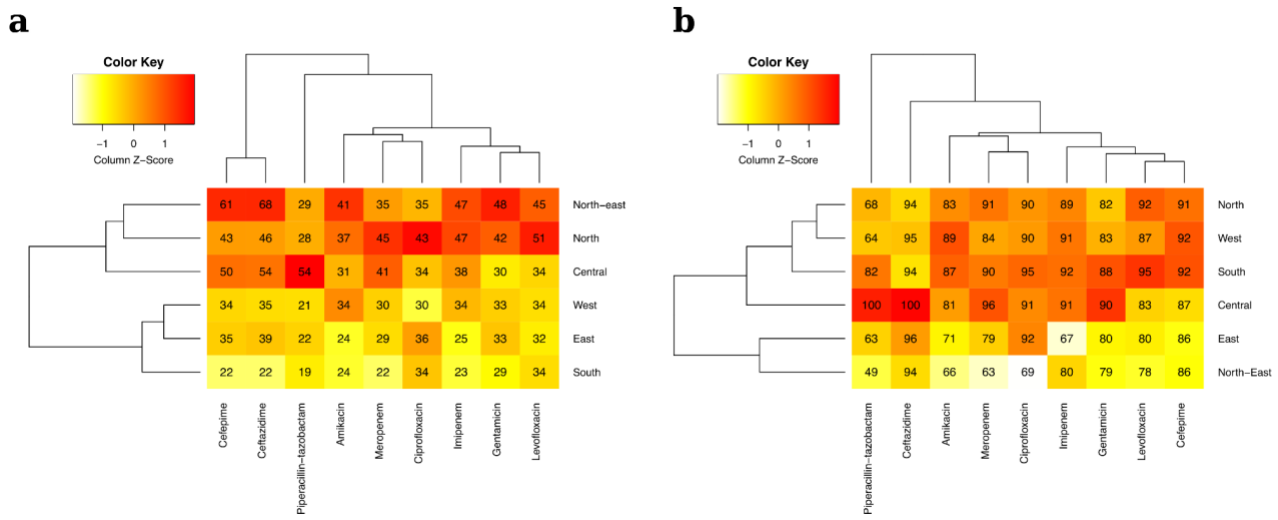


Figure 3.11- Geographical distribution of resistance in *Pseudomonas aeruginosa* BSI a) all samples b) multi-drug resistant samples. Numbers within the boxes represent the proportion of resistance for each antibiotic in the corresponding zone. Boxes are color coded as per the deviation from column Z score.

Staphylococcus

For single drug resistance, the South zone generally had high resistance to all antibiotics except Ciprofloxacin. The North zone had generally low resistance for all antibiotics except Linezolid and Vancomycin, which were also consistent across MDR isolates (Figure 3.12).

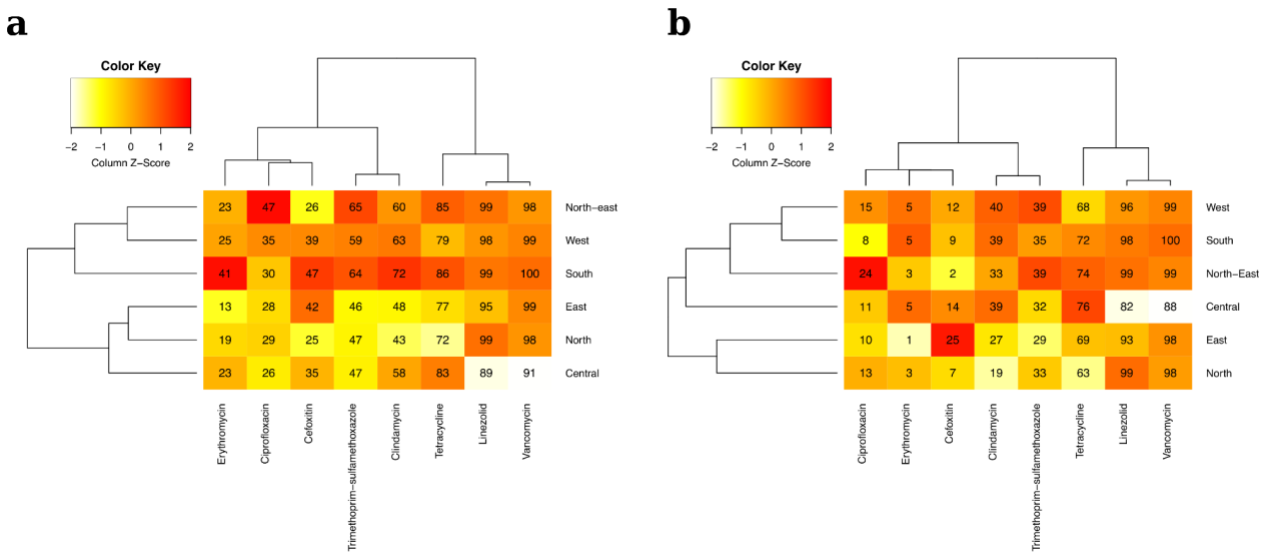


Figure 3.12- Geographical distribution of resistance in *Staphylococcus* BSI a) all samples b) multi-drug resistant samples. Numbers within the boxes represent the proportion of resistance for each antibiotic in the corresponding zone. Boxes are color coded as per the deviation from column Z score.

Enterococcus

Antibiotic classes form two main clusters for single drug resistance (Figure 3.13). The North zone had generally high resistance to all antibiotics except Gentamicin HL and Ampicillin. The East zone had high resistance for Gentamicin HL and Ampicillin. The North-east zone had a generally low resistance for all antibiotics. In MDR isolates, high resistance to Ampicillin and Vancomycin was seen across all zones except North-east in the former and West in the latter.

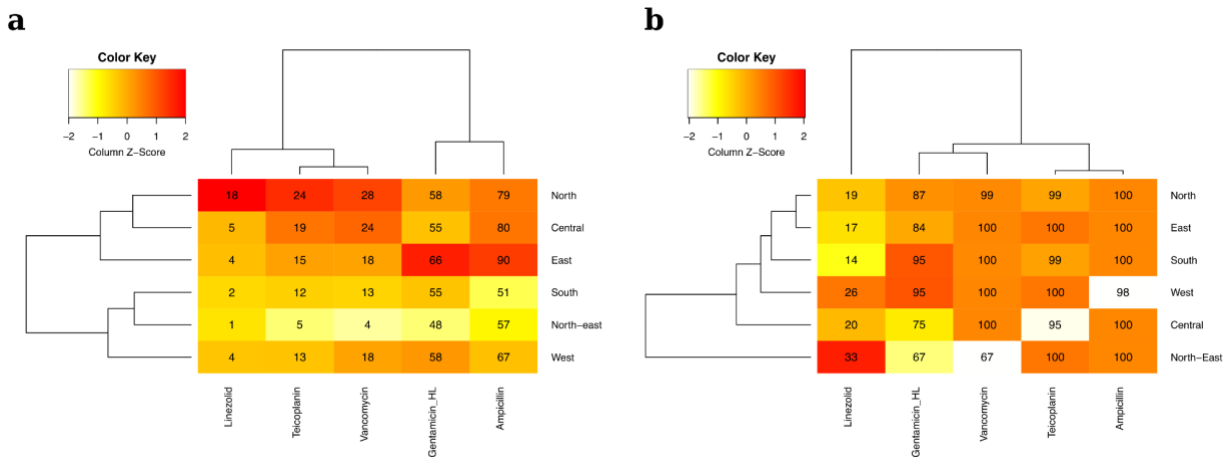


Figure 3.13- Geographical distribution of resistance in *Enterococcus* BSI a) all samples b) multi-drug resistant samples. Numbers within the boxes represent the proportion of resistance for each antibiotic in the corresponding zone. Boxes are color coded as per the deviation from column Z score.

The findings of zonal patterns were then modelled and quantified in the context of SDGs in a data-driven Bayesian network model. For *Klebsiella BSI*s, an association was observed between Imipenem, Amikacin, and Ertapenem resistance and SDG3 (Good Health and Well-being) (Figure 3.15). Further exploration into the variables of SDG3 revealed an association of Amikacin resistance with annual notification of Tb cases, maternal mortality and under-5 mortality. While for *E. coli* BSIs, an association was observed between Ciprofloxacin resistance and SDG3. Quantification of association using the exact inference algorithm revealed the high resistance percentage in aspirant states (84.57%) as compared with the performer (74.17%) and front-runner states (72.1%). Further exploration into the variables of SDG3 revealed an association of Ciprofloxacin resistance with annual notification of Tb cases.

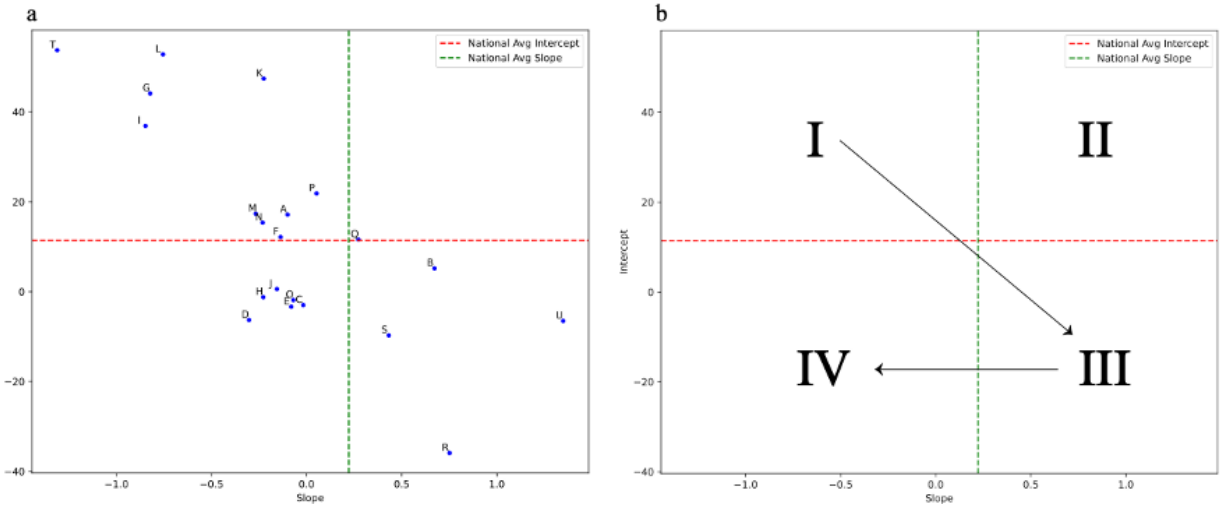


Figure 3.14. The figure contains a) representative plots depicting the position of each hospital relative to national benchmarks. b) The AMR Scorecard displaying four quadrants based on national averages for slope (rate of resistance increase) and intercept (initial resistance levels).

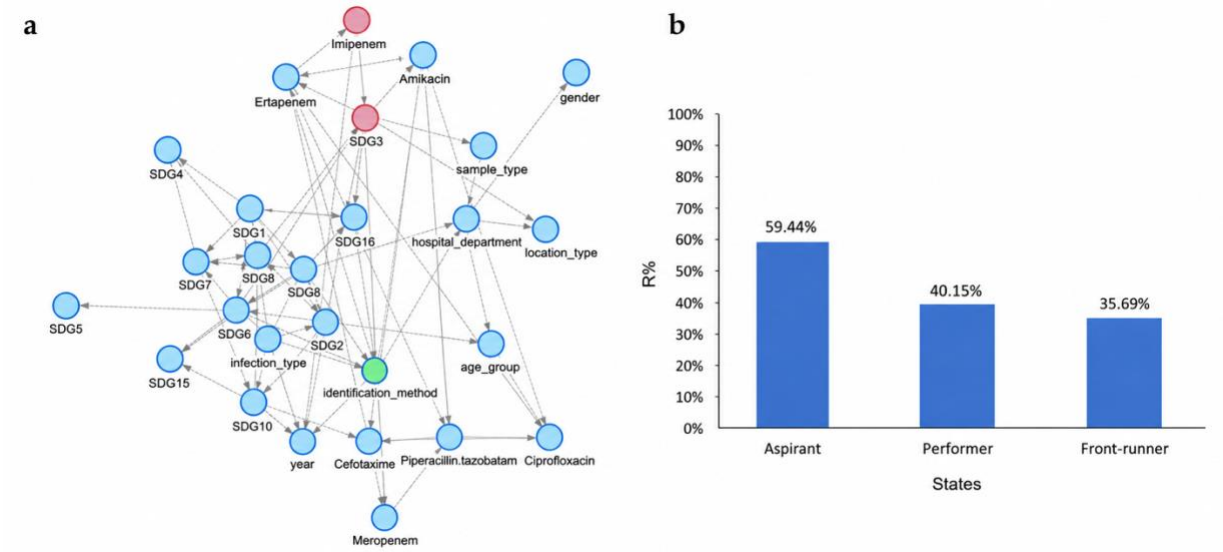


Figure 3.15 a) Bayesian Network model for Klebsiella, depicting the association between SDG3 and Imipenem resistance b) Categorization of states based on their SDG3 index reveals higher resistance rates in aspirant states, underscoring the need for focused healthcare improvements in these regions.

3.3.2 UTI

Primary Analysis

81,865 isolates met the inclusion/exclusion criteria from 20 centers across 13 states/UTs. The proportions of organisms isolated in Table 3.4 show that *E. coli* was the most frequently isolated organism overall (60.78%). Males had a higher proportion of *P. aeruginosa (*10.85%) than females (3.49%). The isolation rates of *E. coli*, *Klebsiella spp.*, *P. aeruginosa,* and *Enterococcus* were highest in the South (65.76%), East (24.47%), North (10.56%), and North-east (19.34%) zones, respectively. More than 50% of *Klebsiella spp*. and *P. aeruginosa* were MDR isolates. Generally, high resistance to Carbapenems, Cephalosporins, and Fluoroquinolones was observed in *E. coli, Klebsiella,* and *P. aeruginosa* isolates. Specifically, high resistance to Imipenem was observed in *P. aeruginosa* (47%), *Klebsiella* (35%), and *E. coli* (21%). High resistance to Ciprofloxacin (81.19%), Ampicillin (51.21%) & Gentamicin HL (52.39%) and low resistance to Linezolid (2.3%) was observed for *Enterococcus*.

Table 3.4 - Distribution of isolates across gender, zones, and overall antibiotic resistance patterns in UTIs.

		E. coli (%)	**Klebsiella$ (%)**	**P. aeruginosa (%)**	**Enterococcus# (%)**
ISOLATION					
Total	Total Isolates (81,865)	49755/81865 (60.78)	16846/81865 (20.58)	5646/81865 (6.90)	9618/81865 (11.75)
Gender	Males (37,884; 46.3%)	20953/37884 (55.31)	8179/37884 (21.59)	4111/37884 (10.85)	4641/37884 (12.25)
	Females (43,970; 53.7%)	28793/43970 (65.48)	8667/43970 (19.71)	1535/43970 (3.49)	4975/43970 (11.31)
	Transgender (11; 0.01%)	9/11 (81.82)	0/11 (0.00)	0/11 (0.00)	2/11 (18.18)

Zone*	North Zone (16,792; 20.5%)	9184/16792 (54.69)	3663/16792 (21.81)	1773/16792 (10.56)	2172/16792 (12.93)
	South Zone (27,051; 33%)	17790/27051 (65.76)	4787/27051 (17.70)	894/27051 (3.30)	3580/27051 (13.23)
	East Zone (6,290; 7.7%)	3727/6290 (59.25)	1539/6290 (24.47)	555/6290 (8.82)	469/6290 (7.46)
	West Zone (21,386; 26.1%)	12902/21386 (60.33)	4877/21386 (22.80)	1941/21386 (9.08)	1666/21386 (7.79)
	Central Zone (2,870; 3.5%)	1805/2870 (62.89)	594/2870 (20.70)	186/2870 (6.48)	285/2870 (9.93)
	North-east Zone (7,476; 9.1%)	4347/7476 (58.15)	1386/7476 (18.54)	297/7476 (3.97)	1446/7476 (19.34)
MDR (%)	Isolates resistant to 3 or more antibiotic classes	19046/49755 (38.28)	9254/16846 (54.93)	2986/5646 (52.89)	3285/9618 (34.15)
RESISTANCE					
Average resistance percentage $ over the entire study duration	Amikacin (AMK)	6903/48409 (14.26)	6280/16420 (38.25)	2593/5540 (46.81)	NA
	Ampicillin (AMP)	NA	NA	NA	4314/8424 (51.21)
	Cefazolin (CFZ)	14519/19153 (75.81)	4708/6297 (74.77)	NA	NA
	Cefepime (FEP)	NA	NA	2738/5299 (51.67)	NA
	Cefotaxime (TAX)	30292/41686 (72.67)	9579/13879 (69.02)	NA	NA
	Ceftazidime (CAZ)	NA	NA	2763/5201 (53.12)	NA
	Ciprofloxacin (CIP)	31166/44752 (69.64)	8580/14822 (57.89)	2993/5358 (55.86)	5946/7324 (81.19)
	Colistin (CST)	55/5779 (0.95)	128/2954 (4.33)	41/1116 (3.67)	NA
	Ertapenem (ETP)	8818/40918 (21.55)	6214/14058 (44.2)	NA	NA

	Fosfomycin (FOS)	848/19332 (4.39)	807/6461 (12.49)	NA	481/5528 (8.7)
	Gentamicin (GEN)	NA	NA	2536/5009 (50.63)	NA
	Gentamicin High Level (HLG)	NA	NA	NA	4260/8132 (52.39)
	Imipenem (IPM)	9795/45624 (21.47)	5525/15626 (35.36)	2495/5356 (46.58)	NA
	Levofloxacin (LVX)	17742/25309 (70.1)	5349/8772 (60.98)	2877/4757 (60.48)	NA
	Linezolid (LZD)	NA	NA	NA	206/8947 (2.3)
	Meropenem (MEM)	8167/44991 (18.15)	5748/14923 (38.52)	2550/5454 (46.75)	NA
	Nitrofurantoin (NIT)	4224/47678 (8.86)	8134/15924 (51.08)	NA	2162/9350 (23.12)
	Piperacillin-tazobactam (PTZ)	13133/47929 (27.4)	7734/16196 (47.75)	2046/5409 (37.83)	NA
	Teicoplanin (TEC)	NA	NA	NA	752/8959 (8.39)
	Tobramycin (TOB)	NA	NA	1278/2384 (53.61)	NA
	Trimethoprim-sulfamethoxazole (TMP-SMZ)	24918/43108 (57.8)	8618/14858 (58)	NA	NA
	Vancomycin (VAN)	NA	NA	NA	890/9498 (9.37)

*North zone includes Himachal Pradesh, Punjab, Uttarakhand, Uttar Pradesh, Haryana, Ladakh, Chandigarh, Delhi, Jammu and Kashmir; South zone includes Andhra Pradesh, Karnataka, Kerala, Telangana, Tamil Nadu, Andaman and Nicobar, Lakshadweep, Puducherry; East zone includes Bihar, Odisha, Jharkhand, West Bengal; West zone includes Rajasthan, Gujarat, Goa, Maharashtra, Dadra and Nagar Haveli, Daman and Diu; Central zone includes Madhya Pradesh, Chhattisgarh; North-east zone includes Assam, Sikkim, Nagaland, Meghalaya, Manipur, Mizoram, Tripura, Arunachal Pradesh

[$] All resistance normalized as n/N (%) [(Resistance)/ (Resistance + Sensitivity +Intermediate)]

NA Not applicable (antibiotic not relevant/tested for the particular organism)

[&] Klebsiella includes *Klebsiella pneumoniae*, *Klebsiella oxytoca* and *Klebsiella species*

[#] Enterococcus includes *Enterococcus faecalis*, *Enterococcus faecium* and *Enterococcus species*

National Trends of Resistance

The cluster-robust modelling of monthly resistance rates for each pathogen revealed significant linear trends for each microorganism-antibiotic combination as follows:

E. coli

A national monthly increase in resistance was observed in Piperacillin-tazobactam (0.16%, $p<10^{-16}$), Imipenem (0.1%, $p<0.005$), Nitrofurantoin (0.08%, $p<10^{-16}$) and Amikacin (0.03%, $p<10^{-15}$). Decreasing resistance was observed for Cefazolin (0.38%, $p<10^{-16}$), Cefotaxime (0.31%, $p<10^{-16}$), Levofloxacin (0.30%, $p<10^{-13}$), Trimethoprim-sulfamethoxazole (0.29%, $p<10^{-11}$), Ciprofloxacin (0.16%, $p<10^{-6}$), Meropenem (0.11%, $p<10^{-16}$), Ertapenem (0.07%, $p<10^{-16}$) and Fosfomycin (0.05%, $p<10^{-16}$) (Figure 3.16).

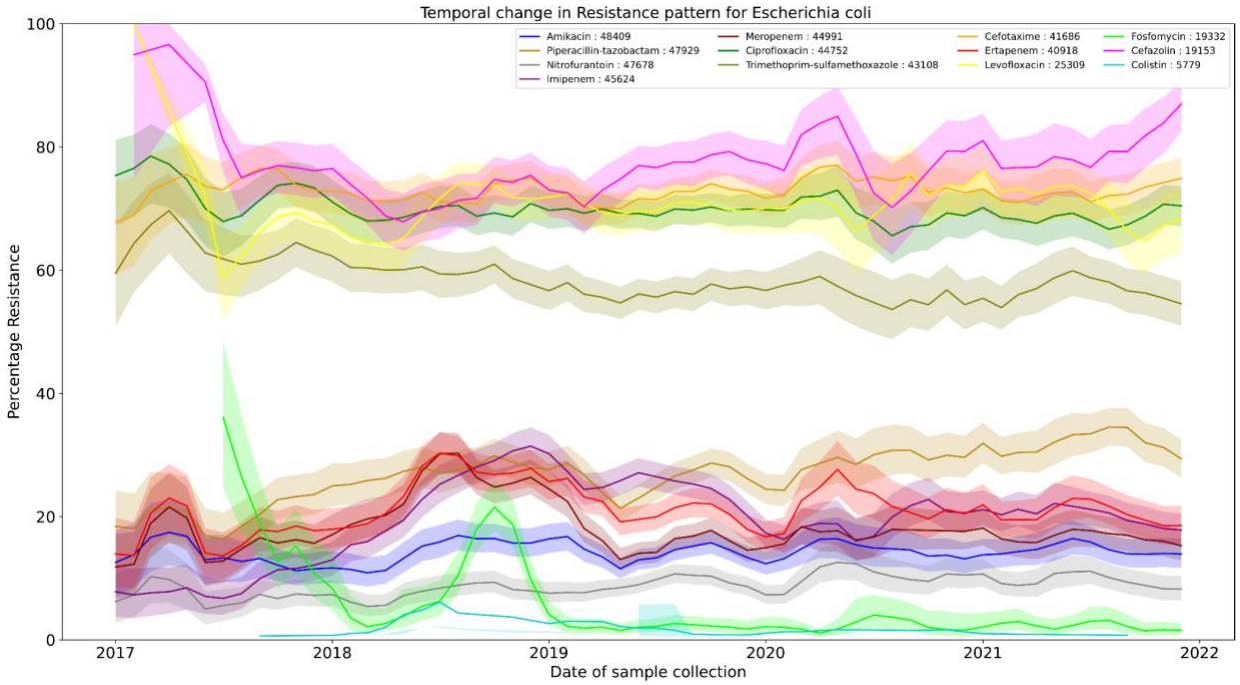


Figure 3.16- This figure shows monthly aggregated trends of antibiotic resistances in *E. coli* UTIs from 2017 to 2021. The average rates are represented by lines with shaded areas indicating 95% confidence intervals generated by bootstrapping.

Klebsiella spp.

A national monthly increase in resistance was observed in Imipenem (0.24%, $p<10^{-16}$), Piperacillin-tazobactam (0.20%, $p<10^{-16}$), Nitrofurantoin (0.06%, $p<0.001$) and Fosfomycin (0.04%, $p<0.001$). Decreasing resistance was observed for Cefotaxime (0.33%, $p<10^{-16}$), Cefazolin (0.30%, $p<10^{-16}$), Trimethoprim-sulfamethoxazole (0.20%, $p<10^{-16}$), Ciprofloxacin (0.15%, $p<10^{-16}$), Meropenem (0.13%, $p<10^{-16}$) and Ertapenem (0.05%, $p<10^{-13}$) (Figure 3.17).

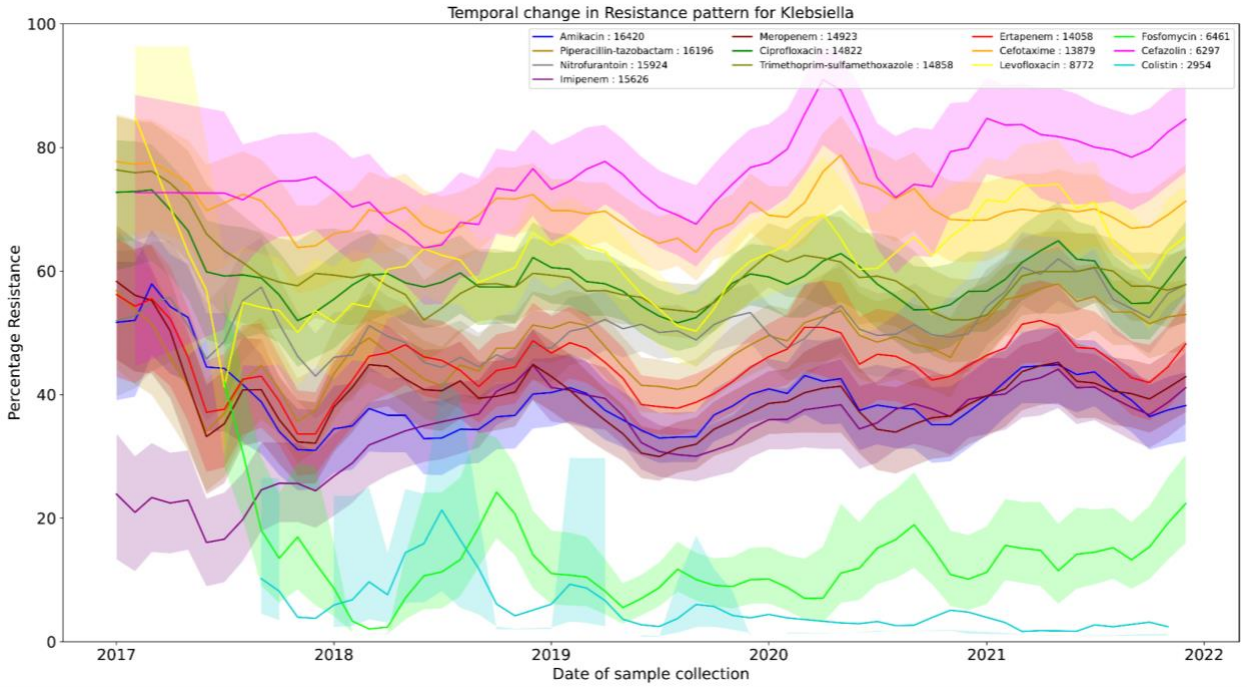


Figure 3.17- This figure shows monthly aggregated trends of antibiotic resistances in *Klebsiella* UTIs from 2017 to 2021. The average rates are represented by lines with shaded areas indicating 95% confidence intervals generated by bootstrapping.

Enterococcus spp.

A national monthly increase in resistance was observed in Nitrofurantoin (0.43%, $p<10^{-16}$), Ampicillin (0.26%, $p<0.05$), Vancomycin (0.06%, 0.0001), and Teicoplanin (0.04%, 0.0001). Decreasing resistance was observed for Ciprofloxacin (0.49%, $p<10^{-9}$), Gentamicin High Level (0.26%, $p<10^{-16}$) and Fosfomycin (0.17%, $p<10^{-16}$) (Figure 3.18).

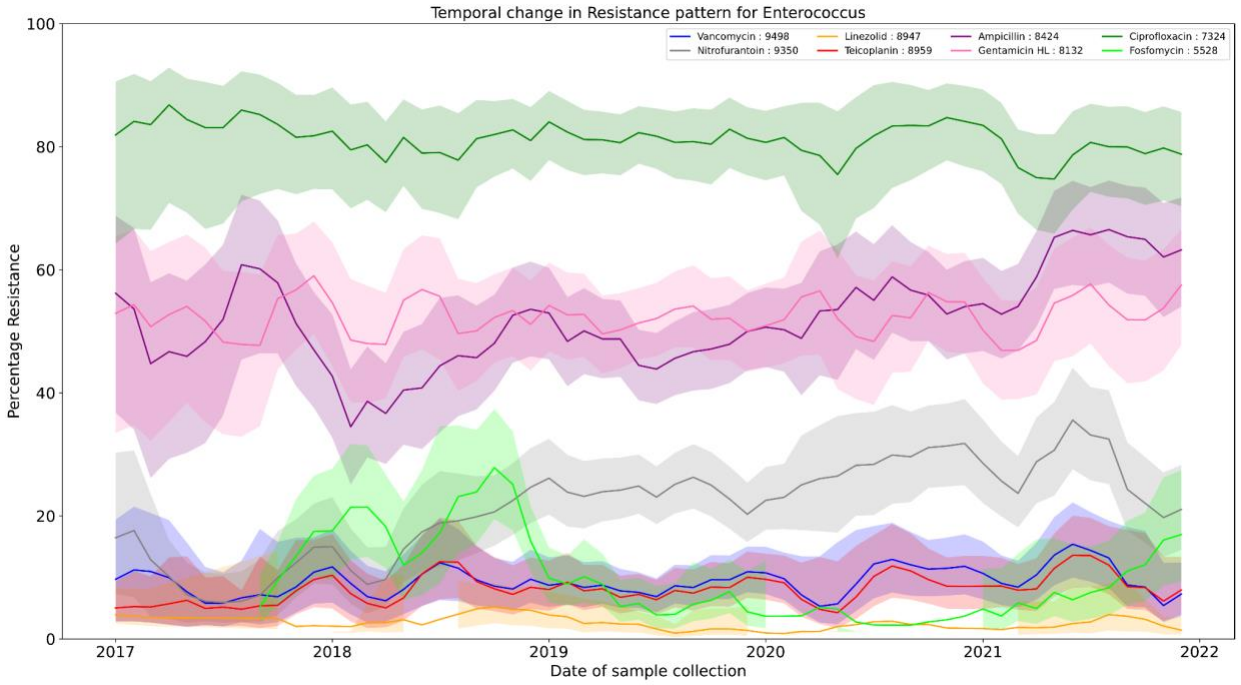


Figure 3.18- This figure shows monthly aggregated trends of antibiotic resistances in *Enterococcus* UTIs from 2017 to 2021. The average rates are represented by lines with shaded areas indicating 95% confidence intervals generated by bootstrapping.

P. aeruginosa

A national monthly increase in resistance was observed in Imipenem (0.37%, $p<10^{-16}$), Piperacillin-tazobactam (0.30%, $p<10^{-16}$), Ceftazidime (0.12%, $p<0.01$), Meropenem (0.06%, $p<10^{-16}$) and Cefepime (0.06%, $p<10^{-8}$). Decreasing resistance was observed for Tobramycin

(0.24%, $p<0.05$), Gentamicin (0.19%, $p<0.001$), Amikacin (0.09%, $p<0.05$) and Ciprofloxacin (0.04%, $p<10^{-6}$) (Figure 3.19).

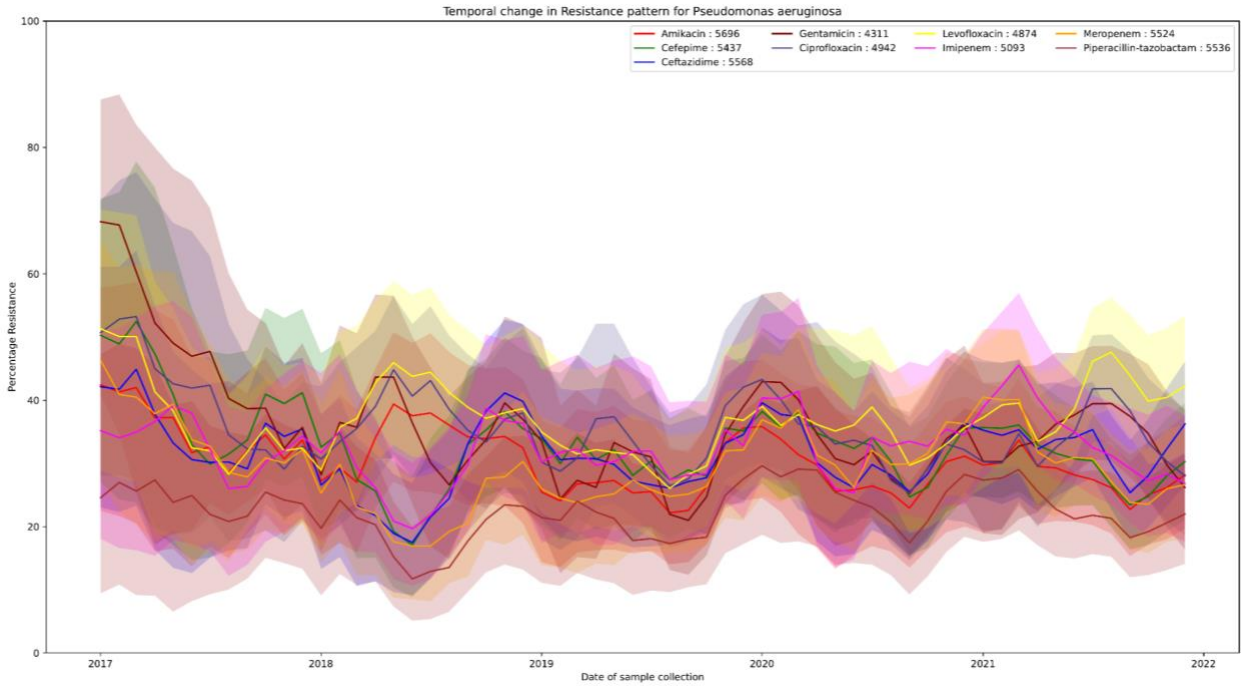


Figure 3.19- This figure shows monthly aggregated trends of antibiotic resistances in Pseudomonas aeruginosa UTIs from 2017 to 2021. The average rates are represented by lines with shaded areas indicating 95% confidence intervals generated by bootstrapping.

Table 3.5 National monthly trends in antibiotic resistance among urinary tract infection isolates, 2017-2021

Antibiotic	*E. coli*	*Klebsiella*	*P. aeruginosa*	*Enterococcus*
Amikacin	+0.03 (p=7.73×10^{-16})	+0.07 (p=0.127)	-0.09 (p=0.013)	-
Ampicillin	-	-	-	+0.26 (p=0.0138)
Cefazolin	-0.38 (p=2.62×10^{-56})	-0.30 (p=2.44×10^{-29})	-	-
Cefepime	-	-	+0.06 (p=1.26×10^{-9})	-
Cefotaxime	-0.31 (p=8.97×10^{-217})	-0.33 (p=1.60×10^{-19})	-	-
Ceftazidime	-	-	+0.12 (p=0.00107)	-
Ciprofloxacin	-0.16 (p=9.13×10^{-7})	-0.15 (p=3.29×10^{-247})	-0.04 (p=4.71×10^{-7})	-0.49 (p=1.21×10^{-10})
Ertapenem	-0.07 (p=3.85×10^{-102})	-0.05 (p=3.02×10^{-14})	-	-
Fosfomycin	-0.05 (p<0.0001)	+0.04 (p=0.0003)	-	-0.17 (p=9.79×10^{-244})
Gentamicin	-	-	-0.19 (p=0.00044)	-
Gentamicin HL	-	-	-	-0.26 (p=3.51×10^{-304})
Imipenem	+0.10 (p=0.002)	+0.24 (p=3.64×10^{-55})	+0.37 (p=7.26×10^{-17})	-
Levofloxacin	-0.30 (p=6.09×10^{-14})	-0.06 (p=0.056)	-0.06 (p=0.228)	-
Linezolid	-	-	-	-0.01 (p=0.3412)
Meropenem	-0.11 (p=7.45×10^{-50})	-0.13 (p=1.84×10^{-31})	+0.06 (p<0.0001)	-
Nitrofurantoin	+0.08 (p=7.49×10^{-158})	+0.06 (p=0.001)	-	+0.43 (p=4.02×10^{-20})

Piperacillin-tazobactam	+0.16 (p=6.06×10^{-93})	+0.20 (p=5.85×10^{-30})	+0.30 (p=2.46×10^{-103})	-
Teicoplanin	-	-	-	+0.04 (p=1.44×10^{-5})
Tobramycin	-	-	-0.24 (p=0.0236)	-
Trimethoprim-sulfamethoxazole	-0.29 (p=9.76×10^{-12})	-0.20 (p=3.51×10^{-60})	-	-
Vancomycin	-	-	-	+0.06 (p=5.56×10^{-5})

Values represent regression-derived national monthly changes in resistance percentage (percentage points per month) from the primary model incorporating time, hospital and time × hospital interaction, with hospital-cluster-robust standard errors. Positive and negative values indicate increasing and decreasing resistance trends, respectively. Exact p-values are shown in parentheses. - indicates that an estimate was not available/not applicable for the corresponding organism-antibiotic combination. Detailed subgroup-specific analyses by sex, age group, geographical zone and acquisition setting are provided in Appendix A.

Local Patterns of AMR and Sustainable Development Goals

In our analysis, 93% of the patients were tested within their zone of residence, and 75% of the patients were tested within their state of residence.

E. coli

For single drug resistance, antibiotic classes for complicated and uncomplicated UTIs formed distinct clusters of resistance (Figure 3.20). The West zone showed very high resistance to Fosfomycin. East zone had generally high resistance for all antibiotics except Imipenem, Colistin and Fosfomycin. In MDR isolates, West zone had lower resistance except for Imipenem and Fosfomycin (Figure 3.20b).

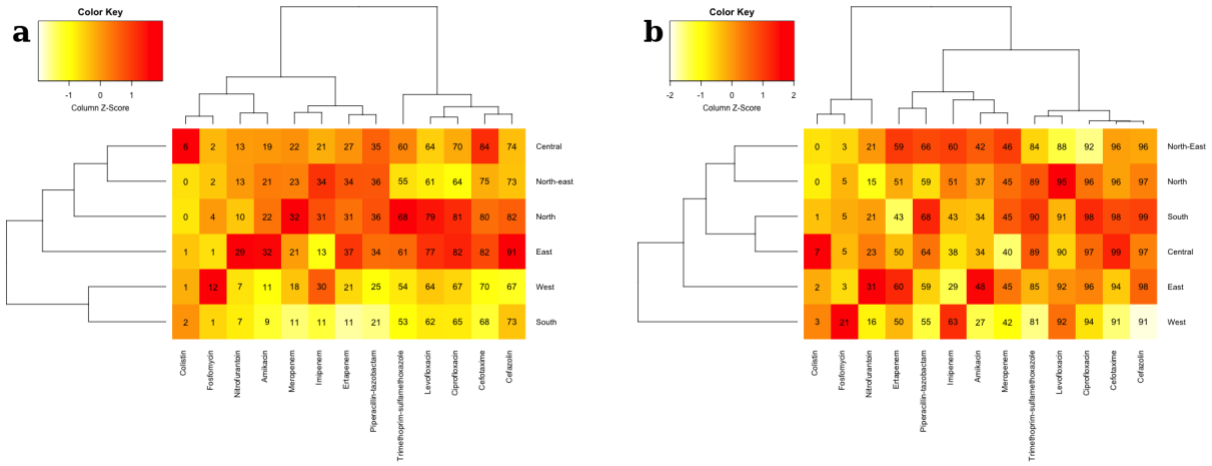


Figure 3.20 represents a heatmap with cluster dendrograms showing the clustering of zones (y-axis) and antibiotics (x-axis) in *E. coli* isolates in (a) all isolates cultured for *E. coli* and (b) MDR isolates of E. coli. The colour represents the deviation of respective zones from nationwide Z-scores. Numbers in boxes represent the actual resistance percentage.

Klebsiella

For single drug resistance, antibiotic classes formed three distinct clusters of resistance (Figure 3.21a). The North zone had generally high resistance for all antibiotics except Colistin and Fosfomycin. The South zone had generally low resistance. Both Central and East zones exhibited high Colistin resistance, while Central and West zones showed high Fosfomycin resistance. Among MDR isolates, the Central zone displayed high resistance to most antibiotics, whereas the North had higher resistance to those targeting uncomplicated MDR infections.

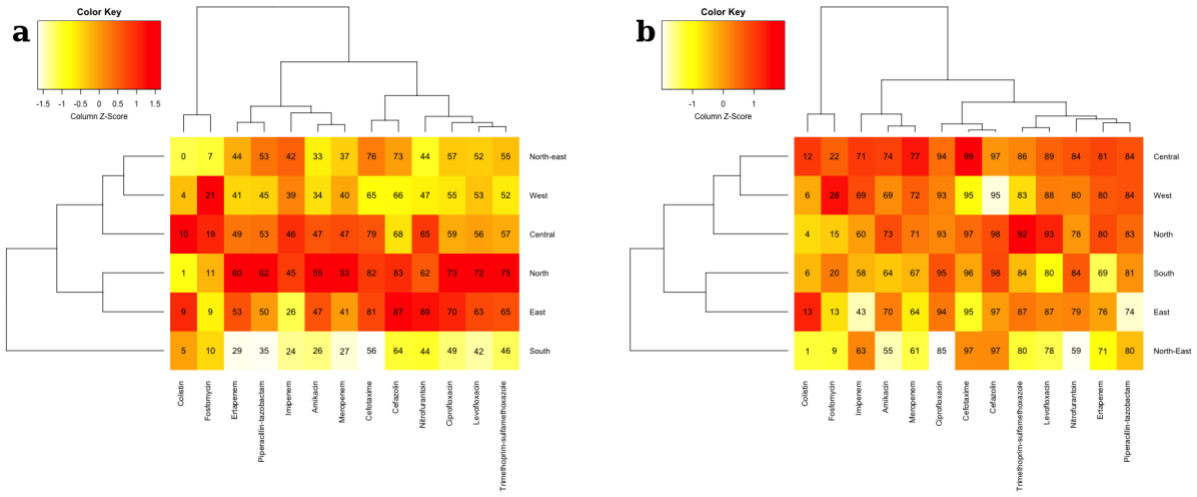


Figure 3.21- Geographical distribution of resistance for *Klebsiella* UTIs a) all samples b) multi-drug resistant samples

Enterococcus

For single drug resistance, antibiotic classes form two main clusters (Figure 3.22a). The East zone had generally high resistance to all antibiotics. The North zone had high resistance for Gentamicin HL. The North, Central, and Northeast zones consistently showed high susceptibility to Fosfomycin in both single and multi-drug resistant isolates. For MDR isolates, the Central zone demonstrated high resistance to Nitrofurantoin but maintained low resistance to Fosfomycin.

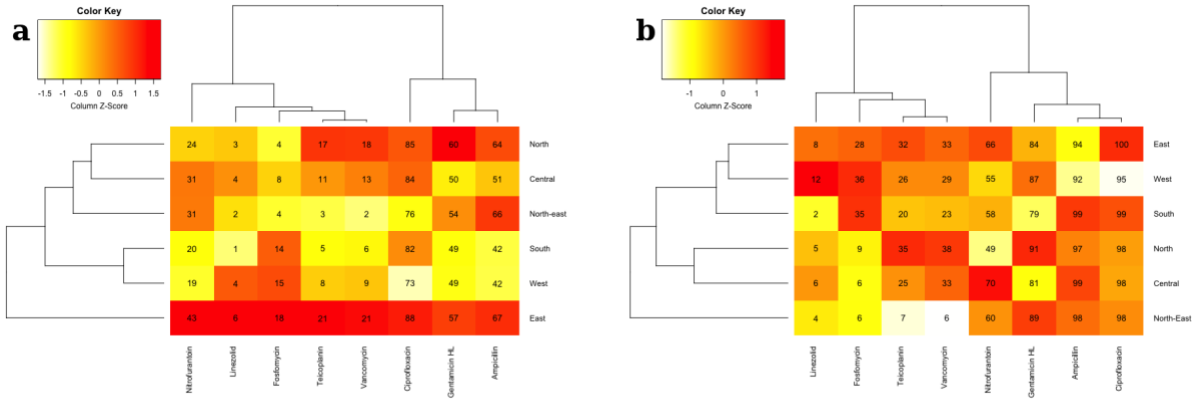


Figure 3.22- Geographical distribution of resistance for *Enterococcus* UTIs a) all samples b) multi-drug resistant samples

P. aeruginosa

For single drug resistance, the East and North zone had generally high resistance for all antibiotics (Figure 3.23a). The Central and northeast zone had generally less resistance for Colistin. South region had overall lesser resistance in single drug-resistant isolates which increases in the case of MDR isolates (Figure 3.23b). Additionally, in MDR isolates, the northeast zone had low resistance to most antibiotics.

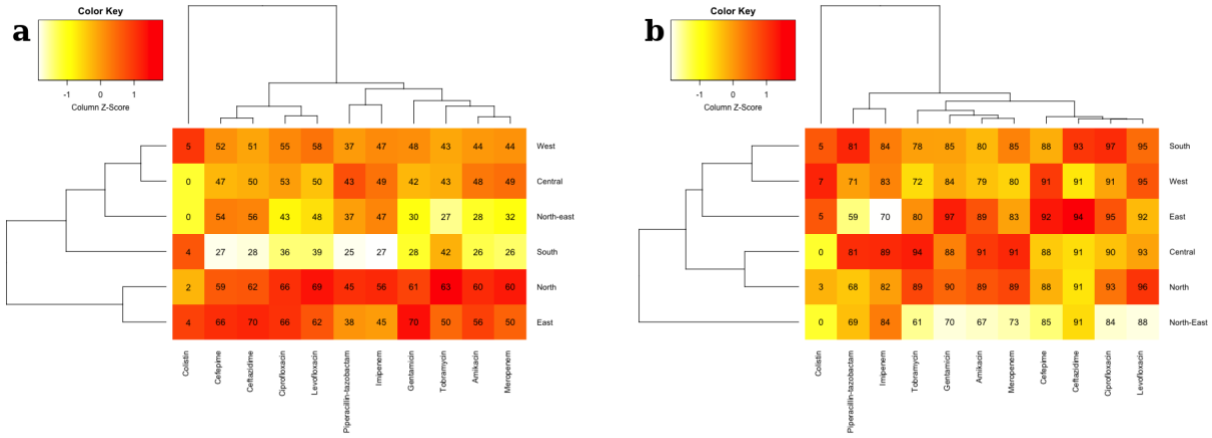


Figure 3.23- Geographical distribution of resistance for *Pseudomonas aeruginosa* UTIs a) all samples b) multi-drug resistant samples

The findings of zonal patterns were then modelled and quantified in the context of SDGs in a data-driven Bayesian network model. For *P. aeruginosa* UTIs, the association between Imipenem resistance and SDG3 was observed (Figure 3.24). For *E. coli* UTIs, the association between resistance to Imipenem and SDG2 (zero hunger) was observed.



Figure 3.24. Bayesian Network model learned for *P. aeruginosa* UTIs showing the association between Imipenem resistance and SDG3 (health and well-being). Categorization of states based on their Sustainable Development Goals 3 (SDG3) Index reveals higher resistance rates in aspirant states (51.5%) as compared with performer (49.3%) and front-runner states (31.7%). This association should be interpreted within a broader public health context, encompassing healthcare access and quality, infection prevention, and socioeconomic and environmental conditions. The analysis does not establish which specific determinants explain the observed differences.

3.4 Discussion

This study is the first to offer a national-scale, multicentric perspective on AMR trends and associations for both UTIs and BSIs, particularly identifying the alarming patterns in Carbapenem resistance. The AMR prevalence in both BSIs and UTIs aligns with smaller, single-centric studies from India, thus consistent with our findings and highlighting the need for ongoing, comprehensive monitoring of AMR at a national level (Hammond et al., 2022, Karuna et al., 2023, Khurana et al., 2018, Mathur et al., 2022, Parveen et al., 2025, Akram et al., 2007, Ravishankar et al., 2021). In the context of limited large-scale longitudinal data from LMICs, these findings are highly consequential for national stewardship strategies.

Our longitudinal analysis revealed high and in several instances, increasing resistance trends for critically important antimicrobials, particularly carbapenems such as imipenem and meropenem, among *Acinetobacter spp.*, *Klebsiella spp.*, and *E. coli*. These findings are particularly concerning given the central role of carbapenems as last-line agents in severe Gram-negative infections. Moreover, these trends were not uniformly concordant across infection syndromes and while increasing resistance was observed in several organism–antibiotic combinations in BSIs, corresponding trends in UTIs were sometimes lesser or even directionally opposite. For example, meropenem resistance demonstrated rising trends in BSIs for *E. coli* and *Klebsiella spp.*, whereas UTI isolates showed declining or slower-growing resistance patterns for the same antibiotic. These findings indicate that resistance dynamics are not only organism- and antibiotic-specific but also syndrome-specific, reflecting differences in antibiotic exposure patterns, patient populations, and healthcare settings. This heterogeneity underscores the need for infection-site–specific surveillance and cautions against extrapolating bloodstream resistance trends to community-

acquired UTIs or vice versa. From a stewardship perspective, these data support differentiated empirical therapy guidelines rather than uniform carbapenem policies across syndromes.

We also observed high resistance levels to fluoroquinolones, second- and third-generation oral cephalosporins, and trimethoprim–sulfamethoxazole render these agents increasingly unsuitable for empirical therapy in many settings. However, we observed relatively low resistance rates to fosfomycin in UTIs, supporting its continued utility as an empiric option for community-acquired UTI (CA-UTI).

Substantial geographic and age-related variation in resistance prevalence and trends was also identified wherein certain regions exhibited increasing trends, while others demonstrated stabilization or decline, highlighting the spatial heterogeneity of AMR across India. This variability likely reflects differences in prescribing practices, infection control measures, and healthcare infrastructure thus emphasizing the need for decentralized, regionally adaptive stewardship strategies rather than a singular national response.

Methodologically, the national trends were estimated using a cluster-robust linear regression model that accounted for heteroskedasticity and within-hospital temporal autocorrelation. We also explored mixed-effects models incorporating random hospital effects; however, these models did not adequately address temporal autocorrelation and did not provide reliable inferential statistics for random-effect components, limiting interpretability. The cluster-robust framework therefore offered a more appropriate balance between robustness and interpretability in longitudinal multicenter surveillance data.

Increasing resistance amid the shortage of new antibiotics can derail the progress towards the 2030 SDG target. While AMR directly impacts SDG 3 (good health and well-being), SDGs 1 (no poverty), SDG 2 (zero hunger), and SDG 8 (decent work and economic growth) are also crucially

linked. The integration of two new AMR indicators into SDG 3 underscores the urgency of joint monitoring efforts. To the best of our knowledge, our study introduces the first empirical evidence of the relationship between state SDG performance and AMR in India, utilising a data-driven Bayesian model. This approach, while not establishing causality, provides a novel way to analyse associations between AMR and SDGs, with our findings highlighting a inverse relationship between SDG 3 performance and Imipenem resistance. This can be understood by a complex adaptive systems perspective. SDG categories capture broad contextual conditions within which infection, antibiotic exposure, healthcare access and transmission occur. Several pathways may operate simultaneously and in opposing directions: improved access may increase opportunities for antibiotic exposure and diagnostic testing, while stronger infection prevention, sanitation and appropriate treatment may reduce infection and transmission. Consequently, an observed SDG–resistance association cannot identify which pathway predominates. Gautham et al.'s (2021) analysis of community antibiotic provision illustrates how provider decisions are embedded within wider commercial, community and regulatory relationships, supporting this contextual interpretation. In the present study, the associations involving SDG 3 should therefore be understood as patterns requiring further investigation within particular organism–antibiotic and surveillance contexts. State-level categories cannot establish individual-level relationships, and differences in sampling, referral and diagnostic access may also influence the observed patterns. The association between SDG 2 and imipenem resistance in *E. coli* urinary isolates illustrates the value of examining development measures beyond SDG 3. However, the aggregate SDG measure does not identify which underlying component or mechanism accounts for this association and provides a hypothesis for further investigation. We would like to acknowledge certain limitations. Since the dataset is derived exclusively from tertiary care centers, the patterns may overrepresent

severe or referral cases. Although stratification by acquisition setting and patient's residence can partially mitigate this concern, true population-level representativeness remains constrained. Additionally, in the absence of integration with reliable nationally representative antibiotic consumption data, we assumed relative stability in antibiotic usage patterns between 2017 and 2022 when interpreting resistance trajectories. While this assumption is reasonable over short intervals, changes in prescribing behavior particularly during the COVID-19 pandemic could have influenced resistance dynamics. Although the network represents conditional dependencies among included variables, unmeasured confounding, ecological aggregation and surveillance selection may influence these associations.

The concordance of broad resistance patterns across BSIs and UTIs, coupled with identified syndrome-specific divergences, suggests that our modelling framework is both generalizable and adaptable. Future work will focus on operational deployment of this modelling framework and associated scorecards for hospitals across the country.

In conclusion, this study establishes a national benchmark for AMR trends in BSIs and UTIs in India. The escalating carbapenem resistance observed in key Gram-negative pathogens, combined with marked geographic and syndrome-specific heterogeneity, underscores the urgency of strengthened surveillance and targeted stewardship. However, addressing AMR at scale will require integrated modelling, decentralized policy adaptation, improved antibiotic consumption data systems, and sustained investment in surveillance infrastructure. Without such measures, the continued erosion of last-line therapies threatens both clinical outcomes and broader development goals.

Chapter 4: Characterising lead–lag relationships in resistance trajectories by identifying Indicator antibiotics

This chapter reorganises the lead–lag analyses reported within the BSI and UTI studies cited in Chapter 3 and the separation of Chapters 3 and 4 is analytical. These analyses are presented separately because they address a distinct methodological objective of examining whether changes in resistance to selected antibiotics temporally precede changes in resistance to other, clinically important agents. The findings are interpreted as exploratory temporal associations and not as evidence of causation or validated early-warning performance.

4.1 Introduction

In the previous chapter, we examined longitudinal trends in AMR across major pathogen–antibiotic–specimen combinations across India. While the trend analyses were useful for identifying trends, they did not address whether the changes in resistance patterns could be detected early, before they become sufficiently pronounced to appear as clear surveillance signals. This is an important gap as the changes in resistance patterns to one antibiotic may accompany changes in related agents, shaped by shared resistance mechanisms, selective pressure, prescribing behaviour, and patterns of transmission. Similar temporal ordering may also be seen across care settings where resistance patterns observed in hospitals may emerge earlier than those in community-linked infections, owing to greater antimicrobial exposure, higher patient load, and more intense opportunities for transmission. Inspite of the biological plausibility and epidemiological relevance of these lead-lag patterns they are not a part of routine surveillance activity. Most surveillance systems generally assess each antibiotic separately and summarise

resistance as parallel trends, with limited attention to how resistance patterns may relate to one another over time.

The present chapter aims to address this gap by examining lead–lag relationships in resistance trajectories and by identifying potential indicator antibiotics. The term indicator antibiotic is used for an antibiotic whose resistance trajectory shows an earlier and potentially informative shift relative to another antibiotic, such that change in the former may serve as a warning signal for subsequent change in the latter. The emphasis, therefore, is on exploratory temporal precedence for surveillance rather than causality.

4.2 Methods

4.2.1 Data Sources

The study utilised anonymised AST reports for suspected BSIs and UTIs from the IAMRSN. For the BSIs, data between 2017 and 2022 for *Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Klebsiella species*, *Acinetobacter baumannii*, *Acinetobacter calcoaceticus*, *Acinetobacter baumannii-calcoaceticu complex, Acinetobacter species*, *Staphylococcus aureus*, *Coagulase-negative Staphylococci* (CoNS), *Staphylococcus species*, *Pseudomonas aeruginosa*, *Enterococcus faecalis*, *Enterococcus faecium*, and *Enterococcus species* with known state information were analysed. For the UTIs, data between 2017 and 2021 for *Escherichia coli*, *Klebsiella (Klebsiella pneumoniae, Klebsiella oxytoca and Klebsiella species)*, *Pseudomonas aeruginosa*, or *Enterococcus (Enterococcus faecalis, Enterococcus faecium and Enterococcus species)* with known state information were analysed. This study focused on analysing monthly-aggregated data and did not attempt to re-identify patients.

4.2.2 AMR Rates

The rate of antimicrobial resistance (AMR) was calculated as in the previous chapter

$$AMR\ rate\ (R\%)\ = \frac{R\ count}{(R + I + S)\ count}$$

$$AMR\ rate\ (S\%)\ = \frac{S\ count}{(R + I + S)\ count}$$

where "R" represents the count of resistant isolates, "I" represents the count of intermediate isolates and "S" represents the count of susceptible isolates.

4.2.3 Lead-lag analysis

Cross-correlation analysis is a statistical tool used to quantify the degree to which two time series move in relation to each other. The analysis involves shifting one time series relative to another to determine whether changes in one series lead or lag changes in the other, and to what extent they are correlated. This shifting is measured in terms of lags (or leads), which are discrete time units (e.g., months, in our case) by which time series X is shifted backwards or forward in time relative to the other series Y. For each organism-antibiotic combination, let X_t denote resistance to antibiotic A and Y_t denote resistance to antibiotic B at month t. The cross-correlation was calculated by ccf in R stats package. Function Rxy (k) at a specific lag k is calculated as the correlation between X_{t+k} and Y_t. This means that, for each value of k, we compare the values of the first time series X at time t+k with those of the second time series Y at time t, where t ranges over all possible time points that allow this comparison given the length of the time series.

For this analysis, minimal pre-processing of the monthly time series of resistance for each antibiotic-sample-organism combination was done to avoid statistical artifacts. Time series with

overall missing values for resistance rates of more than 20% were discarded and less than five consecutive missing values were linearly interpolated. Stationarity of the interpolated time series was examined using the Augmented Dickey-Fuller test and first- or second-order differencing was applied to address non-stationarity in the series. Cross-correlations were computed for the transformed, stationary AMR rates at lags of -15 to 15 months and depicted graphically. Similarly, a lead-lag analysis was conducted for AMR rates in community-acquired and hospital-acquired infections (CAI and HAI).

4.2.4 Patient Consent and Ethics Approval

This study has been approved by the Ethics Committee of the Indraprastha Institute of Information Technology, Delhi (IIITD-IRB/ER/11/2022/2). This study utilized the routinely collected IAMRSN data. The access to anonymized IAMRSN data was provided by ICMR. Each hospital in the network has obtained its own ethics approvals for the collection of the surveillance data.

4.3 RESULTS:

4.3.1 BSI

In BSIs, 81,265 isolates across 21 centers in 14 states/UTs were analysed. Associations between CA-BSI and HA-BSI were analysed separately for 8,786 CA-BSI and 12,079 HA-BSI.

Temporal Associations of Resistance in Community and Hospital-Acquired Infections

This analysis was designed to explore the temporal dynamics of resistance patterns in community-acquired (CA) and hospital-acquired (HA) bloodstream infections (BSIs). We hypothesised that resistance patterns observed in one setting might precede similar patterns in the other, thereby

providing insights into the possible transmission of resistance between contexts. Our analysis revealed significant associations in CA and HA BSIs (all $p<0.05$). For *E. coli* BSIs, Amikacin and Piperacillin-tazobactam resistance in HA-BSI led resistance in CA-BSIs (Figure 4.1).

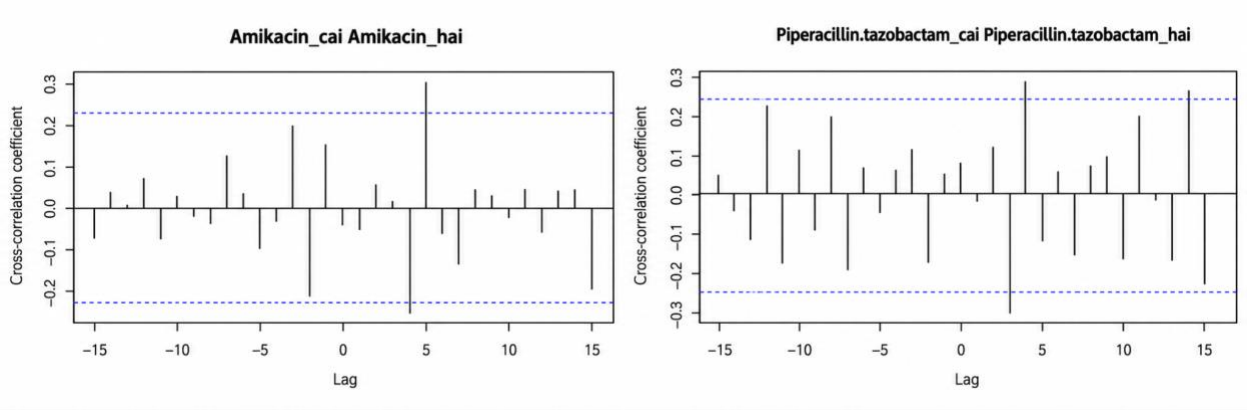


Figure 4.1- Antibiotic cross-correlation analysis of Amikacin and piperacillin-tazobactam in CA-BSI and HA-BSI in *E. coli* BSIs

As anticipated, a leading association between hospitals and the community is evident in the case of *Klebsiella* and *Acinetobacter* species. Notably, a correlation is observed for the following antimicrobial agents: Amikacin, Cefotaxime, Ciprofloxacin, Imipenem, and Meropenem in *Klebsiella* species, and Ceftazidime, Imipenem, and Meropenem in *Acinetobacter* species (Figures 4.2 & 4.3).

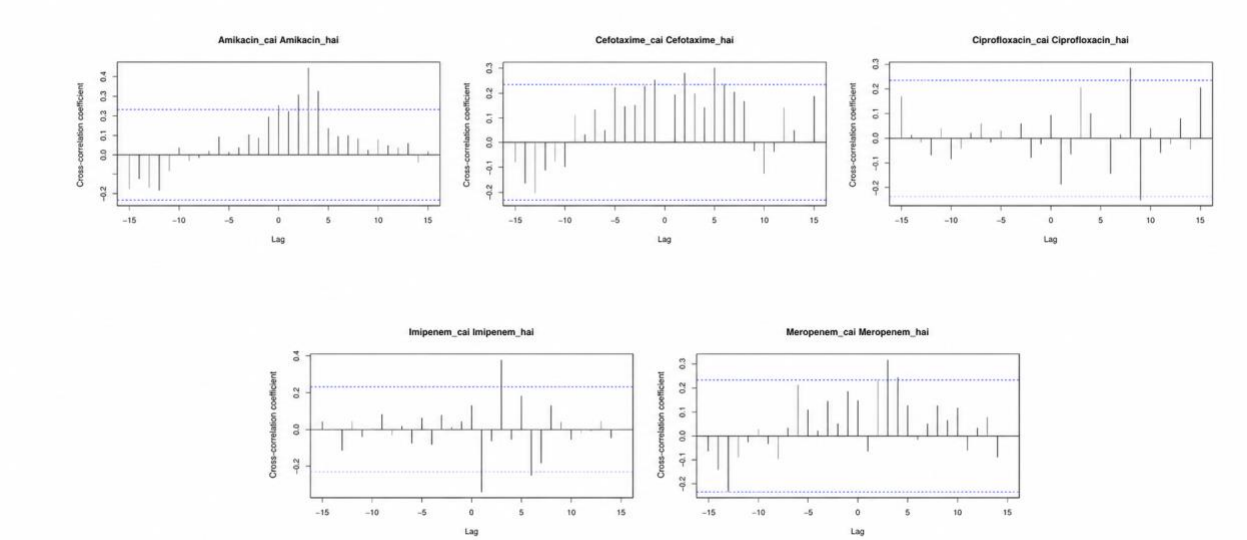


Figure 4.2- Antibiotic cross-correlation analysis of Amikacin, Cefotaxime, Ciprofloxacin, Imipenem, and Meropenem in CA-BSI and HA-BSI in *Klebsiella* BSIs

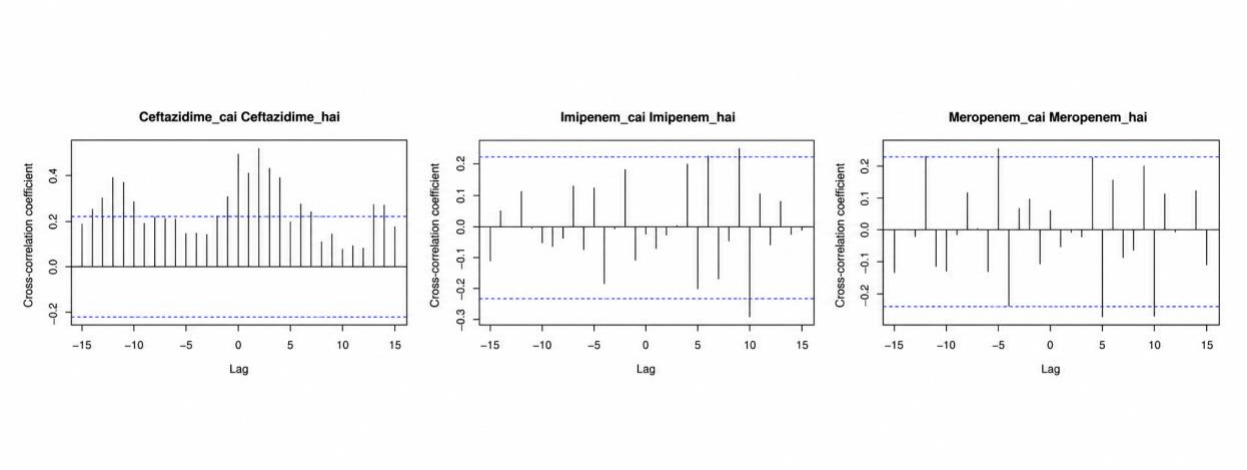


Figure 4.3- Antibiotic cross-correlation analysis of Ceftazidime, Imipenem, and Meropenem in CA-BSI and HA-BSI in *Acinetobacter* BSIs

However, in *Staphylococcus*, Ciprofloxacin and Erythromycin resistance in HA-BSI led resistance in CA-BSI by 3-4 months in the former and 10 months in the latter. In contrast, Clindamycin resistance in CA-BSI led to HA-BSI by 1-2 months (Figure 4.4).

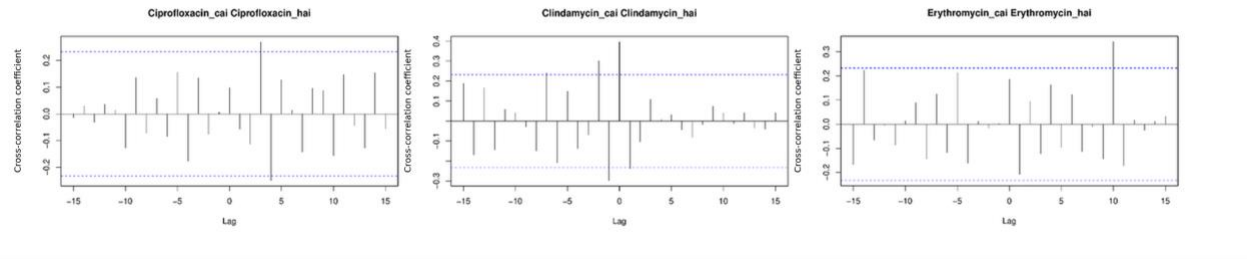


Figure 4.4- Antibiotic cross-correlation analysis of Ciprofloxacin, Erythromycin and Clindamycin in CA-BSI and HA-BSI in *Staphylococcus* BSIs

Indicator Antibiotics as Potential Early Warning Signals for Surveillance

The lead-lag analysis required minimum pre-processing as most of the time series achieved stationarity with the maximum first-order differencing operation. lead-lag cross-correlation analyses between antibiotic pairs revealed significant associations that can serve as early warning signals for critically important antimicrobials, such as Carbapenems (all $p<0.05$).

For *E. coli*, Cefotaxime was seen as a leading indicator for Imipenem and Meropenem resistance (Figure 4.5), with a lead time of 9-10 months.

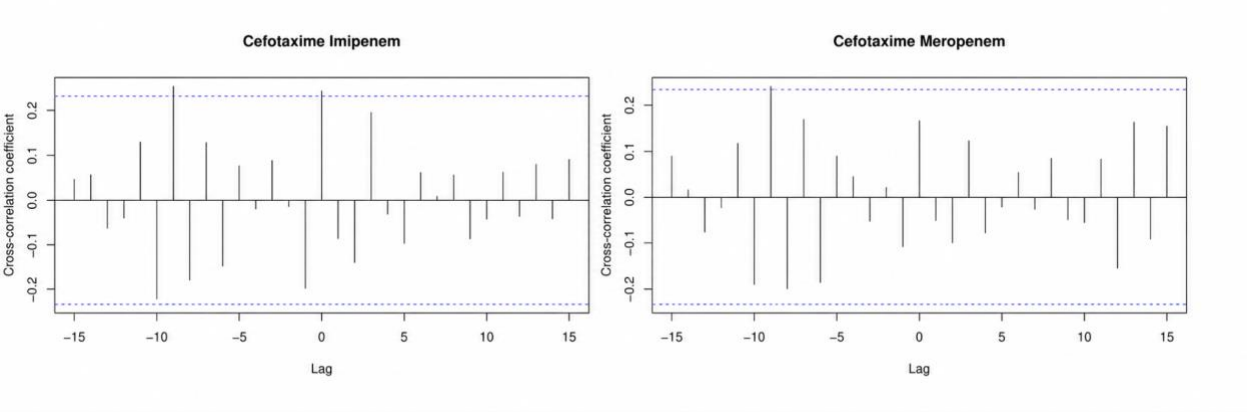


Figure 4.5- Antibiotic cross-correlation analysis of Cefotaxime and Carbapenems in *E. coli* BSIs

Additionally, In case of *Klebsiella* BSIs, Ciprofloxacin and Piperacillin-tazobactam emerged as leading indicators for Imipenem resistance with a lead time of 0-1 months (Figure 4.6).

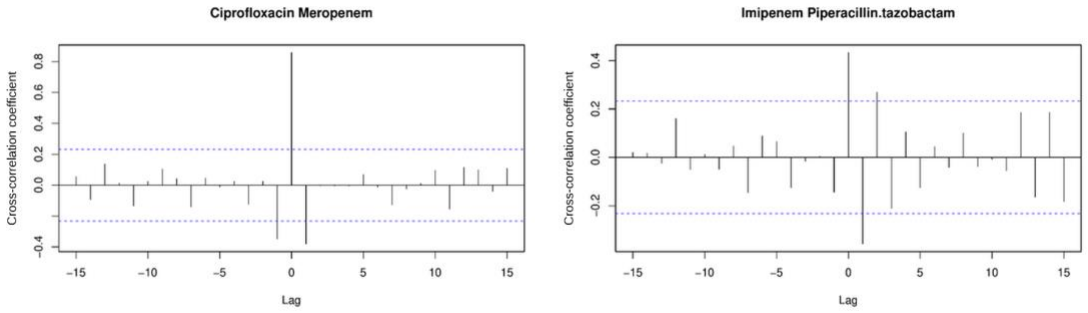


Figure 4.6- Antibiotic cross-correlation analysis of Ciprofloxacin, PTZ, meropenem and Imipenem in *Klebsiella* BSIs

In *Acinetobacter* BSIs, we observed a strong positive association between Ceftazidime/Cefepime resistance and Meropenem resistance at lag 0 (Figure 4.7). This indicates that increases in cephalosporin resistance occurred contemporaneously with increases in Meropenem resistance rather than clearly preceding them. Notably, the correlation at lag -1 month was negative, suggesting short-term divergence immediately prior to the peak contemporaneous association.

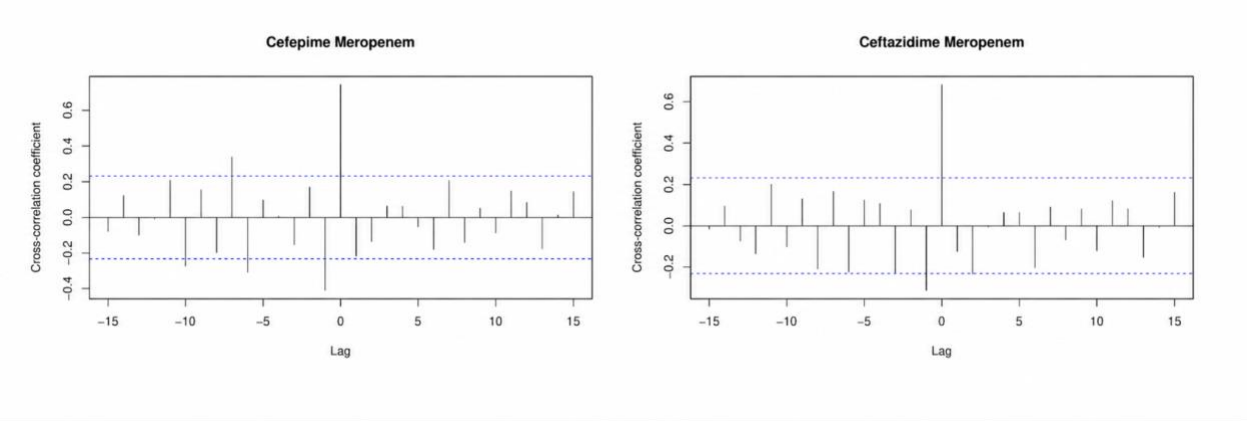


Figure 4.7- Antibiotic cross-correlation analysis of Ceftazidime, Cefepime and Meropenem in *Acinetobacter* BSIs

4.3.2 UTI

81,865 isolates for UTIs from 20 centers across 13 states/UTs were analysed.

Temporal Associations of Resistance in Community and Hospital-Acquired Infections

In *E. coli*, ertapenem and cefazolin resistance showed community-leading temporal associations, whereas nitrofurantoin and ciprofloxacin resistance showed hospital-leading associations (Figure 4.8). For amikacin, cross-correlations exceeded the plotted significance bounds at both negative and positive lags. This pattern indicates temporal associations in both directions, without identifying a single consistently leading setting. It does not establish reciprocal transmission or a causal influence of resistance in one setting on the other.

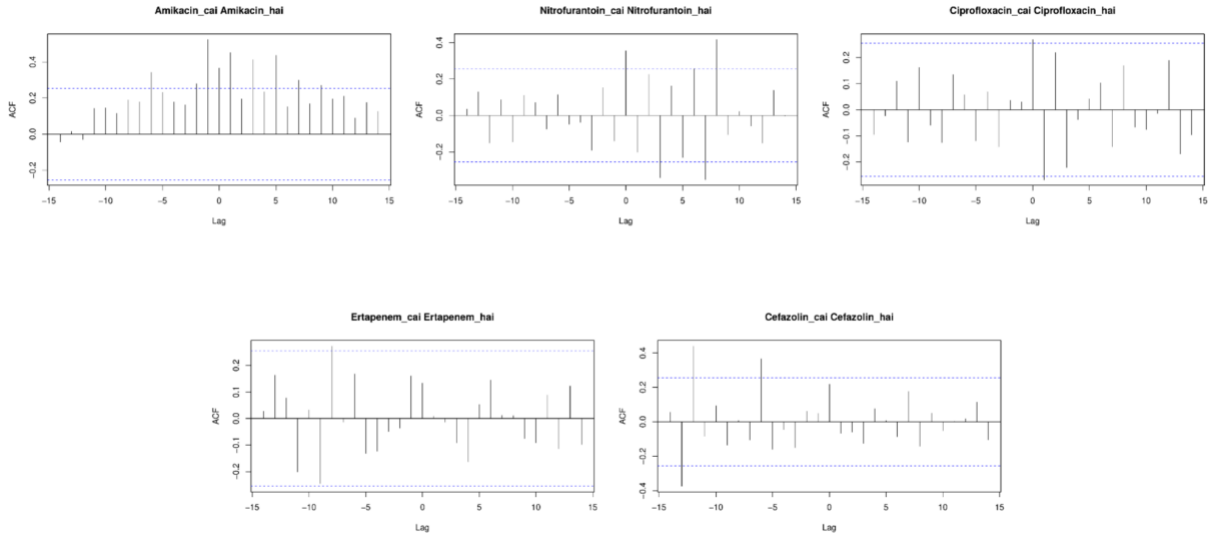


Figure 4.8- Antibiotic cross-correlation analysis of Ertapenem, Amikacin, Cefazolin, Nitrofurantoin and Ciprofloxacin in CA-UTI and HA-UTI for *E. coli* UTIs

However, in *Klebsiella*, Imipenem resistance in HA-UTI led CA-UTI by 2-10 months, Ertapenem resistance was bidirectional and Ciprofloxacin resistance in CA-UTI led HA-UTI by up to 6 months (Figure 4.9).

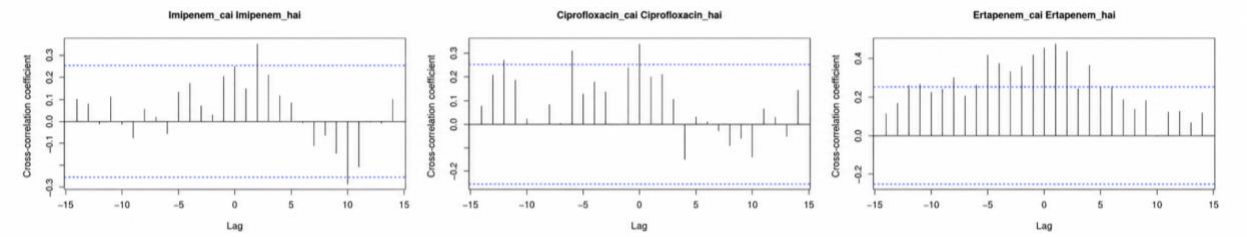


Figure 4.9- Antibiotic cross-correlation analysis of Imipenem, Ciprofloxacin and Ertapenem in CA-UTI and HA-UTI for *Klebsiella* UTIs

These are consistent with our hypothesis revealing statistically significant temporal associations (all $p<0.05$), indicating that resistance patterns in CA-UTIs often precede or follow those in HA-UTIs by several months, depending on the microorganism-antibiotic combination.

4.4 Discussion

This chapter extends the geo-temporal trends presented in the previous chapter by exploring whether the resistance patterns exhibit temporal lead–lag relationships across antibiotic classes and across care settings. Previous time-series studies have examined lagged relationships between antimicrobial consumption and subsequent resistance. For example, Laffont-Lozes et al. (2023) reviewed hospital-based dynamic regression studies investigating these relationships and identified a continuing need to evaluate their predictive usefulness. More directly comparable, Martínez et al. (2025) analysed urinary *E. coli* and *K. pneumoniae* resistance across Dutch primary-care and hospital settings using vector autoregressive models. They found predominantly primary-care-leading associations, with bidirectional associations for ciprofloxacin resistance in *K. pneumoniae*. The present study extends this literature by examining both resistance-to-resistance relationships across antibiotics and temporal relationships between hospital- and community-acquired bloodstream and urinary infections in India. This approach explores whether routinely

available susceptibility data contain candidate signals for closer surveillance, particularly where linked consumption data are unavailable. The observed relationships should be interpreted as exploratory temporal associations requiring further validation.

The CDC framework for evaluating early outbreak detection emphasises timeliness, sensitivity, predictive value and the consequences of false alarms (Buehler et al., 2004). Although developed for outbreak surveillance, these evaluation principles are relevant to assessing candidate AMR warning signals. The present cross-correlation analysis identifies retrospective temporal relationships and it does not establish an operational alert rule or its predictive performance. Further evaluation would require a predefined resistance event, an explicit alert threshold, and testing on subsequent observations using only information available when each alert would have been generated. Performance should be assessed through detection sensitivity, false-alert frequency and usable lead time relative to simpler surveillance approaches.For BSIs we observed that the resistance in HAIs preceded corresponding resistance in CA-BSIs for several pathogen–antibiotic combinations. Resistance to Amikacin and Piperacillin–tazobactam in hospital-acquired *E. coli* infections was leading community-acquired *E. coli* infections. Similar hospital-leading associations were observed for both *Klebsiella* and *Acinetobacter* species across β-lactams and carbapenems. The observed pattern is consistent with the ecological reality of hospitals as high-selection-pressure environments, where broad-spectrum antibiotic exposure and transmission density are greater. The resistant strain that emerge or amplify within hospital settings may disseminate outward into the community through patient movement and referral networks. Epidemiological studies provide plausible explanations for temporal relationships between settings. Hilty et al. (2012) documented household transmission of ESBL-producing Enterobacteriaceae, including probable transmission following hospital acquisition in two index

patients. This supports a possible pathway connecting hospital carriage with subsequent community dissemination. Conversely, Gorrie et al. (2017) identified *K. pneumoniae* carriage among patients admitted directly from the community and found that carriage at admission was associated with subsequent ICU infection. These observations support considering both pre-existing carriage and movement between settings when interpreting the temporal patterns. However, they do not establish the mechanisms underlying our observed lags, which may also reflect shared antibiotic exposure, referral patterns or changes in testing.

However, the directionality is not uniform and differs across pathogen-antibiotic-specimen combinations. In case of BSIs caused by Staphylococcus Ciprofloxacin and Erythromycin resistance in hospital acquired infections preceded community acquired while Clindamycin resistance showed the opposite pattern. Similarly, *E. coli* UTIs, Ertapenem and Cefazolin resistance in community-acquired infections preceded hospital resistance, whereas Nitrofurantoin and Ciprofloxacin demonstrated hospital-leading patterns. In *Klebsiella* UTIs, Imipenem resistance in hospitals preceded community resistance by several months, while Ciprofloxacin resistance showed in the reverse direction. These patterns identify temporal associations in both directions but do not establish the separate contributions of hospital and community antibiotic use. The observed 9–10-month lead of cefotaxime resistance relative to imipenem and meropenem resistance in E. coli BSIs identifies a candidate relationship for further surveillance evaluation. This temporal ordering does not establish that cephalosporin resistance causes subsequent carbapenem resistance, nor that the same lead would reliably recur in future data. Shared resistance determinants, antimicrobial exposure, changes in circulating strains and surveillance practices are possible explanations requiring additional evidence. If the relationship is reproduced in independent settings and subsequent observations, it could support closer monitoring and

stewardship review. Its prospective predictive value and operational usefulness remain to be established.

However several limitations need to be considered while interpreting these results. Aggregation at a monthly level may obscure shorter transmission bursts. Moreover, the lack of linked antibiotic consumption data limits the ability to directly connect prescribing patterns with observed lag structures. Since the data is from tertiary care centers, it may not fully capture resistance dynamics in smaller or private healthcare facilities. Future work will involve integration with antibiotic consumption and genomic surveillance data to validate and refine these temporal relationships. The lead–lag associations were identified retrospectively and were not evaluated as forecasts. Establishing predictive validity will require testing on later, unseen observations, comparison with models using the target antibiotic's own resistance history, and replication across hospitals and time periods. Further robustness assessment should examine sensitivity to preprocessing, lag selection and multiple comparisons. Prospective evaluation is needed to determine whether these associations can support reliable surveillance alerts.

Overall, this chapter extends descriptive surveillance by identifying candidate temporal relationships across antibiotics and care settings. Its contribution is the generation of testable hypotheses about potential leading resistance signals. Incorporating such signals into surveillance dashboards would require further evaluation of their reproducibility, predictive performance and usefulness for stewardship decisions.

Chapter 5: *AMROrbit Scorecard*: translating routinely generated AST data into dynamic trajectory-based stewardship intelligence

This chapter is based on the *AMROrbit* study accepted for publication in JAC-Antimicrobial Resistance. The presentation has been adapted to align the terminology, interpretation and narrative with the broader thesis. Within the thesis, *AMROrbit* is positioned as the methodological culmination of the preceding analyses: Chapter 3 establishes resistance burden and temporal change, Chapter 4 examines candidate temporal signals, and Chapter 5 combines burden and velocity into an interpretable trajectory-based prioritisation framework.

5.1 Introduction

AMR Surveillance and stewardship have been the two foundational pillars in the global response to AMR. While surveillance provides data on resistance patterns, the stewardship programmes translate these data into interventions to optimise antibiotic use and improve patient outcomes (Barlam et al., 2016; Dyar et al., 2017; Laxminarayan et al., 2013). Traditionally, stewardship approaches depend on retrospective insights, such as annual antibiograms (Laxminarayan, 2022; Truong et al., 2021) and by the time such patterns are evident in the aggregate summaries, opportunities for early intervention may already have been reduced (Dyar et al., 2017; Laxminarayan, 2022). Therefore, our stewardship approaches remain more reactive than anticipatory in most settings.

Proactive data-driven stewardship requires analytic frameworks capable of detecting shifts in resistance patterns early enough to inform clinical decisions. Statistical and machine-learning approaches available as alerts and dashboards have shown the potential to augment decision-making by providing interpretable, near-real-time signals to frontline clinicians and policymakers (Fu et al., 2025; Howard et al., 2024; Lim et al., 2021). Regression-based surveillance models are being used to estimate temporal trends (Hernandez et al., 2021) and to predict resistance phenotypes at the isolate or pathogen–antibiotic level (Ardila et al., 2025; Mediouni et al., 2025; Valavarasu et al., 2025). Dynamic regression and related time-series models are extending this approach by linking antimicrobial consumption with resistance, estimating lagged associations, and generating short-term forecasts where sufficiently granular antimicrobial use and resistance data are available (Laffont-Lozes et al., 2023). These approaches address important but distinct operational questions on estimating trends, but many available approaches either lack interpretability or remain closely tied to specific datasets and implementation contexts, limiting their broader applicability (Fu et al., 2025; Howard et al., 2024). Moreover, fewer frameworks have focused on jointly capturing both the current burden of resistance and its direction of change across countries, organisms, specimens, and antibiotics.

In the previous chapters, we showed that routinely collected surveillance data can provide identify resistance trends and candidate temporal indicators for further surveillance evaluation. With the IAMRSN data, we introduced a model-based AMR scorecard for focused interventions and continuous monitoring in tertiary care settings (Kaur et al, 2024). However, the scorecard lacked understanding of the dynamics of resistance.

To address this gap, we developed *AMROrbit*, an explainable trajectory-based scorecard that converts routine microbiology data into comparative stewardship insights. *AMROrbit* uses model-

derived estimates of baseline resistance burden and temporal change to define two interpretable dimensions: amplitude and velocity. By mapping these dimensions into a shared phase space, the framework distinguishes trajectories with similar resistance trends but different baseline burdens, or similar burdens but different temporal directions. *AMROrbit* is intended not as a replacement for regression, forecasting, or resistance prediction models, but as a translational layer that summarises observed AMR dynamics into trajectory states that can support surveillance interpretation, prioritisation, and stewardship review.

5.2 Methods

Data Source

ATLAS is a global antimicrobial resistance surveillance initiative that monitors resistance trends using standardised antimicrobial susceptibility testing (AST) data from clinical microbiology laboratories worldwide. In this study, the Pfizer ATLAS dataset was accessed through the Vivli AMR platform as part of the AMR Surveillance Data Challenge (Vivli AMR, 2024; Pfizer ATLAS, 2024; Vivli AMR Data Challenge, 2024). The dataset comprised longitudinal AST data (2004 onwards) from clinical microbiology laboratories worldwide, with isolates tested against a predefined panel of antimicrobials. This study included data for ESKAPE pathogens (*Enterococcus faecium*, *Staphylococcus aureus (*MRSA), *Staphylococcus aureus (*MSSA)*, Klebsiella pneumoniae*, *Klebsiella aerogenes*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, Enterobacter cloacae and *Enterobacter spp.*) and *Escherichia coli* from Bloodstream, Urine, Sputum, and Wound infections.

To ensure sufficient temporal depth for resistance trajectory modelling, only countries with comprehensive surveillance data spanning from 2014 to 2022 were included. Missing annual resistance values were not imputed. The analysis retained combinations with complete longitudinal data because the limited number of annual observations would make trajectory estimates particularly dependent on any imputation assumptions. The inclusion criteria for each country were assessed separately for each organism–antibiotic–specimen combination. For each combination, countries were retained only if they had a complete time series across the study period. Consequently, the number and identity of included countries varied across analytical strata rather than constituting a single fixed set of countries. Antimicrobial susceptibility results were analysed using the preclassified susceptible, intermediate, and resistant categories available in the ATLAS dataset. *AMROrbit* did not apply additional clinical breakpoints to raw MIC or zone-diameter values. Susceptible dose-dependent was not available as a separate category in the extracted data and was therefore not separately analysed. All analyses were performed on yearly aggregated data, with no patient-level identifiers used.

Exploratory Data Analysis

The isolation percentage of an organism was calculated as follows:

$$Total\ isolation\ rate\ (Organism\ 1)\ = \frac{Count\ of\ isolates\ for\ organism\ 1\ (nO1)}{Count\ of\ total\ positive\ cultures\ (N)}\ *\ 100$$

$$Sample-wise\ isolation\ rate\ (Organism\ 1\ in\ sample\ 1)\ =$$

$$\frac{Count\ of\ isolates\ for\ organism\ 1\ in\ sample\ 1}{Count\ of\ total\ positive\ cultures\ for\ sample\ 1} * 100$$

$$Country - wise\ isolation\ rate\ (Organism\ 1\ in\ Country\ 1)\ =$$

$$\frac{Count\ of\ isolates\ for\ organism\ 1\ in\ country\ 1}{Count\ of\ total\ positive\ cultures\ for\ country\ 1} * 100$$

Yearly aggregated resistance percentages were calculated for each antibiotic-organism-sample-country combination to generate a time series of resistance as

$$AMR\ Rate\ (R\%)\ =\ \frac{R}{R+I+S} * 100$$

where R is the count of resistant isolates, S is the count of susceptible isolates, and I is the count of Intermediate isolates

AMROrbit Scorecard

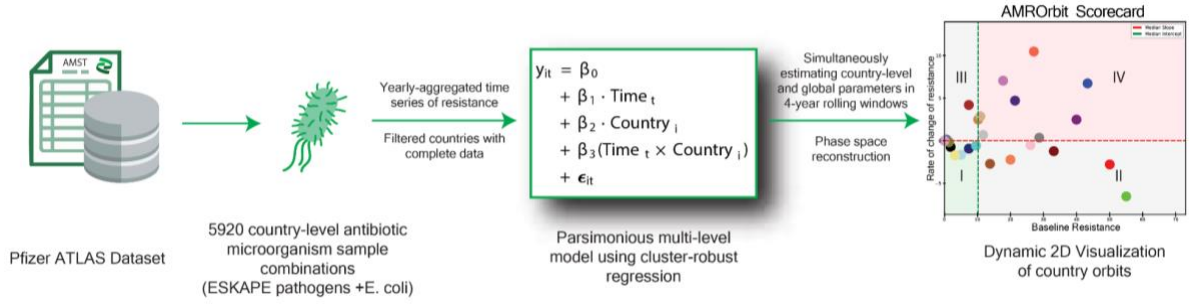


Figure 5.1- From snapshots to trajectories: *AMROrbit* pipeline and visualisation of antimicrobial resistance (AMR) dynamics. Antimicrobial susceptibility testing (AST) data for ESKAPE pathogens and *Escherichia coli* from 84 countries across 4 specimen types (urinary tract, bloodstream, respiratory, and wound infections) were used to estimate resistance Intercept (baseline level) and slope (rate of change). Estimates were derived within overlapping four-year rolling windows (three-year overlap), allowing both global and country-level resistance patterns to be examined over time. These estimates were then plotted in a two-dimensional phase space based on global medians. Quadrant I represents low slope (rate of change of resistance) and low intercept (baseline resistance); Quadrant II low slope and high intercept; Quadrant III high slope and low intercept; and Quadrant IV high slope and high intercept.

The complete methodology is described in Figure 5.1. Countries with complete time series (aggregated values for all years from 2014 to 2022) for the entire duration were used for modelling. All statistical analyses were performed in R (R Core Team, 2022). Data preprocessing was conducted using dplyr and lubridate. For each country–organism–specimen–antibiotic combination, annual resistance percentages were calculated as the number of resistant isolates divided by the total number of isolates with valid antimicrobial susceptibility interpretations. A centred 3-year moving average was applied to the annual resistance percentage using rollmean () from the zoo package (Zeileis & Grothendieck, 2005). Temporal trajectories were then estimated within rolling 4-year windows from 2014 to 2022. For each window, linear regression models were fitted using the base R lm () function from the stats package, with annual resistance percentage as the outcome and year, country, and year-by-country interaction terms as predictors. The regression equation is:

$$y_{it} = \beta_0 + \beta_1 \cdot Time_t + \beta_2 \cdot Country_i + \beta_3 \cdot (Time_t \times Country_i) + \epsilon_{it}$$

Where:

- y_{it} = AMR resistance percentage for country i at time t
- $Time_t$ = Temporal variable (e.g., year in this case)
- $Country_i$ = Categorical variable for the country
- $\beta_0, \beta_1, \beta_2, \beta_3$ = Model coefficients (intercept, slopes, and interaction term)
- ϵ_{it} = Error term

This model ensures that each country can have its own slope, reflecting different AMR trends over time. The interaction term ($Time_t \times Country_i$) allows for country-specific trends, addressing heterogeneity across countries.

From each fitted model, two parameters were extracted (i) the intercept, representing baseline resistance (amplitude), and (ii) the slope, representing the annual rate of change (velocity). Model summaries were obtained using summary (), and coefficient tests were generated using coeftest () from the lmtest package with robust estimates from the sandwich package (Zeileis & Hothorn, 2002; Zeileis et al., 2020).

The *AMROrbit* scorecard visualisation was performed in Python using pandas, numpy and matplotlib (Harris et al., 2020; Hunter, 2007; McKinney, 2010). Regression-derived amplitude and velocity estimates were mapped into a two-dimensional phase space and stratified using global medians into four quadrants: Q1 (ideal): low baseline resistance and low rate of change; Q2: high baseline resistance and low rate of change; Q3: low baseline resistance and high rate of change; Q4 (concerning): high baseline resistance and high rate of change.

Country-level trajectories were classified by comparing the first and final rolling-window quadrants. Spiral-in (containment) was defined as movement from Q2, Q3, or Q4 to Q1; spiral-out (emerging risk) as movement from Q1, Q2, or Q3 to Q4; persistent as remaining in the same quadrant; and mixed as all other quadrant transitions.

The global median thresholds were not used for statistical estimation itself, but rather for the interpretive phase-space representation layered on top of the continuous regression-derived parameters. The underlying model retained resistance burden and temporal change as continuous

quantities, while the quadrant-based scorecard provided a pragmatic stewardship abstraction for communicating dynamic AMR states.

To account for the non-independence of trajectory observations from the same country across antibiotics, we used a country-level cluster bootstrap (10,000 replicates). In each replicate, countries were resampled with replacement within each organism-source stratum, and all antibiotic-specific trajectory records for each sampled country were retained. The 2.5th and 97.5th percentiles of the bootstrap distribution were taken as the 95% confidence interval for the proportion of country-antibiotic observations in each trajectory category.

Sensitivity analysis for the global median threshold

To assess sensitivity to the choice of phase-space thresholds, we repeated the trajectory classification using region-specific medians instead of global medians. Countries were grouped into four geographic regions: Africa & Middle East, the Americas, Asia, and Europe. For each organism–specimen–antibiotic combination, region-specific medians for baseline resistance and velocity were estimated and used to define the corresponding phase-space quadrants. Regional-median-based trajectory classifications were then compared with the original global-median-based classifications across all country-level trajectories.

5.3 Results

Across the full ATLAS dataset, a total of 5,920 country-level antibiotic–microorganism–sample combinations (212,434 records) were analysed from 2014 to 2022. *E. coli* was the most isolated pathogen across bloodstream and urine isolates, while *Staphylococcus aureus* and *P. aeruginosa* dominated across wound and Sputum isolates, respectively (Figure 5.2).

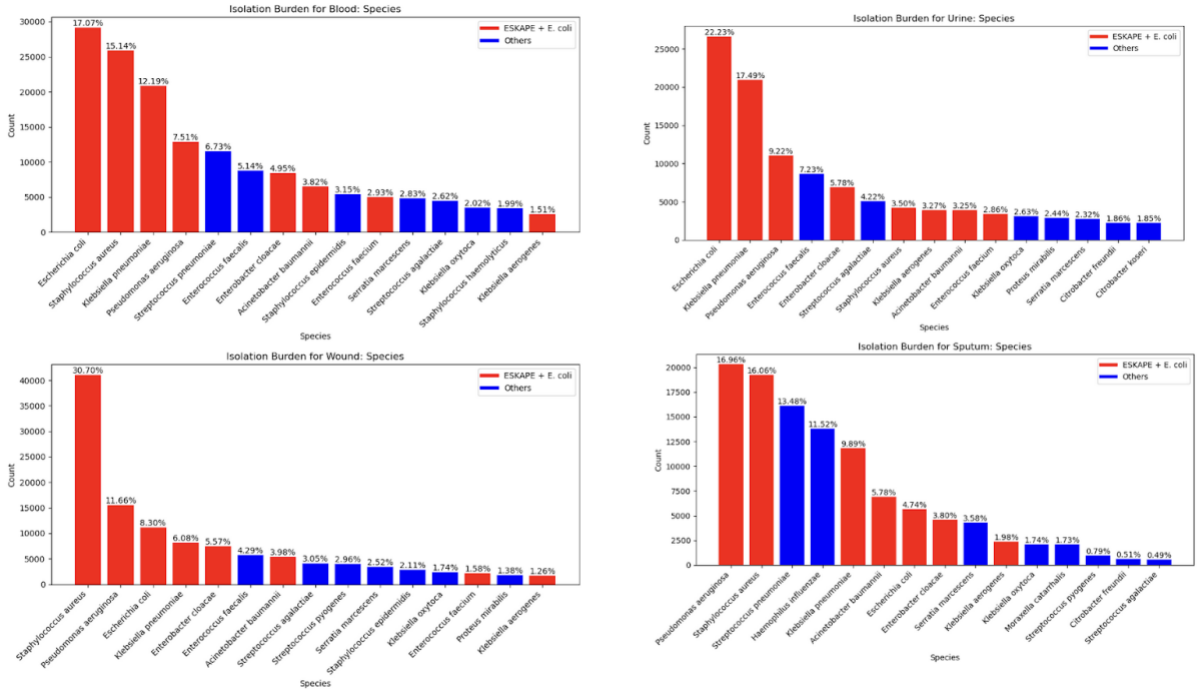


Figure 5.2: Isolation burden across different sample types. The figure shows that *E. coli* was the most isolated pathogen across bloodstream and urine isolates, while *Staphylococcus aureus* and *P. aeruginosa* dominated across wound and Sputum isolates, respectively.

Aggregated global results revealed 62.4% of combinations showed rising baseline resistance, indicating a broad upward shift in AMR burden over time. Among country-level combinations, 17.7% were spiralling out compared to only 13.4% spiralling in, revealing a concerning global imbalance that presents opportunities for policy learning and adaptation. A majority of the combinations followed constant/mixed resistance trajectories, suggesting sustained resistance levels without substantial improvement or deterioration (Table 5.1).

Table 5.1: Summary of country–organism–source–antibiotic *AMROrbit* trajectories by organism and specimen source. Percentages are calculated using the total number of country–antibiotic trajectory observations within each organism–specimen stratum as the denominator. Spiralling-in is defined as movement from QII, QIII, or QIV at baseline to QI in the final time window; spiralling-out is defined as movement from QI, QII, or QIII at baseline to QIV in the final time window; persistent trajectories are defined as trajectories remaining in the same quadrant; and other/mixed trajectories include non-directional, oscillatory, or mixed quadrant sequences that did not meet the predefined criteria for spiralling-in, spiralling-out, or persistent classification. Ninety-five percent confidence intervals for trajectory proportions were estimated using a country-level cluster bootstrap with 10,000 replicates. In each replicate, countries were resampled with replacement within each organism–specimen stratum, retaining all antibiotic-specific trajectory records for the sampled countries, and the 2.5th and 97.5th percentiles of the bootstrap distribution were used as the confidence limits

Organism	Source	Spiralling-in	Spiralling-out	Persistent	Other/Mixed
Acinetobacter baumannii	Blood	23/96 (24.0%; 95% CI 7.3–44.8)	21/96 (21.9%; 95% CI 7.3–39.6)	34/96 (35.4%; 95% CI 22.9–47.9)	18/96 (18.8%; 95% CI 7.3–31.3)
Acinetobacter baumannii	Sputum	26/85 (30.6%; 95% CI 9.2–54.8)	20/85 (23.5%; 95% CI 8.3–40.5)	24/85 (28.2%; 95% CI 9.5–47.7)	15/85 (17.6%; 95% CI 4.7–34.1)
Acinetobacter baumannii	Urine	22/84 (26.2%; 95% CI 8.3–47.6)	19/84 (22.6%; 95% CI 4.8–44.0)	24/84 (28.6%; 95% CI 11.9–47.6)	19/84 (22.6%; 95% CI 7.1–40.5)
Acinetobacter baumannii	Wound	8/72 (11.1%; 95% CI 0.0–25.0)	8/72 (11.1%; 95% CI 0.0–29.2)	27/72 (37.5%; 95% CI 20.8–55.6)	29/72 (40.3%; 95% CI 22.2–59.7)
Enterobacter cloacae	Blood	24/181 (13.3%; 95% CI 8.1–18.9)	27/181 (14.9%; 95% CI 9.6–20.7)	38/181 (21.0%; 95% CI 16.9–25.0)	92/181 (50.8%; 95% CI 45.9–56.0)
Enterobacter cloacae	Sputum	18/145 (12.4%; 95% CI 5.9–19.0)	35/145 (24.1%; 95% CI 16.2–31.8)	31/145 (21.4%; 95% CI 13.9–28.8)	61/145 (42.1%; 95% CI 32.7–53.3)
Enterobacter cloacae	Urine	23/153 (15.0%; 95% CI 6.9–23.9)	34/153 (22.2%; 95% CI 15.0–29.0)	37/153 (24.2%; 95% CI 17.6–29.5)	59/153 (38.6%; 95% CI 31.0–49.1)
Enterobacter cloacae	Wound	16/164 (9.8%; 95% CI 4.4–15.3)	30/164 (18.3%; 95% CI 12.1–25.4)	42/164 (25.6%; 95% CI 18.7–32.4)	76/164 (46.3%; 95% CI 38.8–55.3)
Enterobacter species	Blood	4/44 (9.1%; 95% CI 2.4–16.0)	2/44 (4.5%; 95% CI 0.0–14.3)	9/44 (20.5%; 95% CI 8.8–28.3)	29/44 (65.9%; 95% CI 54.3–83.3)

Enterobacter species	Sputum	2/35 (5.7%; 95% CI 0.0–9.7)	6/35 (17.1%; 95% CI 0.0–29.0)	10/35 (28.6%; 95% CI 5.3–42.9)	17/35 (48.6%; 95% CI 27.5–73.7)
Enterobacter species	Urine	0/11 (0.0%; 95% CI 0.0–0.0)	0/11 (0.0%; 95% CI 0.0–0.0)	0/11 (0.0%; 95% CI 0.0–0.0)	11/11 (100.0%; 95% CI 100.0–100.0)
Enterobacter species	Wound	3/23 (13.0%; 95% CI 0.0–28.1)	2/23 (8.7%; 95% CI 0.0–18.8)	1/23 (4.3%; 95% CI 0.0–9.4)	17/23 (73.9%; 95% CI 70.7–100.0)
Enterococcus faecium	Blood	6/80 (7.5%; 95% CI 2.4–13.3)	9/80 (11.2%; 95% CI 3.8–20.3)	20/80 (25.0%; 95% CI 15.2–34.1)	45/80 (56.2%; 95% CI 48.8–64.2)
Enterococcus faecium	Sputum	0/1 (0.0%; 95% CI 0.0–0.0)	0/1 (0.0%; 95% CI 0.0–0.0)	0/1 (0.0%; 95% CI 0.0–0.0)	1/1 (100.0%; 95% CI 100.0–100.0)
Enterococcus faecium	Urine	4/56 (7.1%; 95% CI 0.0–16.7)	8/56 (14.3%; 95% CI 3.8–26.7)	20/56 (35.7%; 95% CI 25.0–46.4)	24/56 (42.9%; 95% CI 35.0–51.8)
Enterococcus faecium	Wound	3/30 (10.0%; 95% CI 0.0–23.1)	5/30 (16.7%; 95% CI 0.0–29.4)	10/30 (33.3%; 95% CI 13.6–52.9)	12/30 (40.0%; 95% CI 28.9–61.1)
Escherichia coli	Blood	47/333 (14.1%; 95% CI 9.6–18.9)	60/333 (18.0%; 95% CI 12.5–24.1)	102/333 (30.6%; 95% CI 24.5–36.7)	124/333 (37.2%; 95% CI 30.5–44.4)
Escherichia coli	Sputum	29/218 (13.3%; 95% CI 8.2–18.7)	42/218 (19.3%; 95% CI 11.9–27.7)	79/218 (36.2%; 95% CI 30.6–41.8)	68/218 (31.2%; 95% CI 24.7–38.2)
Escherichia coli	Urine	52/297 (17.5%; 95% CI 11.4–23.9)	51/297 (17.2%; 95% CI 12.2–22.9)	105/297 (35.4%; 95% CI 29.5–41.6)	89/297 (30.0%; 95% CI 24.2–36.4)
Escherichia coli	Wound	37/258 (14.3%; 95% CI 8.9–20.2)	54/258 (20.9%; 95% CI 14.0–28.5)	76/258 (29.5%; 95% CI 23.2–35.9)	91/258 (35.3%; 95% CI 27.5–43.4)
Klebsiella aerogenes	Blood	12/103 (11.7%; 95% CI 3.8–21.6)	10/103 (9.7%; 95% CI 3.4–16.7)	21/103 (20.4%; 95% CI 11.7–29.5)	60/103 (58.3%; 95% CI 51.4–68.0)
Klebsiella aerogenes	Sputum	7/94 (7.4%; 95% CI 2.1–12.9)	18/94 (19.1%; 95% CI 12.0–25.7)	27/94 (28.7%; 95% CI 23.3–34.2)	42/94 (44.7%; 95% CI 36.9–55.4)
Klebsiella aerogenes	Urine	8/94 (8.5%; 95% CI 2.6–14.8)	22/94 (23.4%; 95% CI 13.0–32.7)	24/94 (25.5%; 95% CI 18.8–31.1)	40/94 (42.6%; 95% CI 34.3–54.4)
Klebsiella aerogenes	Wound	4/54 (7.4%; 95% CI 0.0–16.4)	8/54 (14.8%; 95% CI 6.7–20.0)	7/54 (13.0%; 95% CI 3.8–20.0)	35/54 (64.8%; 95% CI 53.8–85.2)

Klebsiella pneumoniae	Blood	58/324 (17.9%; 95% CI 12.0–24.4)	64/324 (19.8%; 95% CI 11.4–29.3)	115/324 (35.5%; 95% CI 29.6–41.7)	87/324 (26.9%; 95% CI 20.7–33.3)
Klebsiella pneumoniae	Sputum	47/361 (13.0%; 95% CI 7.9–18.8)	70/361 (19.4%; 95% CI 12.9–26.6)	122/361 (33.8%; 95% CI 26.6–40.9)	122/361 (33.8%; 95% CI 27.1–40.9)
Klebsiella pneumoniae	Urine	48/325 (14.8%; 95% CI 8.8–21.4)	67/325 (20.6%; 95% CI 11.7–30.4)	98/325 (30.2%; 95% CI 24.2–36.2)	112/325 (34.5%; 95% CI 26.4–42.9)
Klebsiella pneumoniae	Wound	38/317 (12.0%; 95% CI 7.3–17.2)	46/317 (14.5%; 95% CI 8.4–22.0)	109/317 (34.4%; 95% CI 27.4–41.5)	124/317 (39.1%; 95% CI 31.9–46.5)
Pseudomonas aeruginosa	Blood	30/203 (14.8%; 95% CI 7.9–22.4)	32/203 (15.8%; 95% CI 8.0–24.9)	64/203 (31.5%; 95% CI 23.5–39.7)	77/203 (37.9%; 95% CI 29.8–47.0)
Pseudomonas aeruginosa	Sputum	43/330 (13.0%; 95% CI 8.0–18.6)	72/330 (21.8%; 95% CI 13.5–30.9)	105/330 (31.8%; 95% CI 25.5–38.3)	110/330 (33.3%; 95% CI 24.6–42.7)
Pseudomonas aeruginosa	Urine	40/288 (13.9%; 95% CI 8.2–20.2)	54/288 (18.8%; 95% CI 11.1–27.5)	94/288 (32.6%; 95% CI 25.3–40.1)	100/288 (34.7%; 95% CI 25.7–44.6)
Pseudomonas aeruginosa	Wound	52/255 (20.4%; 95% CI 12.3–29.0)	49/255 (19.2%; 95% CI 10.3–29.1)	82/255 (32.2%; 95% CI 24.9–39.8)	72/255 (28.2%; 95% CI 20.3–36.7)
Staphylococcus aureus (MRSA)	Blood	4/25 (16.0%; 95% CI 4.0–32.0)	4/25 (16.0%; 95% CI 4.0–32.0)	10/25 (40.0%; 95% CI 20.0–60.0)	7/25 (28.0%; 95% CI 12.0–48.0)
Staphylococcus aureus (MRSA)	Sputum	6/109 (5.5%; 95% CI 1.5–9.6)	9/109 (8.3%; 95% CI 2.8–14.1)	24/109 (22.0%; 95% CI 14.8–28.1)	70/109 (64.2%; 95% CI 57.0–73.6)
Staphylococcus aureus (MRSA)	Urine	1/34 (2.9%; 95% CI 0.0–8.6)	1/34 (2.9%; 95% CI 0.0–8.5)	5/34 (14.7%; 95% CI 0.0–28.3)	27/34 (79.4%; 95% CI 64.4–100.0)
Staphylococcus aureus (MRSA)	Wound	11/188 (5.9%; 95% CI 2.7–9.2)	31/188 (16.5%; 95% CI 12.6–20.4)	66/188 (35.1%; 95% CI 28.9–41.3)	80/188 (42.6%; 95% CI 35.9–50.0)
Staphylococcus aureus (MSSA)	Blood	7/66 (10.6%; 95% CI 4.5–18.2)	5/66 (7.6%; 95% CI 1.5–13.6)	34/66 (51.5%; 95% CI 39.4–63.6)	20/66 (30.3%; 95% CI 19.7–42.4)
Staphylococcus aureus (MSSA)	Sputum	12/141 (8.5%; 95% CI 3.9–13.2)	25/141 (17.7%; 95% CI 12.1–24.0)	35/141 (24.8%; 95% CI 19.0–30.5)	69/141 (48.9%; 95% CI 44.4–54.1)
Staphylococcus aureus (MSSA)	Urine	6/65 (9.2%; 95% CI 2.9–16.7)	15/65 (23.1%; 95% CI 12.5–33.3)	12/65 (18.5%; 95% CI 8.3–29.0)	32/65 (49.2%; 95% CI 40.3–60.7)

Staphylococcus aureus (MSSA)	Wound	12/178 (6.7%; 95% CI 2.8–11.4)	13/178 (7.3%; 95% CI 3.3–11.9)	58/178 (32.6%; 95% CI 27.2–37.7)	95/178 (53.4%; 95% CI 48.9–58.3)

*Enterobacter species includes *Enterobacter asburiae*, *Enterobacter kobei*, *Enterobacter ludwigii*, *Enterobacter cancerogenus*, *Enterobacter gergoviae*, *Enterobacter spp*.

Variation across microorganism–specimen combinations

Table 5.1 summarises *AMROrbit* trajectory classifications at the level of country–organism–specimen–antibiotic trajectories. A higher proportion of spiral-out trajectories was observed in respiratory isolates for *Enterobacter cloacae* (24.1%), *Acinetobacter baumannii (*23.5%), *Pseudomonas aeruginosa* (21.8%) and urinary isolates for *Staphylococcus (MSSA)* (23.1%) and *Klebsiella aerogenes* (23.4%).

To evaluate the robustness of the scorecard to threshold selection, we performed a sensitivity analysis using region-specific median thresholds as alternative decision boundaries. We defined directional discordance as a direct reversal between the two most stewardship-relevant directional categories: spiralling-in under one thresholding approach and spiralling-out under the other, or vice versa. Reclassifications involving constant or mixed categories were not treated as directional reversals, but were considered changes in exact category assignment.

Using this definition, 5890 of 5920 trajectories showed directional concordance, corresponding to 99.49%. Direct reversal was uncommon, and only 12 trajectories changed from spiralling-in under global thresholds to spiralling-out under regional thresholds (0.20%), while 18 trajectories changed from spiralling-out under global thresholds to spiralling-in under regional thresholds (0.30%). Overall, 30 trajectories were directionally discordant, accounting for 0.51% of all trajectories.

These findings indicate that the principal directional interpretation of *AMROrbit* was largely robust to the use of global versus region-specific threshold boundaries, despite some exact category reclassification.

Early-warning insights

Tracking trajectories through *AMROrbit* can enable identification of directional deterioration in resistance velocity before large changes in absolute resistance burden are apparent, with the achievable time scale of detection determined by the temporal granularity and density of the underlying surveillance data. As an example, in Kuwait's *K. pneumoniae*-Amikacin-blood trajectory, Kuwait remained close to global median levels in the 2014–2017 window, with a stable or declining slope. However, in the subsequent 2015–2018 window, an increase in slope was observed, preceding a transition into a spiral-out trajectory and, later, into the high-risk quadrant (Q4). This example illustrates how changes in trajectory (velocity) can precede increases in baseline resistance (amplitude), providing an earlier signal of deterioration than static summaries. Figure 5.3 depicts the United Kingdom following a spiral-in trajectory consistent with improving resistance dynamics, whereas Kuwait exhibits a spiral-out trajectory indicating progressive deterioration.

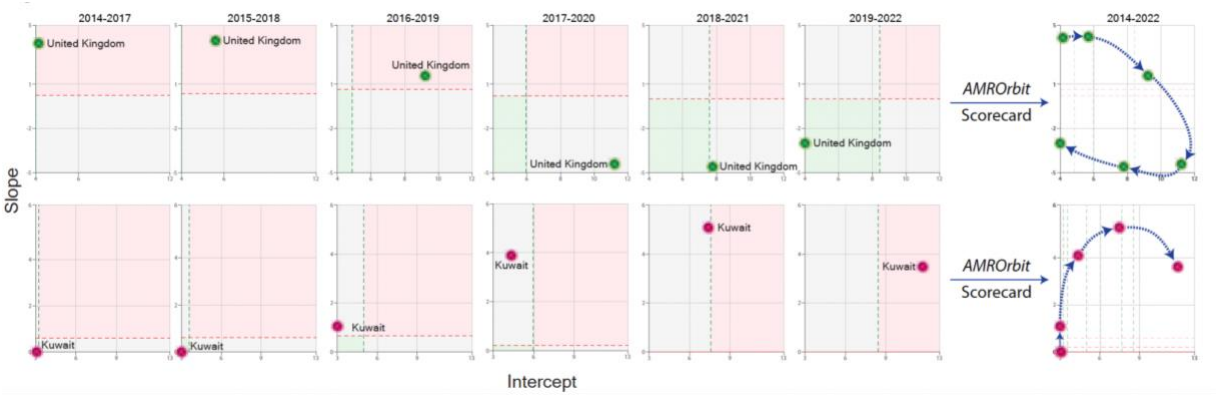


Figure 5.3- *AMROrbit* Scorecard. The X and Y axes represent Intercept (baseline resistance) and slope (rate of change). Country trajectories are classified into intuitive patterns: spiralling in (positive AMR containment), persistent resistance (remaining in the same quadrant), and spiralling out (negative AMR trajectory). The United Kingdom demonstrates a positive trajectory, while Kuwait's trajectory signals deterioration, shifting from Quadrant I to IV, indicating an urgent need for targeted intervention.

Open-source web-based interface for trajectory-based AMR analysis

To support widespread implementation across diverse clinical settings, we developed a web-based data-analysis suite with an end-to-end pipeline that transforms raw, standardized local susceptibility records into comprehensive analytics, including isolation rates, longitudinal resistance patterns, and *AMROrbit* scorecards (Figure 5.4). A core component of the suite is a flexible data-mapping module capable of harmonizing heterogeneous clinical datasets from varying laboratory information systems. Moreover, the web-based architecture allows for all computationally expensive modelling to be performed server-side, ensuring the tool remains fully functional on low-specification hardware with minimal compute resources.

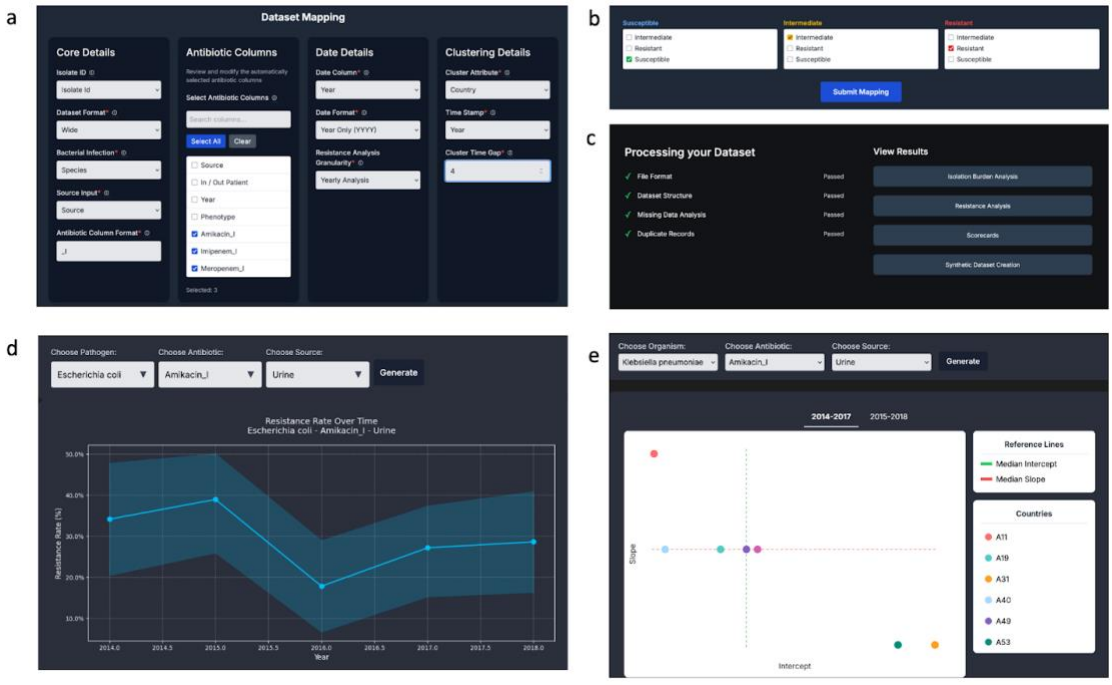


Figure 5.4. Screenshots illustrating the end-to-end workflow available at https://amrorbit.tavlab.iiitd.edu.in:3002 that enables researchers, hospitals, and public health agencies to apply the *AMROrbit* analytical framework to their own routine microbiology data. (a) Dataset and variable mapping interface for harmonizing core metadata, antibiotic columns, temporal information, and clustering attributes. (b) Mapping of antimicrobial susceptibility testing (AST) results to standardized susceptible, intermediate, and resistant categories. (c) Automated data quality checks and selectable analysis modules, including resistance analysis and scorecard generation. (d) Interactive visualization of longitudinal resistance trends for user-selected pathogen–antibiotic–specimen combinations. (e) Trajectory-based *AMROrbit* scorecard depicting country-level intercept (baseline resistance) and slope (temporal trend) relative to reference medians.

Some of the essential features are:

- Data Upload with consent: Users can upload their AST datasets in both long and wide formats with an embedded consent mechanism, ensuring compliance with ethical and data governance norms.
- Variable Mapping: This module allows for mapping user-specific variables as well as resistance categories (resistant, intermediate, susceptible) to the model's schema, allowing flexibility across diverse datasets. Automated Data Validation checks are provided for data completeness and structural consistency, reducing errors prior to analysis.
- Dynamic Visualizations and *AMROrbit* Scorecard: Users can generate resistance trend plots, isolation rate summaries, and *AMROrbit* scorecards through an interactive, no-code interface. The visual outputs include stratification options by organism, antimicrobial class, and time period, facilitating granular data exploration.

5.4 Discussion

AMROrbit extends the analysis of AMR dynamics through the joint representation of model-derived resistance level and temporal velocity within a longitudinal phase-space framework. Tracking these dimensions across successive windows permits differentiation of trajectories with comparable resistance levels but divergent temporal behaviour. The methodological contribution lies in translating this joint evolution into interpretable trajectory classifications, providing a consistent basis for comparative surveillance.

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Most of the conventional AMR outputs often emphasise either resistance prevalence at a given point or temporal trends estimated separately. While both are valuable, neither alone is sufficient for stewardship prioritisation. A high-resistance combination that is stable over time may require a different programmatic response from a lower-resistance combination that is worsening rapidly. *AMROrbit* addresses this interpretive gap by jointly representing baseline resistance burden and temporal velocity within a shared phase space structure. Applied to 5,920 country-level antibiotic–microorganism–specimen trajectories from the ATLAS dataset, *AMROrbit* showed that AMR trajectories were heterogeneous across countries, organisms, specimens, and antibiotics. Importantly, baseline resistance burden and temporal change did not always provide the same signal, some combinations had high resistance levels but relatively stable trends, whereas others had lower baseline resistance but increasing velocity. These findings suggest that *AMROrbit* can move beyond static descriptions of resistance burden and provide a compact framework for comparative AMR surveillance.

WHO GLASS provides an important reference for placing the *AMROrbit* findings within the broader surveillance context. The WHO Global Antibiotic Resistance Surveillance Report 2025 documented increasing resistance in more than 40% of monitored pathogen–antibiotic combinations during 2018–2023 (WHO, 2025). In the present ATLAS analysis, spiralling-out trajectories were more frequent than spiralling-in trajectories (17.7% versus 13.4%) among 5,920 country–organism–antibiotic–specimen trajectories during 2014–2022. This finding is broadly consistent with WHO's evidence of worsening resistance across multiple combinations.

These percentages represent different units of analysis and should not be compared numerically. The datasets differ in contributing sites, sampling structures, included combinations, specimen coverage and observation periods. Furthermore, *AMROrbit* classifications describe movement relative to amplitude and velocity thresholds, and amplitude is a model-derived parameter rather than a single-year prevalence estimate. The comparison therefore provides qualitative epidemiological context rather than external validation. *AMROrbit* complements existing prevalence and trend reporting by jointly representing resistance level and temporal velocity across successive windows, enabling interpretation of persistent high resistance, emerging deterioration and movement towards a more favourable resistance profile.

A more specific comparison is provided by the Kuwait K. pneumoniae–amikacin example. *AMROrbit* identified a spiral-out trajectory among blood isolates during 2014–2022. Al-Fadhli et al. (2026) reported increasing amikacin non-susceptibility in K. pneumoniae at Mubarak Al-Kabeer Hospital, from 2% in 2007 to 22% in 2022. This provides qualitative concordance with the deterioration identified by *AMROrbit*. Direct numerical comparison is inappropriate because the hospital study pooled specimen types, included intermediate isolates as non-susceptible, and covered a different period with reporting gaps. *AMROrbit's* methodological contribution is the

joint representation of resistance level and temporal velocity across successive windows, translating these estimates into interpretable trajectories for surveillance prioritisation. This illustrative comparison provides epidemiological context but does not constitute external validation.

AMROrbit should be viewed as complementary to the existing regression-based, dynamic time-series, and machine-learning approaches in AMR surveillance. While regression and time-series models remain essential for estimating temporal trends, examining antimicrobial consumption–resistance relationships, and supporting forecasts where sufficiently granular data are available. *AMROrbit* adds an interpretive layer that converts continuous estimates of resistance burden and temporal change into trajectory classes that can be compared across settings. This is operationally relevant since the same slope may have different implications depending on the baseline resistance state from which it emerges. Within an adaptive stewardship process, *AMROrbit* could support the tracking and reporting functions of an established hospital antimicrobial stewardship programme, while helping prioritise areas for clinical review. This proposed role aligns with the CDC Core Elements of Hospital Antibiotic Stewardship Programs, which connect accountable leadership and pharmacy expertise with action, monitoring, reporting and education. During local implementation, an adverse trajectory could be reviewed jointly by microbiologists, stewardship clinicians, pharmacists and infection-prevention personnel. The initial review would assess whether changes in testing, breakpoints, specimen composition or patient mix might explain the signal. Where the pattern remained concerning, the team could examine prescribing and consumption data and select an appropriate response, such as targeted prescription audit and feedback, review of local treatment guidance, or investigation of possible transmission. Evaluation would assess whether the scorecard changed review priorities or prescribing practice, alongside

patient-safety outcomes. Subsequent resistance trends would require cautious interpretation because changes cannot automatically be attributed to the intervention.

The ATLAS application illustrates this distinction. Antibiotic–microorganism–specimen combinations classified as spiralling-out may identify settings where resistance is high, increasing, or both, and therefore may warrant closer stewardship review. Persistent high-resistance trajectories may indicate combinations where existing stewardship measures need to be maintained or strengthened, while spiralling-in trajectories may help identify contexts where resistance is moving in a favourable direction and where local practices may warrant further examination. Low-amplitude but increasing-velocity trajectories may also be useful as early-warning signals, as they can identify emerging increases in resistance that may not yet be evident from prevalence-based thresholds alone. From a stewardship perspective, these classifications are best interpreted as prioritisation signals rather than prescriptive treatment rules.

The thresholding strategy is an interpretive choice. Global medians were used in the primary analysis to provide a common reference frame for cross-country comparison. However, global thresholds may not fully reflect regional epidemiology, surveillance practices, or stewardship priorities. The regional-median sensitivity analysis showed that some classifications changed when countries were compared within a more local comparator distribution, although direct reversal between spiralling-in and spiralling-out trajectories was uncommon. This suggests that the main directional signal was generally stable, but that *AMROrbit* labels should be interpreted in relation to the thresholding frame used. Global thresholds may be useful for international benchmarking, whereas regional or local thresholds may be preferable for programme-level stewardship decisions.

Our approach has some limitations. First, the present ATLAS-based analysis was conducted at annual granularity. Because each antibiotic–microorganism–specimen–country series contained a limited number of yearly observations, we did not impute missing annual values. Instead, *AMROrbit* was applied to combinations with complete longitudinal data to avoid introducing model-dependent artefacts into the estimation of resistance trajectories. This conservative approach supports consistent comparison across included combinations, but may under-represent countries, organisms, specimens, or antibiotics with sparse or intermittent reporting. Second, the ATLAS dataset provides a large, standardised, multi-country AMR dataset suitable for demonstrating the *AMROrbit* scorecard, but the resulting trajectories should not be interpreted as fully nationally representative estimates for every included country. Resistance patterns may reflect participating surveillance sites, submitted isolates, patient populations, specimen distribution, diagnostic practices, and antibiotic testing panels within ATLAS. Therefore, *AMROrbit* classifications derived from this dataset should be interpreted as dynamic patterns among analyzable country-level series in ATLAS, rather than as definitive national resistance rankings. Third, although *AMROrbit* was demonstrated here using annual ATLAS data, the scorecard is adaptable to datasets with finer temporal granularity and different geographic levels. In hospital, regional, or national surveillance systems with more granular AST data, missingness could be addressed using pre-specified imputation, smoothing, or sensitivity-analysis approaches before trajectory estimation, provided these choices are appropriate to the data structure, missingness mechanism, and reporting process. The generalizability of *AMROrbit's* outputs will therefore depend not only on the scorecard itself, but also on local data quality, sampling structure, microbiology practices, breakpoint standards, temporal resolution, and stewardship context. Prospective implementation in locally governed surveillance systems will be needed to assess

whether the classifications are stable, actionable, and useful for stewardship review. We are currently implementing *AMROrbit* in two tertiary care hospitals, AIIMS and MAX in New Delhi, which will allow future assessment of its feasibility, interpretability, and operational utility in local stewardship workflows. A further limitation is that resistance-mechanism-specific annotation was not consistently available in ATLAS. For example, although *E. cloacae* complex is highly relevant for chromosomal AmpC-mediated resistance, only a small subset of isolates had known AmpC data. This precluded reliable temporal modelling of AmpC-specific trajectories. *AMROrbit* could be extended to such mechanism-specific surveillance questions where phenotypic or genomic resistance annotations are sufficiently complete over time.

5.5 Acknowledgements

This analysis is based on research using an anonymised dataset from Pfizer ATLAS obtained from https://amr.vivli.org.

5.6 Code availability

All custom scripts and code for the *AMROrbit* scorecard presented in this study are publicly available on the GitHub repository at https://github.com/tavlab-iiitd/AMROrbit. The real-time dashboard and a web-based application to build custom scorecards are available at https://amrorbit.tavlab.iiitd.edu.in:3002.

Chapter 6: Operationalising AMR intelligence: the *AMRSense* ecosystem for community-linked surveillance and stewardship

6.1 Rationale and Positioning

The preceding chapters of this thesis developed analytical approaches for transforming routinely generated antimicrobial susceptibility testing data into interpretable surveillance intelligence. Chapters 3 and 4 demonstrated that routine microbiology data can be used to estimate resistance burden, temporal change, demographic and geographic heterogeneity, and community- versus hospital-associated resistance patterns. The *AMROrbit* framework then extended the analytical framework by characterising both resistance burden and temporal velocity to identify AMR trajectories. However, a contextual barrier in understanding these patterns was the lack of integrated data on community antibiotic exposure, antibiotic use, pharmacy access, prescription practices, diagnostics, care-seeking behaviour, infection-prevention practices, and awareness of AMR. Consequently, with the analytical approaches, our surveillance systems may identify a rising resistance signal, but without adequate contextual information on why that signal is emerging or which intervention pathway is most plausible. Understanding AMR in resource-constrained settings requires attention to the wider social, economic and health-system context (Sulis et al., 2022). Stewardship therefore requires context-specific actions that promote responsible antimicrobial use (Dyar et al., 2017).

AMRSense was designed as a response to this translation problem in continuation of the work of this thesis. While the earlier chapters asked how AMR surveillance data can be modelled to reveal temporal and strategic patterns, this work identifies the ecosystem solution required for such patterns to become operationally useful. Here, operational intelligence refers to the conversion of heterogeneous AMR-relevant data into timely, interpretable, and locally actionable signals for surveillance, stewardship, community awareness, and policy prioritisation.

This chapter is a translational and systems-design chapter that presents the conceptual architecture through which the analytical methods developed earlier in the thesis are being embedded into an implementation-oriented AMR intelligence system while documenting the present state of the work.

6.2 Conceptual Architecture of *AMRSense*

AMRSense is architecturally organised around four interlocking data layers, each addressing a distinct dimension of the AMR problem, intended to inform the proposed multidimensional scorecard, AMRaura. The design philosophy is grounded in the principle that no single data source is sufficient to characterise the full AMR landscape, resistance trends in clinical isolates, antibiotic prescribing behaviour in community settings, population-level awareness, and commercial sales dynamics, each of which captures a distinct and partially independent signal. The four layers are: (i) an Awareness and Behaviour-Change Layer, which captures knowledge, attitudes and reported practices among participating respondents;

(ii) a Longitudinal Health Record and Community Data Layer, which enables structured data collection by community health workers, including extraction of antibiotic information from

handwritten prescriptions using vision-language models and linkage of beneficiary records through the national Ayushman Bharat Health Account (ABHA) identity framework;

(iii) an Antimicrobial Access and Use Layer, which integrates prescription-based aggregated pharmacy sales and prescription data contributed by Tata 1mg to generate granular, pincode-level insights into antibiotic consumption patterns and World Health Organization (WHO) AWaRe classification compliance; and

(iv) a Hospital and Laboratory AMR Surveillance Layer, which adds the hospital-level resistance patterns from IAMRSN reports and TATA 1mg laboratories.

Research, pharmaceutical and private laboratory datasets can complement routine AMR surveillance, provided their quality, accessibility and comparability are assessed (Ashley et al., 2019). *AMRSense* is being developed to establish an integrated baseline evidence base for understanding AMR in the intended implementation settings. Some relevant information may already exist within separate laboratory, clinical, pharmacy or administrative systems, while other dimensions require new data collection. The name *AMRSense* reflects its intended purpose: to "sense" AMR at the community level by triangulating complementary data sources, each necessarily imperfect in the face of substantial gaps in community-level AMR surveillance.

Laboratory surveillance describes resistance among tested clinical isolates; community records and prescriptions provide information on reported antibiotic exposure and care-seeking, pharmacy data capture aspects of antibiotic access and purchasing, and KAP assessments describe knowledge, attitudes and reported practices. ASHA KAP assessments are intended to identify training needs for awareness, documentation and referral activities and they do not measure antibiotic dispensing or represent community-wide knowledge. ABHA provides a mechanism for

linking consenting beneficiaries' records over time, rather than a separate knowledge measure. Tata 1mg data capture prescription-based sales only and do not include OTC purchases. Its users may differ from UPHC attendees, and a shared pincode does not establish population comparability. Comparisons would therefore require assessment of population coverage and alignment of geography and observation periods. Community questions on self-medication and care-seeking provide partial information about antibiotic acquisition outside documented prescriptions, but comprehensive measurement of non-prescription purchasing remains an evidence gap. Each source provides a partial perspective. *AMRSense* aims to generate missing information and bring these perspectives into a shared analytical framework, while retaining their distinct populations, coverage, denominators and time periods. Triangulation would examine both agreement and divergence between sources to identify patterns requiring further investigation.

This rationale is consistent with Gautham et al.'s work, which situates antibiotic practices within interacting individual, community, provider, pharmaceutical and regulatory contexts (Gautham et al., 2021; 2024). Such perspectives support collecting information across these dimensions rather than assuming that resistance patterns or awareness scores alone adequately describe the local AMR context.

The immediate contribution of *AMRSense* is therefore the development of a contextual evidence base. This could inform locally appropriate stewardship priorities, identify stakeholders requiring engagement and provide a baseline for subsequent evaluation. Community health workers would support awareness, documentation and linkage to care, while interpretation of prescribing and access concerns would require engagement with medical officers, qualified pharmacy personnel and programme managers. Establishing this evidence base does not itself demonstrate changes in prescribing, behaviour or resistance outcomes.

6.3 Awareness and Behaviour-Change Layer

6.3.1 Conceptual Basis

Effective stewardship at the population level requires concurrent monitoring of the awareness, attitudes, and practices of the populations that generate antibiotic demand. Community antibiotic practices reflect interactions between knowledge and beliefs, affordability, access to care, provider practices and wider health-system conditions (Gautham et al., 2021; 2024). The Awareness and Behaviour-Change Layer is therefore designed as an intervention and measurement framework that includes the Infection Escape game, AI-generated AMR awareness videos, embedded quizzes, and a Delphi-validated KAP instrument, which are positioned as structured tools for awareness generation, engagement, and longitudinal assessment.

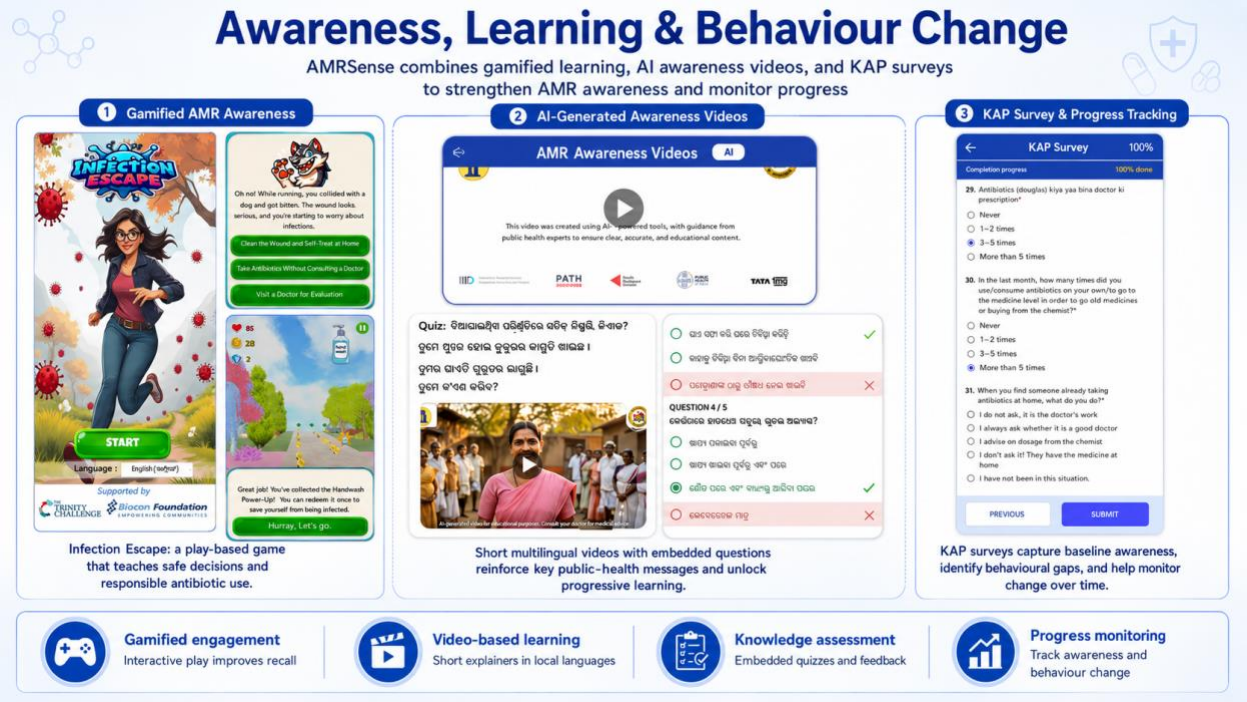


Figure 6.1 Prototype awareness and behaviour-change layer of *AMRSense*, showing gamified AMR education, AI-generated multilingual awareness videos with embedded quizzes, and KAP survey-based progress tracking.

6.3.2 Infection Escape: Gamified AMR Awareness

The Infection Escape (Figure 6.1) game is an interactive, multi-lingual, scenario-based mobile game in which the player navigates decision points that simulate everyday situations involving infection risk and antibiotic use. Players encounter scenarios such as sustaining a wound after contact with an animal and are presented with response options, including self-treatment at home, self-administration of antibiotics, or consultation with a physician, each carrying consequences that unfold within the game narrative. The game also incorporates reward elements, including collectable power-ups awarded for correct decisions that reinforce prosocial antibiotic behaviours and sustain engagement across multiple play sessions.

6.3.3 AI-Generated Awareness Videos with Embedded Quizzes

The awareness component also has built-in AI-generated videos on AMR awareness in both English and Kannada. Each video is paired with an embedded quiz that assesses comprehension of the presented content and gates progression to the subsequent module, creating a structured, adaptive learning pathway. The quiz responses are captured within the *AMRSense* data infrastructure as a time-stamped record of individual-level awareness scores, permitting longitudinal assessment of knowledge change across the intervention period. This design renders the video-quiz component simultaneously an educational intervention and a measurement instrument, reducing the burden of separate KAP assessment activities while generating continuous tracking data.

6.3.4 Delphi-Validated KAP Survey Instrument

A questionnaire for measuring the Knowledge, Attitude and Practices of AMR in the community health workers (Figure 6.1) was developed through a comprehensive Delphi process engaging public health experts, clinical microbiologists, social scientists, and community health practitioners. To our knowledge, it is the first Delphi validated tool from India, capturing KAP in CHWs, including awareness of antibiotic function and the concept of resistance, self-reported antibiotic use behaviours (including non-prescription purchase and incomplete course completion), attitudes toward seeking physician advice for common infections, and practices regarding storage and disposal of unused antibiotics. The KAP survey is embedded within the *AMRSense* application and is administered at enrolment and at regular follow-up intervals, generating longitudinal data that will serve as both the primary outcome measure for the behaviour-change evaluation and an independent data stream for the AMRaura composite score.

6.3.5 Limitations

The Awareness Layer will provide (i) individual-level KAP scores, (ii) game engagement metrics, and (iii) video completion and quiz accuracy rates, which track knowledge acquisition across the educational pathway. However, several limitations of this layer merit acknowledgement. The KAP data are self-reported and are subject to social desirability bias, particularly when community health workers administering the survey are perceived by respondents as authority figures. Also, the awareness components are currently available in English and Kannada. Moreover, the causal attribution of observed KAP change to the AMRSense intervention rather than to concurrent public communication campaigns or secular trends will require a controlled evaluation design that is currently being planned.

6.4 Longitudinal Health Record and Community Data Layer

In India, AMR surveillance remains largely centred on laboratory-confirmed resistance identified in formal healthcare settings, while the selection pressures that drive resistance also build up across outpatient prescribing, antibiotic dispensing, and community antibiotic use. The Community Data Layer of *AMRSense* is designed to generate baseline evidence on AMR in community settings. The layer encompasses a data collection form with integrated ABHA IDs (Ayushman Bharat Digital Mission) for longitudinal health records and a built-in prescription upload tool with vision-language model-assisted antibiotic extraction.

The *AMRSense* community data collection instrument is a structured data collection form capturing sociodemographic characteristics, recent illness episodes, self-medication practices, healthcare seeking behaviour and treatment-related practices, including whether a physician was consulted and, if so, what treatment was prescribed; antibiotic name and dosage when ascertainable; adherence to the prescribed regimen; and disposal practices for unused medication.

A significant technical contribution here is the prescription-digitisation capability for extracting antibiotic information from handwritten prescriptions. Rather than adopting a digitisation architecture by assumption, a systematic model-benchmarking study was conducted to identify the most suitable extraction approach for field deployment (unpublished work; a dedicated benchmarking manuscript is in preparation). A curated evaluation corpus of expert-annotated, real-world prescription images was constructed for this purpose, supplemented with publicly available prescription images and expanded through controlled augmentation to yield a substantially larger

benchmark set. Three architectural paradigms were evaluated: (i) a standalone vision-language model (VLM) direct-pass architecture, which passes the prescription image to a single multimodal model that performs text recognition and antibiotic entity resolution in one step. (ii) a modular OCR-plus-language-model pipeline, couples a dedicated OCR engine for text transcription with a downstream medical-domain large language model performing named-entity recognition and normalisation. (iii) a hybrid VLM-plus-LLM pipeline, which employs a VLM encoder to generate a structured transcript that is subsequently normalised by a medical large language model. Candidate configurations spanned several open multilingual VLMs and medical-domain LLMs, and were assessed on both extraction accuracy and inference latency, and the best-performing configuration identified through this benchmarking has been deployed (unpublished work).

The workflow, as implemented in the *AMRSense* framework, proceeds through five stages as described in Figure 6.2. In the first stage, the ASHA worker or household member captures an image of the prescription using the device camera or uploads an existing photograph. In the second stage, the image is transmitted to the *AMRSense* server, where AI scanning extracts text from the prescription image. In the third stage, detected medicine names are presented to the user for review and editing, with the interface displaying extracted names alongside options to confirm, delete, or manually add items. In the fourth stage, the user confirms the final list of medicines, which is cross-referenced against a curated antibiotic formulary to identify and flag antimicrobial agents. In the fifth stage, the confirmed prescription record, now structured and computable, is appended to the patient record and marked as ready for AMR analytics.

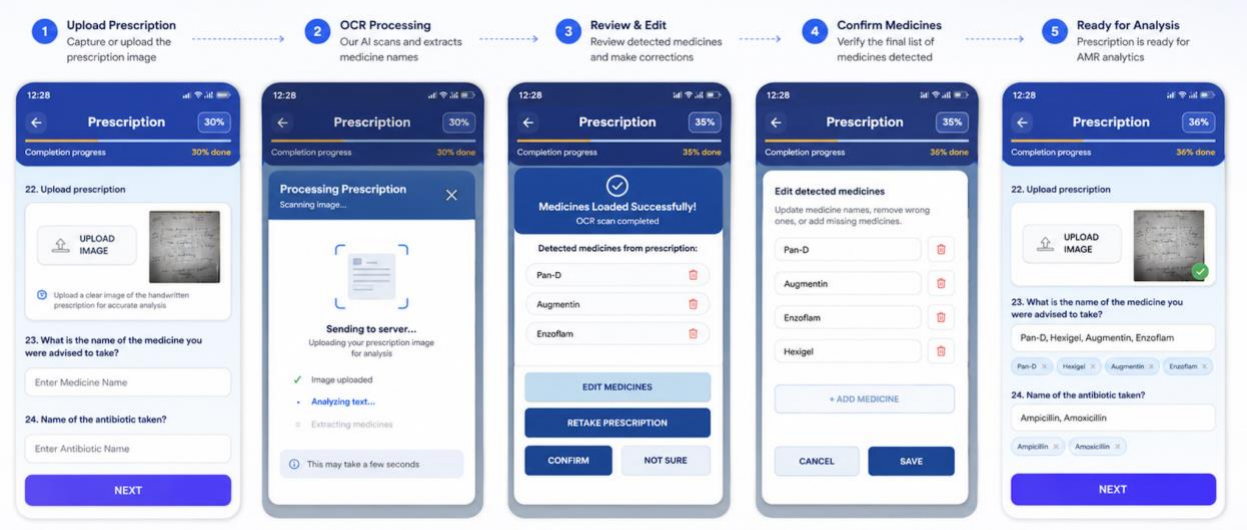


Figure 6.2 Workflow for converting handwritten prescriptions into structured antibiotic-use data through OCR-assisted extraction and user validation in AMRSense.

The community data layer is designed to align with the Ayushman Bharat Digital Mission (ABDM) framework, including the option of linking beneficiary records through an Ayushman Bharat Health Account (ABHA) identifier where appropriate consent and local implementation approvals are in place (Figure 6.3).

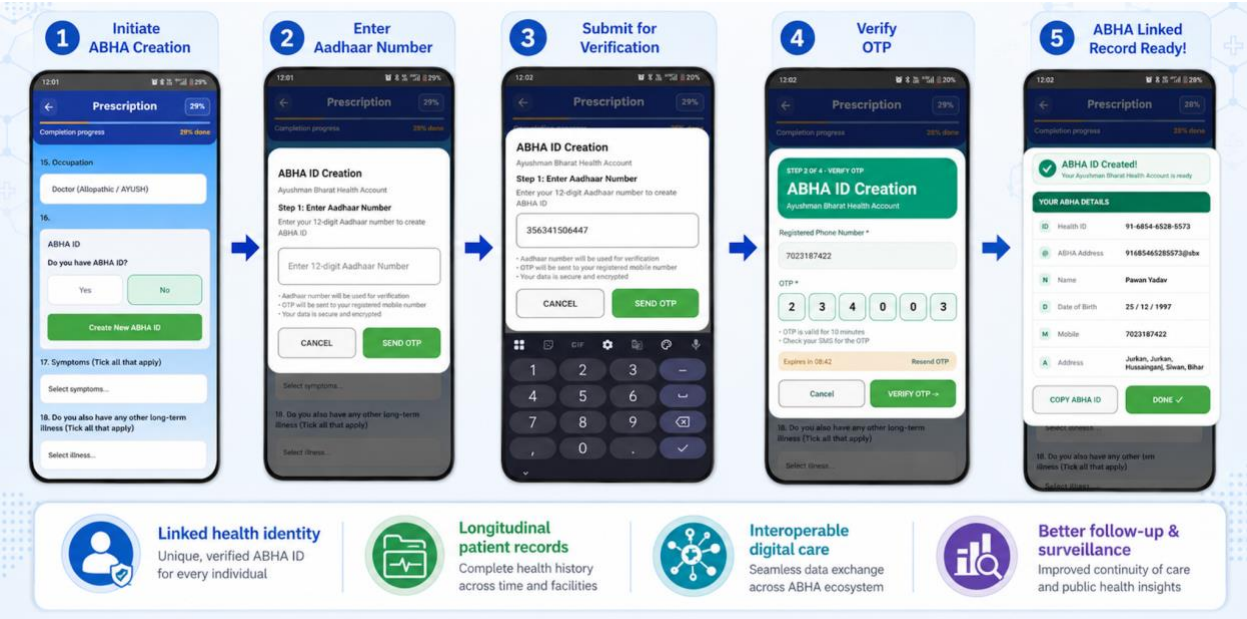


Figure 6.3 ABHA-enabled patient identity linkage workflow in *AMRSense*, illustrating assisted ABHA ID creation/linkage and its intended role in building longitudinal, interoperable health records.

The form has been iteratively refined through human-centred design workshops conducted with ASHA workers and medical officers in Bangalore. The community data collection tool is planned for deployment across 40 Urban Primary Health Centres (UPHCs) within the Greater Bengaluru South Corporation jurisdiction and is to be tested with 230 ASHA workers and 40 medical officers by 2027, intended to be among the first systematic community-level AMR data collection efforts at this scale in an Indian urban setting.

6.5 Antimicrobial Access and Use Layer

Pharmaceutical sales data have been used to describe antibiotic-use patterns by WHO AWaRe category, providing a precedent for descriptive analysis of the Tata 1mg sales dataset (Hsia et al., 2019; World Health Organization, 2023) The Antimicrobial Access and Use Layer operationalises antibiotic sales and prescription data through an interactive dashboard that enables policy-relevant analysis at the pincode level. The prototype dashboard demonstrates the analytical capability of this layer across a sample of Greater Bengaluru at the pincode level (Figure 6.4). For each pincode, it computes antibiotic usage normalised per 1,000 individuals per day, ranks pincodes to surface emerging high-consumption hotspots, decomposes consumption by individual agent to identify the locally dominant antibiotics, and tracks week-on-week change to flag rapidly escalating localities for prioritised investigation. Companion panels present monthly resistance trends for selected agents and the AWaRe-category composition of local consumption. The specific values displayed

in the current prototype derive from a development dataset and are illustrative of the dashboard's analytical functions rather than validated epidemiological findings; the analytic outputs of this layer form part of the in-progress and as-yet-unpublished *AMRSense* work. They are expected to under-represent populations with limited digital access, lower e-pharmacy use, rural residence, or reliance on informal and brick-and-mortar providers. For this reason, Tata 1mg-derived indicators are interpreted as platform-based stewardship signals and are not treated as direct measures of community antibiotic burden without further adjustment, triangulation, and validation against other data sources.



Figure 6.4 Official-facing *AMRSense* dashboard prototypes showing pincode-level antibiotic-use monitoring, AWaRe-category summaries, comparative usage indicators, and longitudinal resistance-trend visualisation for stewardship prioritisation.

6.6 Hospital and Laboratory AMR Surveillance Layer

The Hospital and Laboratory AMR Surveillance Layer provides microbiological evidence on resistance among tested clinical isolates. Interpretation must account for diagnostic access and clinical sampling practices, which influence the representativeness of routine microbiology data (Lim et al., 2021).This layer ingests structured AST data from hospital microbiology laboratories, including IAMRSN-affiliated institutions and TATA 1mg laboratories in Karnataka.

The structured AST data flowing through this layer are processed to generate the trajectory-based resistance profiles required by *AMROrbit*, the stewardship intelligence tool developed in Chapter 5.

6.7 Current Status and Prototype Maturity

The *AMRSense* app prototype is now ready for deployment across 40 UPHCs in the Greater Bengaluru South Corporation, to be tested with 230 ASHA workers, 40 medical officers by the end of the award. We recently received the Health Ministry Screening Committee approvals and have completed the pilot testing of the application. The ecosystem will soon be rolled out in selected geographies in Bangalore.

***AMRSense* component**	**Current status**
Awareness videos	Content developed in Kannada and English, with embedded quizzes in the *AMRSense* application.
Infection Escape game	Game-based AMR awareness developed as an engagement tool within *AMRSense* application.

KAP survey	Delphi-validated KAP instrument developed and embedded into the *AMRSense* data-collection workflow.
Community health-record form	Mobile-based data-collection form co-developed with ASHAs and pilot tested.
Prescription image upload and extraction	VLM-assisted prescription extraction model added in the *AMRSense* app.
ABHA-enabled longitudinal linkage	ABHA integration built inside the app.
Tata 1mg access/use analytics	Aggregated platform-based antibiotic access/use analytics added as a contextual data stream.
Hospital/laboratory AST layer	Data from IAMRSN reports and TATA 1mg labs added and analysed.
AMRaura scorecard	Proposed multidimensional integration framework
Governance and field deployment	HMSC approval received; selected Bangalore geographies planned for rollout.

6.8 Chapter Summary

This chapter has presented *AMRSense* as the translational operationalisation of the doctoral research described in Chapters 3 through 5, documenting the pathway from academic AMR surveillance analytics to a functioning, multi-layer operational intelligence ecosystem recognised through joint second-prize placement in the Trinity Challenge on Antimicrobial Resistance 2024.

The chapter has articulated the rationale for *AMRSense* as a response to the structural data gap that limits AMR stewardship in India, i.e. the absence of integrated, community-level intelligence linking resistance trends in clinical institutions with antibiotic use patterns, awareness levels, and

prescribing behaviour in the communities from which those clinical cases arise. This rationale is consistent with research describing antibiotic practices as embedded within interacting individual, community, provider and health-system contexts (Gautham et al., 2021; 2024). Ebata et al. (2025) emphasise the complementary importance of biomedical guidance, local infection and resistance information, and patients' personal and social circumstances in antibiotic decisions. This provides further conceptual support for developing contextual evidence alongside surveillance outputs. It has described the conceptual architecture of *AMRSense* as a four-layer federated ecosystem, and provided detailed accounts of each layer: the Awareness and Behaviour-Change Layer, encompassing the Infection Escape game, AI-generated multilingual videos with embedded quizzes, and the Delphi-validated KAP instrument the Longitudinal Health Record and Community Data Layer, encompassing the ASHA worker data collection form, the OCR-VLM prescription extraction pipeline, and ABHA-linked longitudinal record creation; the Antimicrobial Access and Use Layer, encompassing Tata 1mg pharmacy sales analytics with pincode-level WHO AWaRe category (World Health Organization, 2023); and the Hospital and Laboratory AMR Surveillance Layer, encompassing WHONET-compatible AST data ingest and *AMROrbit*-compatible trajectory generation.

Further validation will include formative research with ASHAs, community members, medical officers, pharmacists and intended data users. Interviews, group discussions and observation of existing workflows will explore antibiotic-access pathways, users' information needs, acceptability, data-collection burden and interpretation of the proposed outputs. These findings will inform refinement of the instruments, implementation workflow and feedback mechanisms before wider deployment, including approaches to capturing non-prescription antibiotic

acquisition. This planned approach is consistent with complex-intervention guidance emphasising context, stakeholder engagement, feasibility and iterative refinement (Skivington et al., 2021)

The AMRaura integration framework has been proposed as the analytical spine that synthesises signals across all four layers into a composite multidimensional stewardship intelligence score, with *AMROrbit* trajectory outputs from Chapter 5 constituting one of its four constituent dimensions.

AMRSense therefore establishes a pathway for developing the contextual evidence needed to inform future stewardship action, while the proposed AMRaura integration and its operational usefulness require further development and evaluation.

Chapter 7: Conclusion and Future Directions

7.1 Conclusion

Although AST data are produced every day across hospital laboratories, their use often remains confined to cumulative antibiograms or periodic reports. This thesis addresses a central limitation in contemporary AMR surveillance, i.e the gap between the generation of routine microbiology data and its translation into timely, interpretable, and actionable stewardship intelligence. The early chapters established the conceptual and public health foundation for AMR surveillance and stewardship, including the need to interpret resistance patterns within broader health-system and development contexts. The analytical chapters then examined longitudinal resistance trajectories, early warning signals, and interpretable scorecard-based methods for stewardship prioritisation. The final translational chapter extended this work into the *AMRSense* ecosystem, which positions AMR intelligence not as a single dashboard or data-capture application, but as an integrated framework linking awareness, community-level engagement, longitudinal health records, laboratory data, hospital reports, prescription and sales signals, and multidimensional risk scoring.

The central argument of this thesis is that AMR surveillance should include the direction, velocity, and context of resistance change for proactive stewardship. A high resistance burden that is stable may require a different response from a moderate resistance burden that is rapidly increasing. Similarly, a hospital-level resistance signal may have different implications when interpreted alongside community antibiotic use, prescribing behaviour, self-medication practices, and awareness levels. The broader contribution of this thesis is therefore not only empirical, but

translational as it shows how routinely generated AMR data can be transformed into more dynamic, locally relevant, and action-oriented intelligence.

7.2 Synthesis of Key Findings

7.2.1 Foundations: from AMR surveillance to stewardship intelligence

AMR is a complex phenomenon affected by antimicrobial exposure, infection burden, healthcare access, laboratory capacity, prescribing behaviour, community practices, and broader health-system conditions. The background chapters positioned AMR as a complex public health challenge where resistance proportions are conditional estimates depending on who is tested, where cultures are performed, which specimens are submitted, how isolates are deduplicated, what breakpoints are applied, and how hospitals differ in case-mix and laboratory practices. These factors define the methodological caution required when transforming surveillance data into stewardship recommendations. Within this framing, SDG and health-system indicators are used as contextual background to support the argument that AMR trajectories are embedded within broader development, health-system, and infrastructure conditions.

7.2.2 Longitudinal AMR trajectories

The first major analytical contribution of the thesis was the characterisation of longitudinal AMR trends using multicentric IAMRSN data. Across bloodstream and urinary tract infections, the analysis showed that AMR in India is dynamic, pathogen-specific, and geographically heterogeneous. The findings demonstrated sustained increases in resistance among major Gram-negative pathogens, particularly for clinically important antibiotic classes such as carbapenems.

This chapter answered the descriptive question: what is happening to AMR over time? Do the trends differ across geographies? How are AMR patterns associated with state-level SDG performance? Its contribution was to move beyond single-period resistance estimates and show that resistance burden must be interpreted as a trajectory. A national average may conceal divergent local patterns; similarly, a high resistance proportion may have different implications depending on whether it is increasing, decreasing, or stable. The chapter, therefore, established the empirical foundation for a trajectory-centred approach to AMR surveillance.

The findings also reinforced the need for local stewardship intelligence. Resistance patterns differed across organisms, antibiotics, infection syndromes, hospitals, and geographical zones. Such heterogeneity limits the usefulness of generic stewardship recommendations based only on national-level summaries. Instead, stewardship programmes require tools that can identify locally relevant drug–bug combinations and distinguish long-standing high-burden problems from emerging high-momentum threats.

7.2.3 Early-warning signals and indicator antibiotics

The second analytical contribution examined whether routine AMR data contain signals that may precede future resistance changes. Lead–lag analyses were used to explore temporal relationships between resistance trajectories of different antibiotics and between community-acquired and hospital-acquired infections. This shifted the surveillance question from only what is happening now to what may be beginning to change. The analysis suggested that, in some settings, resistance to selected antibiotics may precede changes in resistance to clinically important agents, including carbapenems. These findings support the concept of indicator antibiotics: organism–antibiotic combinations that may provide earlier signals of increasing resistance pressure. In resource-

constrained surveillance systems, such indicators may be useful for prioritising monitoring efforts, especially when continuous high-resolution analysis of all possible organism–antibiotic combinations is not feasible.

However, the temporal precedence should not be interpreted as causality. A leading resistance signal may reflect shared antibiotic exposure, co-selection, laboratory testing practices, patient referral patterns, infection control dynamics, or unmeasured institutional factors. The chapter also showed that AMR movement across the hospital–community interface is not necessarily one-directional. Some signals appeared hospital-leading, while others appeared community-leading. This finding supports a more integrated view of AMR surveillance, where hospitals and communities are connected reservoirs of resistance selection and transmission rather than separate epidemiological spaces.

7.2.4 *AMROrbit*: translating resistance trajectories into stewardship prioritisation

The third major contribution was the development of *AMROrbit* as an interpretable framework for converting routine AST data into stewardship-relevant intelligence. *AMROrbit* uses two simple but operationally meaningful dimensions: baseline resistance burden and velocity of change. Together, these dimensions allow organism–antibiotic combinations to be placed into a phase-space scorecard that distinguishes high-burden, rapidly worsening, stable, emerging, and lower-priority resistance patterns.

The importance of *AMROrbit* lies in its shift from descriptive reporting to prioritisation. Traditional antibiograms usually answer the question: what proportion of isolates are resistant?

AMROrbit extends this by asking: which resistance patterns are already severe, which are worsening, and which require urgent attention because of their current position and momentum? This distinction is directly relevant for antimicrobial stewardship committees, microbiologists, infection-control teams, and programme managers as a moderately resistant organism–antibiotic combination with rapid upward velocity may represent a more urgent stewardship signal than a highly resistant combination that has remained stable over several years. Conversely, a high but stable resistance pattern may require sustained policy attention but not necessarily the same escalation as a rapidly worsening pattern. By making this distinction visible, *AMROrbit* provides a structured way to convert routine surveillance data into interpretable decision-support outputs.

AMROrbit also addresses an implementation gap. Many institutions generate AST data but lack advanced analytical capacity to perform repeated trajectory modelling, trend classification, and visual prioritisation. A no-code scorecard framework can lower this barrier and make trajectory-based surveillance more accessible to hospital laboratories and stewardship teams.

7.2.5 *AMRSense*: from analytical intelligence to an operational ecosystem

The final translational contribution of the thesis is the *AMRSense* ecosystem. *AMRSense* extends the trajectory-centred logic of the earlier chapters into a broader operational framework for AMR awareness, community surveillance, longitudinal health records, data integration, and multidimensional risk scoring.

AMRSense should be understood as an ecosystem solution with four interconnected layers. The awareness layer includes AI-generated multilingual videos, the Infection Escape game, embedded quizzes, and a Delphi-validated KAP instrument. These components are designed to support

awareness generation, structured engagement, and measurement of knowledge, attitudes, and practices related to antibiotic use and AMR to understand the behaviour change. The sales and prescription layer brings together prescription and sales data from one of the largest online pharmacy platforms. The community data layer aims to connect individual and community-level AMR-relevant information through structured data capture, including the *AMRSense* form and potential ABHA-linked continuity of records. Thus, moving beyond one-time awareness activities toward repeated, longitudinal observation of antibiotic exposure, symptoms, care-seeking, diagnostic testing, and treatment behaviour. The hospital and laboratory layer adds on information on resistance patterns in hospital settings. AMRaura is the proposed multidimensional scorecard wherein all these components are integrated. While *AMROrbit* focuses primarily on resistance burden and velocity, AMRaura is positioned as a broader scorecard that may combine resistance trajectories with awareness, prescribing behaviour, self-medication, access, diagnostic, and contextual indicators. Therefore, *AMROrbit* provides the analytical core for resistance momentum, while AMRaura extends the framework toward a more comprehensive stewardship and public health intelligence layer.

7.3 Original Contribution of the Thesis

Contribution type	Original contribution	Evidence and validation	Chapter
Empirical	Multicentre longitudinal characterisation of AMR across BSI and UTI, including temporal, demographic, geographic and healthcare-associated variation	IAMRSN data from participating tertiary-care centres; published BSI and UTI studies	Chapter 3
Methodological	Systematic examination of lead–lag relationships between antibiotic-	Differenced monthly time series and exploratory cross-correlation	Chapter 4

	resistance trajectories across organisms and healthcare settings	analyses reported in the BSI and UTI studies	
Methodological and software	Development of *AMROrbit*, which jointly represents resistance burden and velocity and classifies longitudinal resistance trajectories	Multicountry ATLAS analysis, sensitivity analysis, open-source code and web implementation; accepted in JAC-AMR	Chapter 5
Translational	Design of *AMRSense* as a pathway for connecting analytical surveillance outputs with awareness, community, prescription and institutional data	Implemented components, internal prototypes and planned integrations, each identified by maturity status	Chapter 6

These thesis contributions establish a progression from describing AMR patterns, to detecting candidate temporal signals, to prioritising resistance trajectories, and finally to specifying how these outputs may be operationalised for surveillance and stewardship. The central contribution of the thesis is therefore not any individual dataset or paper, but the integration of these empirical, methodological and translational components into a trajectory-centred and action-oriented framework.

7.4 Limitations

7.4.1 Data and representativeness limitations

Several limitations arise from the nature of the datasets used. The IAMRSN analyses were based on passive surveillance data generated through routine clinical care and reflect patients who were tested in participating hospitals. This, therefore, does not represent the true population-level burden of AMR in India. Patients with severe infections, prior antibiotic exposure, treatment failure, referral histories, or tertiary-care access are likely to be over-represented. The findings should

therefore be interpreted as describing important resistance trajectories within hospital and hospital-linked settings, not as direct national burden estimates.

The use of contextual indicators also has limitations. SDG and health-system indicators are aggregated at the state level and may not reflect within-state heterogeneity, temporal changes during the surveillance period, or district-level differences in health access, sanitation, diagnostic capacity, and antibiotic availability. These indicators are useful for framing AMR within broader development and health-system contexts, but they cannot establish causal relationships with resistance trajectories.

For *AMRSense*, digital and platform-derived data streams also require caution. Prescription, sales, diagnostic, and community-app data may reflect differential platform penetration, smartphone access, literacy, urban bias, health-seeking behaviour, and user engagement. These sources can generate useful high-frequency signals in areas with adequate coverage, but they should not be treated as national antibiotic consumption.

7.4.2 Methodological limitations

The trend analyses and *AMROrbit* framework rely on estimating resistance trajectories within defined time windows. This improves interpretability, but it also means that abrupt outbreaks, breakpoint changes, seasonal effects, sudden shifts in testing policy, formulary changes, or infection-control interventions may not be fully captured by linear velocity estimates.

Lead–lag analysis identifies temporal precedence and not causality. A resistance signal that appears to lead another may reflect shared selective pressure, co-resistance, testing practices, specimen mix, hospital referral pathways, or unmeasured confounding. Therefore, these findings

should, therefore, be interpreted as early-warning surveillance signals requiring microbiological, clinical, and epidemiological validation.

The *AMROrbit* scorecard simplifies complex resistance dynamics into interpretable categories. This is useful for decision-making, but any categorisation involves threshold choices, different time windows, minimum isolate counts, slope definitions, or classification cut-offs which may change the quadrant or priority category assigned to a given organism–antibiotic combination. Also, integration of contextual information on genomic resistance mechanisms, plasmid dynamics, ward-level transmission, patient-level antibiotic exposure, environmental AMR, veterinary antibiotic use, or One Health data streams may help explain trajectories.

7.4.3 Translational and implementation limitations

The translational components of the thesis, especially *AMROrbit* deployment and *AMRSense*, are at different stages of development and validation. *AMROrbit* has a clearer analytical foundation because it builds directly on routine AST data and trajectory modelling. *AMRSense* is broader and more ambitious, but several of its components require prospective evaluation before claims can be made about behavioural change, stewardship impact, or population-level effectiveness. The AI-generated videos, games, quizzes, and KAP instruments can support engagement and measurement, but they do not automatically translate into durable antibiotic-use behaviour change, and their impact must be assessed empirically.

7.5 Future Directions

The future work will involve clinical and operational validation of *AMROrbit* scorecard across hospitals in India. The entire framework is being deployed and evaluated in two tertiary care

hospitals, AIIMS New Delhi and Max Hospital. Future studies should be planned to examine whether scorecard-based prioritisation changes stewardship discussions, antibiotic policy updates, formulary review, empirical therapy guidelines, infection-control alerts, or laboratory reporting practices. This evaluation should include usability, interpretability, time-to-insight, and concordance between *AMROrbit*-generated priorities and expert judgement. Future work will also involve onground deployment and expansion of the *AMRSense* ecosystem and the development of AMRaura as a multidimensional AMR scorecard. Future versions should integrate resistance burden and velocity from *AMROrbit* with community-level awareness, self-medication, prescription behaviour, diagnostic access, antibiotic availability, and contextual health-system indicators. This would allow AMRaura to capture both microbiological risk and behavioural or system-level drivers of AMR. Future methodological work should also incorporate additional data streams like Prescription-level data, ward-level antibiotic consumption, pharmacy dispensing data, genomic surveillance, patient outcomes, environmental AMR, veterinary antibiotic use, and One Health indicators to substantially strengthen the interpretability of resistance trajectories. The long-term goal should be to move from resistance monitoring alone toward integrated AMR intelligence that captures burden, momentum, selection pressure, transmission context, and stewardship response.

7.6 Final Remarks

This thesis shows that the main barrier to effective AMR stewardship is not only the absence of data, but the limited transformation of existing data into usable intelligence. Routine AST data already contain signals of resistance burden, direction, and momentum, antibiotic-use data contain signals of selection pressure, community and behavioural data provide context on how antibiotics

are accessed, demanded, prescribed, and consumed and the health-system indicators help situate these patterns within broader structural conditions. The challenge is to connect these signals and return them to decision-makers in a form that is timely, interpretable, and locally actionable. This thesis contributes to that goal by moving from longitudinal AMR description, to early-warning analysis, to *AMROrbit*-based stewardship prioritisation, and finally to the *AMRSense* ecosystem for broader operational intelligence.

More broadly, the thesis argues for AMR surveillance that is dynamic rather than static, contextual rather than isolated, and action-oriented rather than merely descriptive. It does not claim that analytics alone can solve AMR. But it shows that without better translation of surveillance data into usable intelligence, stewardship will remain slower than the resistance patterns it is trying to control.

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Appendix A: Detailed Regression Estimates for Longitudinal AMR Trend Analyses

A.1 Bloodstream infection analyses

Table A.1.1. Trends for time series decomposition analysis for antibiotics used to treat *E. coli* BSI derived from Simple Linear Regression between resistance percentage and time. Decreasing trend is denoted by a -ve value, Increasing trend is denoted by +ve value. (* Denotes $p < 0.05$, ** $p < 0.001$, *** $p < 0.0001$)

Variable/ Antibiotic →	Amikacin	Cefotaxime	Ciprofloxacin	Ertapenem	Imipenem	Meropenem	Piperacillin-tazobactam
Male	0.05***	-0.03***	0.01	0.01	0.29***	0.18***	0.22***
Female	0.07***	0.07***	0.08***	-0.05	0.21***	0.13***	0.21***
Neonate	NA	0.04	0.19***	0.06	0.07	0.22***	0.16***
Pediatric	-0.02	-0.15***	-0.18***	0.08	0.33***	-0.02	0.05
Reproductive	0.01	0.01	0.06***	-0.05	0.33***	0.13***	0.19***
Middle	0.08***	0.02*	0.03*	0.05*	0.17***	0.17***	0.26***
Elderly	-0.01	0.07*	0.01	-0.05	0.08**	0.06*	0.13***
North Zone	-0.1*	-0.05***	-0.05*	-0.08*	0.41***	-0.24***	0.1**
South zone	0.05***	0.02	0.1***	0.09***	0.16***	0.16***	0.2***
East zone	NA	NA	0.05	-0.05	NA	0.15***	-0.07*
West zone	0.07***	0	0.11***	0.16***	-0.13**	0.1***	0.28***
Central zone	NA	NA	0.46***	NA	NA	NA	NA
North-east zone	NA	0.01	0	NA	NA	NA	0.62***

CA-BSI	0.1***	0.1***	0.1***	0.24***	0.16***	0.17***	0.25***
HA-BSI	0.21***	0.14***	0.18***	0.55***	0.16***	0.24***	0.36***

Table A.1.2. Trends for time series decomposition analysis for antibiotics used to treat Klebsiella BSI derived from Simple Linear Regression between resistance percentage and time. (* Denotes $p < 0.05$, ** $p < 0.001$, *** $p < 0.0001$, Decreasing trend is denoted by a -ve value, Increasing trend is denoted by +ve value)

Variable/ Antibiotic →	**Amikacin**	**Cefotaxime**	**Ciprofloxacin**	**Ertapenem**	**Imipenem**	**Meropenem**	**Piperacillin-tazobactam**
Male	-0.07***	0.01	0.13***	0.01	0.32***	0.14***	0.14***
Female	-0.01	0.01	0.12***	-0.06*	0.33***	0.15***	0.19***
Neonate	-0.25***	0.05*	0.05	-0.16*	0.03	-0.03	0
Pediatric	-0.15***	-0.05*	0.08*	-0.01	0.26***	0.07*	0.08*
Reproductive	-0.04	0.05***	0.14***	-0.04	0.34***	0.12***	0.16***
Middle	-0.08*	-0.04***	0.09***	-0.05**	0.3***	0.11***	0.13***
Elderly	-0.07	0.13***	0.12***	-0.06	0.4***	0.23***	0.23***
North	-0.13***	-0.01	0.11***	0.06***	0.42***	0.08***	0.12***
South	-0.02	-0.02	0.15***	0.14***	0.32***	0.22***	0.21***
East	0.11	NA	0.18***	0.16*	0.01	0.2*	0.14*
West	-0.15*	0.19***	0.2***	-0.08*	-0.17***	-0.17***	-0.03
Central	NA	NA	0.24***	-0.25***	-0.01	0.16*	-0.07
North-east	0.25***	-0.09*	0.44***	-0.07	0.36***	0.16*	0.5***
CA-BSI	0.31***	0.15**	0.34***	0.35***	0.34***	0.27***	0.33***
HA-BSI	0.28***	0.24***	0.23***	0.49***	0.18***	0.13***	0.22***

NA- Not Available

Table A.1.3. Trends for time series decomposition analysis for antibiotics used to treat Acinetobacter BSI derived from Simple Linear Regression between resistance percentage and time. (* Denotes $p < 0.05$, ** $p < 0.001$, *** $p < 0.0001$, Decreasing trend is denoted by a -ve value, Increasing trend is denoted by +ve value)

Variable/ Antibiotic →	**Amikacin**	**Cefepime**	**Ceftazidime**	**Imipenem**	**Levofloxacin**	**Meropenem**	**Piperacillin-tazobactam**	**Minocycline**
Male	0.07***	0.12***	0.17***	0.29***	0.15***	0.42***	0.2***	-0.42***
Female	0.02	0.03*	0.12***	0.13***	0.11***	0.3***	0.1***	-0.46***
Neonate	-0.03	-0.09**	0.23***	0.13*	-0.13*	0.12*	-0.08*	NA
Pediatric age group	-0.01	-0.01	0.07*	0.15***	0.04	0.37***	0.08**	-0.57***
Reproductive age group	0.07***	0.09***	0.13***	0.23***	0.16***	0.36***	0.19***	-0.38***
Middle age group	0.03*	0.16***	0.16***	0.23***	0.13***	0.38***	0.18***	-0.49***
Elderly age group	-0.01	0	0	0.14***	0.11*	0.38***	0.16***	-0.5***
North Zone	-0.02	-0.04*	0.01	0.23***	0.08*	0.55***	0.14***	-0.86***
South zone	0.3***	0.32***	0.28***	0.31***	0.44***	0.32***	0.31***	-0.02
East zone	NA	-0.09*	NA	-0.01	0.29**	-0.1*	0.17*	NA
West zone	0.16***	0.05	0.12***	0.4***	0.06	0.48***	0.27***	0.09*
Central zone	NA	0.47***	0.28*	0.71***	0.66***	0.64***	0.85***	NA
North-east zone	-0.64***	0.02	0.44***	-0.25*	-0.14	-0.37*	-0.48***	NA
CA-BSI	0.29***	0.44***	0.54***	0.39***	0.29***	0.29***	0.43***	NA
HA-BSI	0.26***	0.26***	0.35***	0.26***	0.69***	0.28***	0.28***	0.13***

Table A.1.4. Trends for time series decomposition analysis for antibiotics used to treat Pseudomonas aeruginosa BSI derived from Simple Linear Regression between resistance percentage and time. (* Denotes $p < 0.05$, ** $p < 0.001$, *** $p < 0.0001$, Decreasing trend is denoted by a -ve value, Increasing trend is denoted by +ve value)

Variable/ Antibiotic →	**Amikacin**	**Cefepime**	**Ceftazidime**	**Ciprofloxacin**	**Levofloxacin**	**Imipenem**	**Meropenem**	**Piperacillin-tazobactam**	**Gentamicin**
Male	-0.04*	0.01	0.15***	0.03	0.12***	0.17***	0.11***	0.11***	-0.07*
Female	-0.07***	0.01	0.15***	-0.1***	0.06*	0.12***	0.22***	0.07*	-0.07*
Neonate	NA	NA	NA	NA	NA	NA	NA	NA	NA
Paediatric	-0.05*	0.01	0.15***	-0.02	0.07	0.11*	-0.08	0.01	-0.07
Reproductive	-0.07**	-0.02	0.13***	0.02	0.1***	0.21***	0.23***	0.15***	0.01
Middle	-0.14***	-0.01	0.1**	-0.1**	0.1**	0.02	0.01	-0.05*	-0.2***
Elderly	NA	NA	NA	NA	NA	NA	NA	NA	
North	-0.12**	-0.2***	0.13***	-0.05	0.34***	0.16***	-0.12*	-0.11*	-0.22***
South	-0.17**	0	0.08**	-0.16*	-0.03	0.01	0.14***	0.14***	-0.14*
East	NA	NA	NA	NA	NA	NA	NA	NA	NA
West	-0.08*	-0.32***	-0.27***	-0.24***	-0.25***	-0.08*	0.05	-0.03	-0.3***
Central	NA	NA	NA	NA	NA	NA	NA	NA	NA
North-east	NA	NA	NA	NA	NA	NA	NA	NA	NA

CA-BSI	NA	NA	NA	NA	NA	NA	NA	NA	NA
HA-BSI	-0.27**	NA	0.21**	- 0.15*	NA	0.11*	0.19***	0.17***	NA

NA- Not Available

Table A.1.5. Trends for time series decomposition analysis for antibiotics used to treat Staphylococcus BSI derived from Simple Linear Regression between resistance percentage and time. (* Denotes $p < 0.05$, ** $p < 0.001$, *** $p < 0.0001$, Decreasing trend is denoted by a -ve value, Increasing trend is denoted by +ve value)

Variable/ Antibiotic →	**Cefoxitin**	**Ciprofloxacin**	**Clindamycin**	**Erythromycin**	**Trimethoprim-sulfamethoxazole**	**Linezolid**	**Tetracycline**	**Vancomycin**
Male	0.15***	0.13***	0.15***	0.09***	-0.16***	-0.04***	0.19***	NA
Female	0.14***	0.15***	0.18***	0.15***	-0.1***	NA	0.23***	NA
Neonate	0.12***	-0.07*	0	-0.25***	-0.26***	NA	NA	NA
Pediatric age group	0.17***	0.13***	0.08**	0.01	-0.25***	NA	0.17***	NA
Reproductive age group	0.16***	0.14***	0.17***	0.16***	-0.12***	NA	0.22***	NA
Middle age group	0.1***	0.12***	0.16***	0.11***	-0.11***	NA	0.18***	NA
Elderly age group	0.18***	-0.01	0.26***	0.25***	-0.01	NA	0.24***	NA
North Zone	0.26***	0.12***	0.14***	0.06*	-0.45***	NA	0.38***	NA
South zone	0.01	0.16***	0.04***	0.23***	-0.17***	NA	0.14***	NA
East zone	-0.25***	0.41***	0.56***	0.07***	0.04*	NA	-0.01	NA

West zone	-0.43***	-0.15***	-0.03	0.01	-0.17***	NA	-0.1**	NA
Central zone	NA	0.85***	NA	NA	NA	NA	NA	NA
North-east zone	0.86***	0.06	0.33***	-0.2*	0.08	NA	NA	NA
CA-BSI	0.25***	0.07	0.17***	0.17*	0.03	NA	0.06**	NA
HA-BSI	-0.29***	0.19***	0.24***	0.16***	-0.11**	NA	0.12***	NA

Table A.1.6. Trends for time series decomposition analysis for antibiotics used to treat Enterococcus BSI derived from Simple Linear Regression between resistance percentage and time.(* Denotes $p < 0.05$, ** $p < 0.001$, *** $p < 0.0001$, Decreasing trend is denoted by a -ve value, Increasing trend is denoted by +ve value)

Antibiotic→	**Teicoplanin**	**Ampicillin**	**Gentamicin HL**	**Vancomycin**	**Linezolid**
Male	0.03	0.12***	-0.32***	0.06*	NA
Female	0.02	0.24***	-0.52***	0	NA
Neonate	NA	-0.27***	-1.07***	NA	NA
Paediatric	NA	0.16**	-0.49***	-0.11***	NA
Reproductive	0.02	0.15***	-0.36***	0.03	NA
Middle	0.05**	0.19***	-0.3***	0.07**	NA
Elderly	NA	0.19***	-0.51***	NA	NA
North	0.04*	0.02	-0.69***	-0.14***	NA
South	-0.03	-0.02	-0.19***	-0.01	NA
East	NA	NA	-0.21**	NA	NA
West	NA	-0.05	-0.16*	NA	NA
Central	NA	NA	NA	NA	NA

North-east	NA	0.35***	-0.66***	NA	NA
CA-BSI	NA	0.1*	-0.19**	NA	NA
HA-BSI	NA	0.08*	-0.16***	NA	NA

NA- Not Available

A.2 Urinary Tract Infection Analyses

Table A.2.1. Resistance trend estimates for *E. coli* UTIs derived from Simple Linear Regression between resistance percentage and time. (* Denotes $p < 0.05$, ** $p < 0.001$, *** $p < 0.0001$, Decreasing trend is denoted by a -ve value, Increasing trend is denoted by +ve value)

Variable/ Ab	**Amikacin**	**Cefazolin**	**Cefotaxime**	**Ciprofloxacin**	**Ertapenem**	**Fosfomycin**	**Imipenem**	**Levofloxacin**	**Meropenem**	**Nitrofurantoin**	**Piperacillin-tazobactam**	**Trimethoprim-sulfamethoxazole**
Male	0.04***	0.04	0.02*	-0.07***	0.01	-0.26***	0.12*	0.05*	-0.09*	0.14***	0.23***	-0.19***
Female	0.03*	0.17***	0.02	-0.04***	0.01	-0.18***	0.11*	0.16***	-0.08*	0.05***	0.15***	-0.12***
Neonate	NA	NA	-0.08	-0.3***	NA	NA	NA	NA	NA	NA	-0.48**	-0.53***
Pediatric	-0.08***	0.1***	-0.07***	-0.11***	-0.13***	NA	0.2*	0.14***	-0.24***	0.09***	0.09***	-0.25***
Infant	0.15***	0.09**	-0.1***	-0.1**	0.17***	NA	0.4***	0.22***	0.04	NA	0.24***	-0.14***

Toddler	NA	-0.14***	-0.05*	-0.11*	NA	NA	NA	0.2***	NA	NA	0.07*	-0.38***
Pre-schooler	-0.22***	0.13***	-0.07*	-0.17***	-0.35***	NA	-0.05	0.01	-0.32***	NA	-0.11*	-0.34***
Middle childhood	-0.12***	0.38***	0.09**	-0.18***	-0.15***	NA	NA	0.11*	-0.25***	NA	0.11**	-0.39***
Teenager	0.12***	0.06	-0.07*	0	0.05	NA	0.19*	0.08*	-0.27**	NA	0.17*	-0.13*
Reproductive	0.06***	0.1*	0.04*	0.01	0.03	-0.19***	0.11*	0.13***	-0.06	0.14***	0.2***	-0.11***
Middle	0.06***	0.11***	0.03*	-0.07***	0.05*	-0.25***	0.16**	0.08***	-0.04	0.05***	0.24***	-0.15***
Elderly	0.02	0.13***	-0.01	-0.08***	0.01	NA	0	0	-0.1***	0.06***	0.15***	-0.14***
North	-0.14***	0.12***	0.08***	0.01	-0.49***	NA	0.72***	-0.08***	-0.67***	0.14***	-0.04	-0.12***
South	-0.01*	NA	-0.07*	-0.04*	0.09***	NA	0.04***	NA	0.06***	0	0.19***	-0.36***
East	0.73***	NA	NA	0.19***	1.38***	NA	0.11*	0.09*	0.72***	1.26***	0.16***	0.13*
West	-0.05*	0.25***	-0.17***	-0.17***	-0.39***	-0.7***	-0.94***	-0.06	-0.28***	0.01**	0.08***	-0.07**

Central	-1.03***	0.5***	NA	0.42***	-0.02	NA	0.39***	0.03	0.4***	0.03	0.57***	0.61***
North-east	-0.02	-0.33***	0.09*	0.22***	-0.72***	NA	0.01	0.04	0.11**	-0.34***	0.97***	0.09***
CA-UTI	0.13***	0.06	0	-0.05***	0.28***	NA	0.16**	0.07*	0.14***	0.06***	0.3***	-0.2***
HA-UTI	0.21***	0.22***	0	0.16***	0.84***	NA	-0.04	0.41***	0.14***	0.28***	0.33***	0.02

NA = estimate not available for the corresponding subgroup-antibiotic combination.

Table A.2.2. Resistance trend estimates for Klebsiella UTIs derived from Simple Linear Regression between resistance percentage and time. (* Denotes $p < 0.05$, ** $p < 0.001$, *** $p < 0.0001$, Decreasing trend is denoted by a -ve value, Increasing trend is denoted by +ve value)

Variable/ Antibiotic →	**Amikacin**	**Cefazolin**	**Cefotaxime**	**Ciprofloxacin**	**Ertapenem**	**Fosfomycin**	**Imipenem**	**Levofloxacin**	**Meropenem**	**Nitrofurantoin**	**Piperacillin-tazobactam**	**Trimethoprim-sulfamethoxazole**
Male	0	0.23***	0.02	0.01	0.11***	0.02	0.29***	0.18***	-0.06	0.21***	0.29***	-0.11***
Female	0.11***	0.33***	0.07***	-0.03*	0.11***	0.04	0.24***	0.31***	-0.01	0.07*	0.18***	-0.04*
Neonate	NA	NA	-0.91***	-0.31**	NA	NA	NA	NA	NA	-0.36**	NA	-0.87***
Pediatric	0.11*	0.32***	-0.06*	-0.01	0.17***	NA	0.38***	0.38***	0.09*	0.28***	0.32***	-0.07*

Infant	0.06	0.25*	-0.23***	-0.12*	0.09	NA	0.43***	0.58***	0.28***	0.39***	0.22**	-0.17*
Toddler	NA	NA	-0.21*	NA	NA	NA	NA	NA	NA	NA	NA	NA
Pre-schooler	NA	NA	0.09	-0.09	NA	NA	NA	NA	NA	0.01	0.14*	0.01
Middle childhood	-0.15	NA	0.05	-0.32***	-0.21**	NA	0.3**	NA	-0.23*	0.16*	0.1	-0.04
Teenager	0	NA	-0.09*	0.27**	0.49***	NA	NA	NA	0.09	0.3***	0.33***	0.12*
Reproductive	0.13***	0.31***	0.16***	0.08**	0.15***	0.09**	0.25***	0.42***	0.01	0.27***	0.3***	0.02
Middle	0.12***	0.28***	0.1*	0.01	0.23***	-0.02	0.41***	0.23***	0.07*	0.12***	0.32***	0.01
Elderly	-0.04*	0.28***	-0.07***	-0.14***	-0.11***	NA	0.01	0.14***	-0.22***	-0.12**	0.06*	-0.24***
North	0.18***	0.14***	0.07**	0.12*	0.03	NA	1.04***	0.08	-0.17*	0.42***	0.31***	-0.07
South	0.09***	NA	-0.1***	0.07*	0.26***	NA	0.12***	NA	0.2***	0.08*	0.32***	-0.3***
East	0.19*	NA	NA	0.03	0.74***	NA	0.26*	-0.13*	0.59**	0.22***	-0.31**	-0.04
West	0.02	0.31***	-0.22***	-0.2***	-0.3***	-0.34***	-0.55***	-0.07	-0.22***	0.01	0.02	-0.03

Central	-0.15	0.83***	NA	0.77**	0.81***	NA	0.95***	0.95***	1.04***	0.63*	1.45***	0.59*
North-east	0.26***	-0.22*	0.15***	0.46***	-0.28**	NA	0.28**	0.37***	0.13***	0	1.01***	0.17***
CA-UTI	0.27***	0.54***	0.24***	0.19***	0.62***	NA	0.32***	0.42***	0.39***	0.18***	0.47***	0.06***
HA-UTI	0.23***	0.32***	0.05*	0.26***	0.49***	NA	0.14**	0.45***	0.19***	0.21***	0.3***	0.06

NA = estimate not available for the corresponding subgroup-antibiotic combination.

Table A.2.3. Resistance trend estimates for P. aeruginosa UTIs derived from Simple Linear Regression between resistance percentage and time. (* Denotes $p < 0.05$, ** $p < 0.001$, *** $p < 0.0001$, Decreasing trend is denoted by a -ve value, Increasing trend is denoted by +ve value)

Variable/ Antibiotic →	**Amikacin**	**Cefepime**	**Ceftazidime**	**Ciprofloxacin**	**Gentamicin**	**Imipenem**	**Levofloxacin**	**Meropenem**	**Piperacillin-tazobactam**	**Tobramycin**
Male	-0.07*	0.04*	0.18***	0.03	-0.13***	0.37***	0.15***	0.06*	0.3***	-0.02
Female	-0.18***	-0.01	0.06	-0.06*	-0.14***	0.28***	-0.07**	-0.04*	0.28***	0.04
Neonate	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Pediatric	-0.32***	-0.16*	0.06	-0.12	-0.15*	0.44***	-0.1	-0.02	0.29*	0.1
Infant	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Toddler	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Pre-schooler	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Middle childhood	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Teenager	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Reproductive	0.05	0.14***	0.27***	0.17***	0.02	0.54***	0.27***	0.16*	0.45***	0.06
Middle	0.1**	0.11**	0.29***	0.07*	0.06*	0.4***	0.16***	0.19***	0.41***	-0.05
Elderly	-0.26***	-0.11*	-0.06	-0.18***	-0.38***	-0.09	0.01	-0.12**	-0.21***	NA
North	0.21***	0.45***	0.6***	0.43***	0.25***	1.05***	0.49***	0.35***	0.89***	0.33***
South	-0.69***	-0.46***	-0.3***	-0.65***	-0.83***	-0.32***	-0.69***	-0.24***	-0.38***	NA
East	0.56***	0.98***	0.87***	0.91***	0.65***	0.44***	0.57**	0.58***	NA	NA
West	-0.04	-0.42***	-0.42***	-0.14***	-0.25***	-0.44***	-0.11*	-0.15***	0.06	-0.44**
Central	NA	NA	NA	0.77***	NA	0.81***	NA	0.55***	NA	NA
North-east	NA	1.39***	1.58***	0.82***	NA	1.01***	0.93***	NA	NA	NA

CA-UTI	0.02	0.39***	0.38***	-0.07	-0.28***	0.01	0.03	0.1*	NA	NA
HA-UTI	-0.61***	-0.42***	-0.33***	-0.56***	-0.57***	-0.29***	-0.16***	-0.46***	-0.39***	NA

NA = estimate not available for the corresponding subgroup-antibiotic combination.

Table A.2.4. Resistance trend estimates for Enterococcus UTIs derived from Simple Linear Regression between resistance percentage and time. (* Denotes $p < 0.05$, ** $p < 0.001$, *** $p < 0.0001$, Decreasing trend is denoted by a -ve value, Increasing trend is denoted by +ve value)

Variable/Antibiotic →	**Ampicillin**	**Ciprofloxacin**	**Fosfomycin**	**Gentamicin HL**	**Nitrofurantoin**	**Teicoplanin**	**Vancomycin**
Male	0.28***	0.04*	-	0.10***	0.44***	0.08***	0.09***
Female	0.27***	-0.10***	-	-0.10***	0.39***	-0.01	0.00
Neonate	-	-0.16	-	-	-	-	-
Pediatric	0.19***	0.16***	-	0.11***	-	-	-
Reproductive	0.30***	-0.03*	-	0.05*	0.38***	0.02*	0.01
Middle	0.38***	-0.06**	-	-0.10***	0.50***	0.08***	0.11***
Elderly	0.03	-0.04*	-	-0.09*	0.17***	-	-0.03
North	-0.11	-0.20***	-	-0.72***	-0.08*	-0.18***	-0.29***
South	-0.04	-0.02*	-	0.02	0.60***	0.10***	0.15***
East	-	0.02	-	-	-	-	-
West	0.14***	0.07	-	0.31***	0.22***	0.03	-0.04
Central	1.26***	0.50***	-	-	1.46***	-	-
North-east	0.55***	0.50***	-	-0.07	0.13	-	-
CA-UTI	0.43***	0.01	-	0.14*	0.41***	-	-
HA-UTI	-0.14***	-0.05*	-0.95***	-0.14**	0.62***	0.09***	0.13***