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HYBRID AGENT-BASED AND SYSTEM DYNAMICS MODELING OF ANTI-BACTERIAL RESISTANCE IN COMMUNITY

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ABSTRACT

Antibiotic resistance (ABR) is a major global health threat, contributing to increased mortality and economic losses. The emergence and spread of ABR is driven by healthcare practices, environmental contamination, and human-to-human transmission. In low and middle income countries (LMICs), limited healthcare infrastructure and environmental factors, such as contaminated water and poor sanitation, exacerbate the situation. In these regions, inappropriate antibiotic use and insufficient infection control measures further promote resistance. This paper presents a hybrid model that combines System Dynamics (SD) and Agent-Based Modeling (ABM) to explore complex interactions between healthcare systems, environmental factors, and human behavior in community settings. The SD approach models aggregated within-host bacterial dynamics and external environmental factors, while ABM captures individual person behaviors community interactions and interactions with healthcare. By integrating these methods, this study offers a more comprehensive framework for understanding the emergence of ABR in LMICs. Preliminary results and future directions are discussed.

1 INTRODUCTION

Antibiotic resistance (ABR) is a growing global health crisis, driven by complex interactions between healthcare practices, community dynamics, and environmental factors. The misuse and overuse of antibiotics in healthcare, combined with human-to-human transmission and environmental contamination, contribute to the emergence and spread of resistant bacteria. Addressing ABR requires a multi-dimensional approach that considers the interconnected roles of medical treatment, social behavior, and environmental exposure in shaping resistance patterns.

In Mayer et al. (1995), a foundational mathematical model was proposed to capture the interactions between the bacterial population and the immune response. Ibargüen-Mondragón et al. (2014) extended this model by incorporating the dynamics of bacterial populations in the presence of antibiotics, categorizing them into sensitive and resistant groups. They demonstrated that the current antibiotic dosages recommended by the WHO could contribute to resistance, particularly in the case of tuberculosis. Expanding further, Daşbaşı and Öztürk (2016) integrated the immune response into the model and found similar results. More recently, Nashebi et al. (2024) advanced the modeling framework by incorporating minimum inhibitory concentration (MIC) values, offering a more detailed analytical approach to understanding antibiotic interactions and resistance evolution. Despite these contributions, there remains a notable gap in comprehensive system-level modeling approaches that integrate immune dynamics, community transmission, treatment strategies, and environmental factors. Caudill and Lawson (2013) developed a hybrid simulation model to investigate patient–healthcare worker interactions within hospital settings by combining intra-host and inter-host dynamics. The within-host bacterial population dynamics were modeled using differential equations, while hosts were represented as heterogeneous agents in an agent-based modeling framework. A novel concept called the Bacterial Population Vector (BPV) was introduced to efficiently track multiple bacterial strains with varying resistance profiles. This vector was updated through differential equations to balance biological

accuracy with computational efficiency, while agent-based modeling captured the complex patterns of interactions and infection transmission between individuals. Transmission was categorized into six distinct types, allowing a detailed representation of how infections spread in clinical environments. Building on this work, Caudill and Lawson (2017) further enhanced the model by incorporating immune response dynamics and accounting for antibiotic treatment history, enabling a more comprehensive understanding of the evolutionary pathways leading to antibiotic resistance. Djanatliev et al. (2012) highlighted the growing use of hybrid simulation approaches—specifically the combination of System Dynamics (SD) and Agent-Based Modeling (ABM)—in healthcare technology assessments. These hybrid models leverage the strengths of SD in capturing system-level feedback and long-term trends, alongside the granularity of ABM in representing individual-level heterogeneity. The loosely coupled architecture of such models facilitates the integration of diverse healthcare scenarios, enabling comprehensive simulations that inform economic, demographic, and health-related outcomes prior to the large-scale implementation of new technologies. Extending the application of hybrid modeling, Kang et al. (2021) introduced a hybrid simulation framework integrated with simulation-based optimization to evaluate the impact of various social distancing policies during the COVID-19 pandemic, demonstrating the approach's flexibility in informing real-time policy decisions. Olesen (2022) explores how mathematical modeling can be used to estimate the impact of mass drug administration (MDA) of antibiotics, particularly azithromycin, on the development and spread of antimicrobial resistance within and between communities. Letten et al. (2021) apply ecological coexistence theory to antibiotic resistance, highlighting how resource competition and niche overlap influence the persistence of resistant microbes and offering new perspectives for understanding microbial interactions and resistance dynamics. Paterson et al. (2016) employs mathematical modeling and a genetic algorithm to optimize antibiotic treatment regimens, aiming to maximize bacterial eradication while minimizing antibiotic usage. It demonstrates that a high initial dose followed by gradually tapering doses consistently outperforms traditional regimens in terms of efficacy and efficiency. VanScoy et al. (2021) investigates the pharmacokinetics and pharmacodynamics (PK-PD) of gepotidacin, a novel antibiotic, against Escherichia coli using in vitro infection models. The research identifies the AUC/MIC ratio as the key PK-PD index for determining bacterial reduction efficacy and assesses the relationship between gepotidacin exposure and resistance amplification. Results indicate that higher AUC/MIC ratios are associated with improved bacterial eradication and resistance suppression, providing valuable insights for optimizing dosing regimens for future clinical trials.

In this paper, we propose a hybrid simulation approach to model within-host bacterial infection dynamics and investigate the emergence of infection within a community. By combining SD and ABM, we study bacterial infection dynamics at both the individual and population levels. Each individual's bacterial dynamics are governed by an SD model that reflects its bacterial dynamics, influenced by unique physical and behavioral traits. These individual traits (ABM), along with their interactions, drive the population-level infection dynamics. The SD approach is also used to capture environmental bacterial dynamics, particularly focusing on the bacterial populations in water sources that affect community health. ABM is applied to model the interactions between individuals and healthcare providers (doctors and quacks), as these interactions significantly influence treatment decisions and infection transmission. SD captures aggregate dynamics but struggles with heterogeneity, while ABM effectively handles individual variability but is computationally expensive (Hunter and Kelleher 2022). By integrating both approaches, we overcome their respective limitations, creating a more realistic and scalable framework. We use the proposed framework to evaluate the emergence of ABR in a community, considering environmental transmission and the presence of diverse healthcare facilities.

2 MODELING SCENARIO

In this study, we explore the emergence and transmission of antibiotic resistance within a community. The community in this setting relies on a shared environment say water source—such as a nearby lake, reservoir, or river—which is contaminated, possibly including strains like Escherichia coli. Individuals are

exposed to bacterial pathogens primarily through the environment. Environmental transmission stems from the ingestion of contaminated water, where the risk of infection is proportional to the bacterial concentration and the volume consumed. Interpersonal transmission occurs when individuals interact with one another and transfer bacterial loads during those contacts. As they fall ill, infected persons shed bacteria back into the environment, exacerbating contamination levels. Over time, the bacterial load in the environment fluctuates in response to both the number of infected individuals and environmental cleanup interventions. Once the contamination or infection prevalence exceeds a defined threshold, the community initiates decontamination measures to reduce the environmental risk. Transmission of infection in the community occurs through two primary mechanisms: environmental and interpersonal.

Once individuals become infected, they seek treatment from healthcare providers available within the same community. The healthcare infrastructure in the community comprises both formally trained doctors and informal practitioners, commonly referred to as "quacks", as well as over-the-counter (OTC) sales of antibiotics, and self-medication. The decision of where to seek treatment is influenced by several factors, including accessibility, cost, and individual preferences. In many cases, individuals may opt for quacks due to convenience, lower costs, or social familiarity, despite the associated risks discussed in Das et al. (2016).

There is a significant difference in how these two types of providers administer antibiotics. Doctors are assumed to possess formal medical training and have a better understanding of bacterial infections and antibiotic stewardship. They are more likely to diagnose infections correctly and prescribe antibiotics cautiously—only when necessary and in the appropriate dosage and duration. Additionally, they are assumed to be aware of the broader implications of antimicrobial resistance and may even educate patients about responsible antibiotic use. In contrast, quacks often lack formal education or professional oversight and tend to overprescribe antibiotics, even for viral infections or mild symptoms where such medication is ineffective. Over time, individuals treated by quacks may experience treatment failures due to resistant infections, potentially leading to more severe illness or repeated infections. This can further burden the local healthcare system and increase environmental contamination through prolonged bacterial shedding. By incorporating these behavioral and systemic factors, the model provides a nuanced view of how healthcare access, provider behavior, and antibiotic misuse contribute to the possible emergence and amplification of antibiotic resistance.

Antibiotic resistance is a complex, multidimensional problem involving biological, social, environmental, and healthcare-related factors. In this study, we focus on four key dimensions: (i) within-host bacterial dynamics, capturing the evolution of bacterial populations inside individuals; (ii) between-host transmission models, addressing human-to-human spread of resistant strains; (iii) environmental pathways, encompassing the role of natural and built environments in resistance propagation; and (iv) healthcare facility dynamics, accounting for clinical practices and institutional contributions to resistance. Furthermore, we explicitly model the interactions between these dimensions to provide an integrated understanding of the system-level drivers of antibiotic resistance.

3 METHODOLOGY

A hybrid simulation model integrates multiple modeling paradigms to capture complex systems more comprehensively than any single approach. By combining SD, ABM, these models represent different aspects of a system across various levels of abstraction. All simulations were conducted using AnyLogic 8.9.2 Personal Learning Edition (Borshchev 2013).

System Dynamics (SD): System dynamics captures complex systems through feedback loops, stock-and-flow structures, and time delays. Operating at an aggregate level, SD uses differential or difference equations to model how variables change over time (Forrester 1987). For antibiotic resistance, SD effectively models interactions between sensitive and resistant bacterial populations within hosts. It captures how antibiotic use creates selection pressure favoring resistant strains, while enabling analysis of long-term

resistance trends and intervention impacts. SD is particularly valuable for evaluating factors like mutation rates and treatment policy effects on resistance development at population scales.

Agent-Based Modeling (ABM): ABM simulates individual entities (agents) with distinct behaviors, interactions, and decision-making capabilities (Macal and North 2005). Each agent—whether a patient or healthcare worker—operates autonomously while interacting within an environment. ABM excels at capturing heterogeneity in host characteristics and behaviors, allowing for modeling of adaptive behaviors and complex social dynamics. It simulates host-pathogen interactions (transmission) at the individual level, representing transmission pathways through various contact networks. ABM incorporates crucial factors like immune responses and antibiotic adherence patterns that vary across individuals, making it ideal for studying how diversity in treatment behaviors affects resistance spread.

4 MODELING FRAMEWORK

In this section, we present our modeling framework for the emergence of the ABR. The pictorial representation of the framework is presented in the Figure 1.

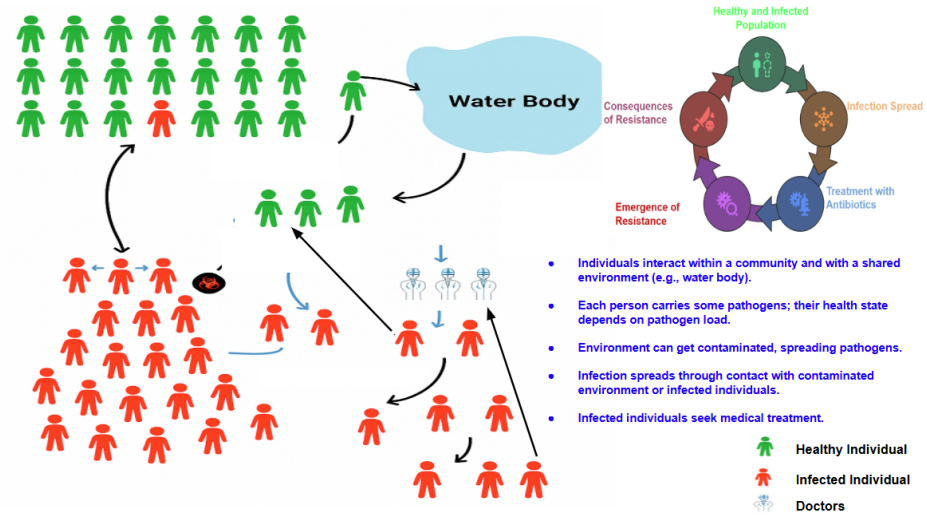

Figure 1: Pictorial representation of modeling framework.

4.1 Person Agent Infection Dynamics:

In this section, we describe the infection dynamics of the host. The infection dynamics are governed by the bacterial population and, immunity of the host, but sometimes when the bacterial population goes beyond a certain threshold, then the antibiotics play a crucial role. Here, we consider system dynamics approach for modeling the infection dynamics within the host. Four stocks are considered: two stocks representing sensitive and resistant bacterial strains, one stock representing the aggregated immunity of the host, and one stock for the antibiotics. The course of infection within each person is shaped by two main factors: the external bacterial loads and the strength of their immune system. Individuals with stronger immunity may be able to suppress higher bacterial loads without medical treatment, while others may require antibiotics even at moderate levels of exposure. Once antibiotics are required, their dosage and duration are influenced by the type of healthcare facility the person accesses. If this total bacterial load remains below a certain individual-specific infection threshold, the person's immune system can effectively eliminate the pathogens, and the infection does not manifest clinically. However, if the bacterial population surpasses this threshold, the immune response alone may not be sufficient, and antibiotic intervention becomes necessary. The SD model can be found in the Figure 2.

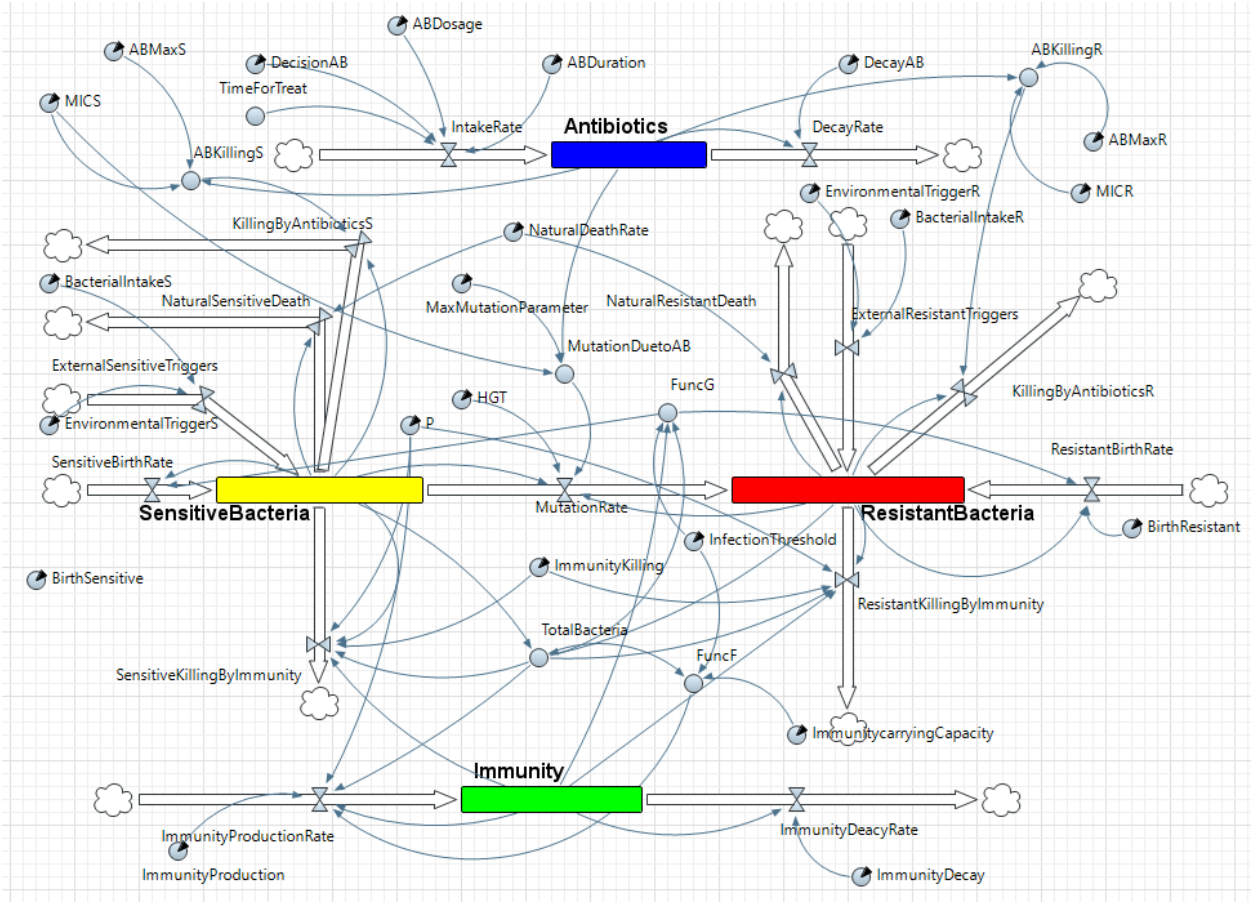

Figure 2: System Dynamics Model of bacterial dynamics within Person agent.

Here, S(SensitiveBacteria), R(ResistantBacteria), I(Immunity) and A(AB) represent the sensitive bacterial stock, the resistant bacterial stock, the aggregated immunity stock, and the antibiotics stock, respectively. The dynamics are described by the following equations:

$$\frac{dS}{dt} = r_S S f(S,R,K,I) - \mu_S S - k_I \frac{SI}{p+(S+R)} - \alpha(A)S - m(A)S - hSR + \sum M_S \delta(t), \tag{1}$$

$$\frac{dR}{dt} = r_R R f(S,R,K,I) - \mu_R R - k_I \frac{RI}{p+(S+R)} - \alpha(A)R + m(A)S + hSR + \sum M_R \delta(t), \tag{2}$$

$$\frac{dI}{dt} = r_I \frac{I(S+R)}{(S+R)+p}\left(1 - \frac{I}{g(S,R,K,I_{max})}\right) - \mu_I I, \tag{3}$$

$$\frac{dA}{dt} = \Delta - \mu_A A, \tag{4}$$

where the auxiliary functions are:

$$f(S,R,K,I) = \begin{cases} 1 - \frac{S+R}{K} & \text{if } \frac{S+R}{K} \leq 1 \text{ and } I > 0 \\ 1 - \frac{S+R}{10K} & \text{otherwise} \end{cases}$$

and

$$g(S,R,K,I_{\max}) = \begin{cases} S+R+1 & \text{if } S+R < K \text{ and } S+R < I_{\max} \\ I_{\max} & \text{otherwise.} \end{cases}$$

For the killing rates by antibiotics and antibiotics-induced mutation rates, we use the Emax model (Knechtle et al. 2021),

$$\alpha(A) = \frac{A^2}{A^2 + MIC_i^2}, \forall i \in \{S, R\}$$

and

$$m(A) = \frac{A^2}{A^2 + MIC_S^2}.$$

In (1), the first and second terms denote the natural birth and death rates of the sensitive bacteria, respectively. The third term represents the killing of sensitive bacteria by the immune system. The fourth term denotes the rate at which sensitive bacteria are killed by antibiotics, depending on the concentration of the antibiotics. The fifth term describes the mutation rate induced by the administration of antibiotics ($m(A)$, MutationDueToAB), which is an outflow. The sixth term represents the natural mutation rate((h) from sensitive to resistant bacteria. The last term is for the external triggers, consisting of environmental and human-to-human transmission of sensitive bacteria (M_S, BacterailIntakeS+ExternalSensitiveTrigger).
In (2), the first and second terms denote the natural birth and death rates of the resistant bacteria, respectively. The third term represents the killing of resistant bacteria by the immune system. The fourth term denotes the rate at which resistant bacteria are killed by antibiotics. The fifth term describes the mutation rate induced by the administration of antibiotics ($m(A)$, MutationDueToAB), which is an inflow. The sixth term represents the natural mutation rate (h) from sensitive to resistant bacteria. The last term is for the external triggers, consisting of environmental and human-to-human transmission of resistant bacteria (M_R, BacterailIntakeR+ExternalResistantTrigger).
In (3), the first term denotes the immunity production rate that depends on the total bacterial population and variable immunity-carrying capacity. The second term is related to the natural decay rate of immunity.
In (4) denotes the intake and decay of antibiotics. Here, we only consider one antibiotic. Antibiotic intake is characterized by three key parameters: “ABDosage" (the amount administered), “ABDuration" (the duration of the treatment), and the initiation time of the dosage. Additionally, in certain cases, a decision must be made on whether to administer antibiotics at all, captured by the variable “DecisionAB". This decision is influenced by the treatment pathway selected by the infected agent. A detailed discussion on the administration strategy and decision-making process regarding antibiotic use is provided in a later section. In this model, we have considered two transmission channels: environmental transmission and human-to-human transmission. It captures the external influences in the within-host infection dynamics. In the next section, we discuss the modeling of the environmental contamination.

4.2 Person Agent State Chart:

In this section, we will discuss the person agent model chart. Person agent’s infection dynamics can be viewed as the agent’s state chart. The state chart contains one composite state and seven states. The composite state is “Healthy” and consists of two states: “Susceptible” and “PartiallyImmune”. The other states are “Infected”, “SeekingTreatment”, “ImproperTreatment”, “ProperTreatment”, “ProperTreatment1”, “ProperTreatment2” and “TreatmentFailure”. All the agents having a total bacterial population under an infection threshold (different for different agents) are considered in the ”Healthy” state. The Agent State chart is shown in Figure 3.

Upon exposure to an external bacterial load—arising from a ContaminationEvent, environmental transmission, or human-to-human transmission, each characterized by attributes such as ContactRate and ProbOfInfEnv—an agent’s infection status is determined by whether the cumulative bacterial load exceeds a predefined infection threshold (Threshold1). If this threshold is surpassed, the agent transitions to the Infected state; otherwise, the agent remains Susceptible. Once infected, the agent may return to the Susceptible state if the immune system successfully reduces the total bacterial population ($S+R$, representing susceptible and resistant strains) below Threshold1. However, if the immune response alone fails to control the infection,

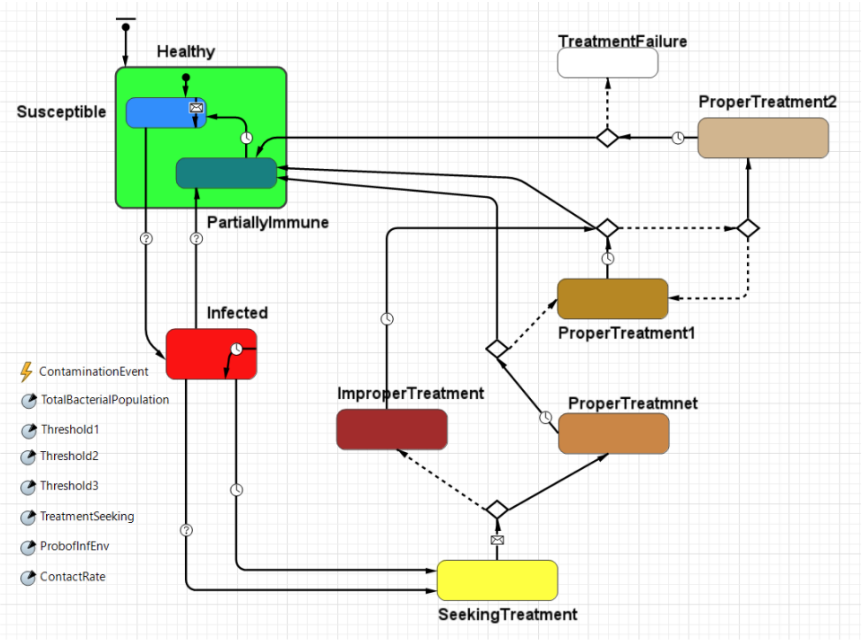

Figure 3: Agent state-chart.

the agent may enter treatment through one of two routes: either the bacterial load continues to increase and exceeds a higher, critical treatment threshold (Threshold2), or the agent autonomously seeks treatment after a predefined period (TreatmentSeeking), regardless of the current bacterial level.

When an agent enters the “SeekingTreatment" state, a decision must be made between pursuing proper or improper treatment. This choice is influenced by multiple factors, such as the individual’s education level, awareness, socioeconomic status, and proximity to healthcare services (Debsarma and Choudhary 2025). However, in our modeling framework, we only consider two key determinants: the distance to the nearest healthcare facility and the availability of medical personnel (including qualified doctors and informal practitioners or quacks). Based on these factors, the agent transitions either to “ProperTreatment" or “ImproperTreatment".

In the “ImproperTreatment" state, the agent receives care from an unqualified practitioner (quack or self-medicate), who is assumed to prescribe antibiotics immediately, without conducting any diagnostic tests or following standard treatment protocols. The antibiotic course is administered for a fixed duration, and it is assumed that the agent adheres to the prescribed regimen. Upon completion of this treatment period, the agent’s bacterial load is reassessed. If the bacterial population falls below the infection threshold, the agent transitions to the “PartiallyImmune" state, indicating a temporary recovery. However, if the bacterial load remains above the threshold, the agent proceeds to the “ProperTreatment1" state, seeking appropriate medical care.

If the agent opts for proper treatment, it enters the “ProperTreatment" state, where it is evaluated by a qualified doctor. In line with standard medical protocols, it is assumed that antibiotics are not prescribed during the initial consultation. Instead, the doctor advises the agent to return for a follow-up if symptoms persist after a few days. Following this waiting period, two outcomes are possible: if the bacterial load has fallen below the infection threshold due to its immunity, the agent transitions to the “PartiallyImmune" state, indicating recovery without antibiotic intervention; however, if the bacterial load remains above the threshold, the agent proceeds to the “ProperTreatment1" state, where appropriate antibiotic treatment is initiated.

In the “ProperTreatment1" state, the agent is re-evaluated by the doctor, who prescribes antibiotics based on the agent’s bacterial load and in accordance with established antibiotic prescribing protocols.

The treatment is administered for a fixed, prescribed duration. Upon completion of the antibiotic course, the agent's bacterial load is reassessed. If it falls below the infection threshold, the agent transitions to the "PartiallyImmune" state, indicating recovery. However, if the bacterial load remains above the threshold, the agent either re-enters the "ProperTreatment1" state for continued treatment or progresses to the "ProperTreatment2" state, depending on the severity of the infection(TotalBacterialPopulation exceeds Threshlod3).

In the "ProperTreatment2" state, the doctor administers a higher dosage of antibiotics over an extended duration, aiming to suppress resistant bacterial strains and reduce the overall bacterial population below the infection threshold. If the treatment is successful, the agent transitions to the "PartiallyImmune" state, indicating partial recovery and the development of some level of immunity. However, if the bacterial load remains above the threshold despite the intensified treatment, the case is considered a treatment failure, and the agent moves to the "TreatmentFailure" state. Finally, when the agent is in the "PartiallyImmune" state, then it can only move to the "Susceptible" state, after some delay.

4.3 Environmental Modeling:

We model the environment (common water body) using the system dynamics approach. In this model, we consider two key components: the stock of sensitive bacteria and the stock of resistant bacteria present in the environment. Both bacterial strains are subject to natural birth and death processes. We consider that the water body may be polluted with various chemicals, some of which exert selective pressure that drives the mutation (sensitive to resistant). Additionally, infected individuals contribute to environmental contamination by shedding bacterial loads into the water body. Both bacterial stocks share the same capacity. Here, S_E and R_E denote the environmental sensitive and resistant bacterial stocks, respectively. The SD model can be found in the Figure 4.

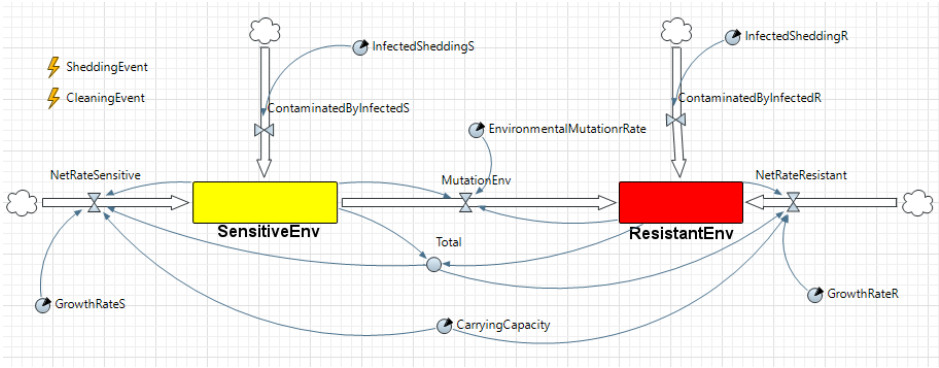

Figure 4: Environmental System Dynamics Model consisting Sensitive and Resistant bacterial stock.

The equations as follows:

$$\frac{dS_E}{dt} = r_{E,S}S_E(1-\frac{S_E+R_E}{K_E}) - d_{E,S}S_E - \mu_E S_E R_E + \sum_{infected} B_S\delta(t) \text{ and} \tag{5}$$

$$\frac{dR_E}{dt} = r_{E,R}R_E(1-\frac{S_E+R_E}{K_E}) - d_{E,R}R_E + \mu_E S_E R_E + \sum_{infected} B_R\delta(t). \tag{6}$$

Here, the above two equations, (5) and (6), represents the sensitive-resistant bacterial dynamics in the environment. The first and second term denotes the natural birth and death rates in the environment. The third term denotes the mutation rate (μ_E) of sensitive to resistant. The last term denotes that the infected people shed a bacterial load (B_S, B_R) into the environment, $\delta(t)$ is the pulse function.

4.4 Healthcare Facility:

When a host becomes infected with a bacterial population, comprising both sensitive and resistant strains, the decision to seek treatment is influenced by factors such as bacterial load and the individual's tolerance to illness. Upon the onset of symptoms, the host chooses to consult a qualified doctor or an informal practitioner (quack, taking self-medication, etc.). In this model, both doctors and quacks are represented as autonomous agents with identical statecharts but differing in their treatment behavior. Each Doctor/Quack (determined by the attribute "Type") agent transitions through two states: "Idle" and "Busy", which can be seen in the figure Figure 5. In the "Idle" state, the agent is available and awaits patient requests. Upon receiving a trigger message from a host in the "SeekingTreatment" state, the doctor agent transitions to the "Busy" state, where they interact with the patient, make diagnostic decisions("TreatmentProcess")), and prescribe antibiotics—doctors adhering to clinical guidelines, while unqualified person prescribe without protocol or testing. Following the consultation, the agent returns to the "Idle" state after a short delay, ready to attend to the next patient. Qualified doctors are assumed to prescribe antibiotics in optimal doses and for appropriate durations, considering the patient's condition and resistance concerns. In contrast, an unqualified person may overprescribe or administer incorrect dosages, contributing not only to treatment inefficacy but also to the selection pressure that favors resistant bacterial strains. This coupling of community-level infection spread with within-host infection dynamics adds a crucial layer of biological realism and allows the model to evaluate both public health and clinical outcomes in tandem. The parameters value can be

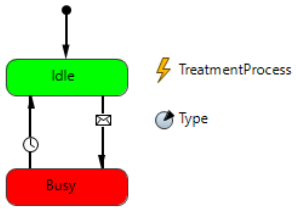

Figure 5: Doctor/Quack state-chart.

found in the Table 1.

Table 1: Key parameters of the model.

Model Variable	Parameter Range	Units
Initial number of agents	1000	Person
ProbofInfEnv	0.6	unit less
EnvironmentalTrigger	0-10^7	Cells
BacterialIntake	0-15000	Cells
GrowthRate ($r_{E,i}, i \in \{S,R\}$)	0.001-1	Cells/day
InfectedShedding ($B_i, i \in \{S,R\}$)	0-10^7	Cells
InfectionThreshold (K)	1000-2000	Cells
ImmuneCapacity (I_{max})	750-1200	Cells
MaxMutationRate (m)	10^{-6}	Cells/day
CarryingCapacity (K_E)	10^7	Cells
ToleranceLevel	2-10	days
TreatmentSeeking	2-5	days

5 SIMULATION AND PRELIMINARY RESULTS

In this paper, we consider a closed community consisting of 1,000 individuals, with no migration, births, or deaths—thus maintaining a fixed population throughout the simulation period. Each individual is modeled as an autonomous agent that interacts randomly with others at a predefined contact rate, simulating everyday

social interactions. Initially, all agents are in the Susceptible state, meaning they are healthy but vulnerable to infection. Disease transmission occurs through two primary pathways: direct human-to-human contact and environmental contamination. The environmental component specifically refers to water sources within the community, which can become reservoirs of bacterial contamination. The environment harbors two bacterial strains—antibiotic-sensitive and antibiotic-resistant—and the contamination level is dynamically updated based on infected individuals shedding bacteria into the water. Community members use this shared water source for daily activities, thereby creating a feedback loop between environmental contamination and infection risk.

For treatment modeling, the community includes two healthcare providers: one qualified doctor and one informal practitioner or quack. Both are represented as agents with identical statecharts (Idle, Busy), but differ in their treatment behavior and adherence to antibiotic prescribing protocols. When an agent decides to seek treatment, they randomly choose between consulting the doctor or the quack, reflecting a simplified assumption of equal probability in healthcare-seeking behavior. This framework enables the study of how treatment decisions and environmental factors interact to influence the dynamics of antibiotic resistance within the population.

We consider a total simulation period of 10 years to capture long-term trends in infection, resistance development, and treatment outcomes. The simulation results are shown in the Figure 6. Also, we examine three treatment scenarios: (i) all patients receive improper treatment, (ii) 50% of patients receive improper treatment while the remaining 50% receive proper treatment, and (iii) all patients receive proper treatment, results in Table 2

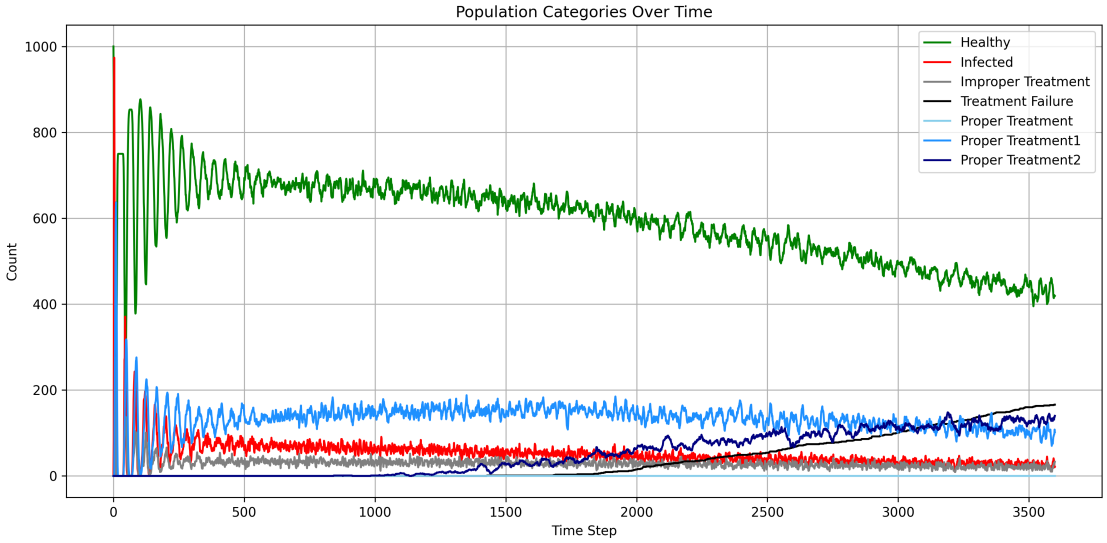

Figure 6: Population count over time, when 50% patients go to proper treatment.

The graph in Figure 6 illustrates a concerning evolution of antimicrobial resistance through multiple treatment outcome trajectories. Initially, standard treatments (represented by blue lines) demonstrate reasonable effectiveness in managing infections. However, as the timeline progresses, a marked increase in treatment failures (black line) becomes evident, rising steadily to 166 cases by the observation's end. This upward trend in failures coincides with declining effectiveness of conventional treatment approaches, shown by the decreasing populations in the standard treatment categories. Simultaneously, the prolonged treatment option (Proper Treatment2) sees increased adoption as healthcare providers likely respond to standard treatment failures. The red line showing consistent treatment failures throughout suggests a persistent baseline of cases unresponsive to intervention. This pattern clearly indicates antimicrobial resistance development: early treatment success gradually compromised by growing failure rates, necessitating longer

treatment durations, with even these enhanced protocols eventually showing diminishing returns as resistance mechanisms strengthen over time.

Table 2: Treatment Failure in the end of simulation run.

Time Span	0% Proper Treatment	50% Proper Treatment	100% Proper Treatment
10 years	172	166	154

6 CONCLUSIONS AND FUTURE WORK

Antibiotic resistance (ABR) is a complex, multi-dimensional problem that demands an integrated approach to understand its various components in conjunction. In this paper, we propose a comprehensive framework that not only couples within-host dynamics with between-host transmission but also incorporates environmental pathways and healthcare facility interactions, offering a more holistic perspective on the ABR challenge. The framework enables exploration of how environmental contamination influences the emergence and spread of resistance and serves as a tool to evaluate treatment outcomes across diverse contexts. To fully leverage this framework, we will conduct extensive simulations to examine intervention strategies, behavioral patterns, and system dynamics under varying assumptions and epidemiological conditions. Through explorative modeling, we aim to investigate structural uncertainties, alternative scenarios, and the sensitivity of key parameters that govern resistance evolution. Several case studies will be undertaken to test the robustness and flexibility of the model, highlighting how it can be adapted to different real-world settings characterized by varying levels of healthcare access, infrastructure, and antibiotic usage patterns.

Improper antibiotic use is widespread in LMICs due to poor regulation and limited healthcare access, worsening the antibiotic ABR crisis. Our study demonstrates that these practices accelerate treatment failure and the spread of resistance (Table 2). While some treatment failures occur even with optimal care, our data shows failure rates are highest when patients rely entirely on improper treatment pathways. This highlights that inappropriate antibiotic use is a primary driver that dramatically exacerbates the problem of ABR.

To build on these findings, we plan to refine the model by incorporating a broader and more realistic range of treatment pathways, capturing the complexity of how antibiotics are used and misused in practice. This includes modeling disparities in access to formal and informal healthcare, variability in patient decision-making, and differences in treatment adherence. While the current model provides valuable insights into how resistance emerges and spreads, validating such a complex and layered system remains challenging due to limited data and the uncertainties surrounding both biological and behavioral factors. Moreover, the current framework is limited to a single antibiotic, whereas real-world treatment involves multiple drugs with varied resistance patterns. It also does not yet include bacteria with varying levels of resistance or co-resistance, nor interactions between bacterial species and host immune responses. Addressing these limitations is essential to better capture the real-world consequences of improper treatment and to inform more effective interventions against ABR.

These limitations point to critical directions for future work. We aim to incorporate detailed resistance mechanisms at the genomic level, poly-microbial dynamics that consider competition and synergy among pathogens, and multi-drug treatment protocols that reflect current clinical practices. Ultimately, this framework serves not only as a simulation tool but as a decision-support platform for researchers and policymakers seeking to design more effective, context-sensitive interventions against the growing threat of antibiotic resistance.

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