# CHAPTER ONE

# INTRODUCTION

## 1.1 Background to the Study

Hospitals are primarily intended to be places of healing, where patients receive care that alleviates or cures their illnesses. Unfortunately, the hospital environment itself is often a significant source of infection. Patients, healthcare workers, visitors, and even family caregivers face risks of acquiring infections through various transmission pathways within healthcare settings.

In many cases, individuals admitted for one condition may develop additional infections unrelated to their initial illness. Such infections are referred to as nosocomial infections, also known as hospital-acquired infections (HAIs) or healthcare-associated infections (HCAIs) (McBryde et al., 2004). Common examples include urinary tract infections (UTIs), surgical site infections (SSIs), wound infections (WIs), and ventilator-associated pneumonia (VAP), etc. These infections are frequently caused by bacterial pathogens such as Staphylococcus aureus, Escherichia coli, and Enterococci etc.

A major challenge arises from the prevalence of antibiotic-resistant strains. Commonly used antibiotics such as penicillin, tetracycline, ampicillin, methicillin, and vancomycin are increasingly ineffective due to bacterial resistance. For instance, strains such as Methicillin-Resistant Staphylococcus aureus (MRSA), Vancomycin-Resistant Enterococci (VRE), and Carbapenem-Resistant E. coli (CRE) have been widely documented in the literature (McBryde et al., 2004). Consequently, nosocomial infections represent a serious threat, particularly to inpatients who serve as major reservoirs.

Healthcare workers, have been recognized as key agents in the transmission of these infections (Semmelweiss, 1861), and they play a central role in infection dynamics. This has motivated researchers to model nosocomial transmission using compartmental mathematical frameworks, often based on sporadic contact patterns between patients and healthcare workers (Cooper et al., 1999).

The public health burden of nosocomial infections is profound. They are associated with extended hospital stays, increased morbidity and mortality, and substantial financial costs (Abalkhail and Marzouk, 2025). The World Health Organization (WHO, 2024) reported that nearly 3.5 million people can lose their lives due to nosocomial infections every year up to 2050. In Nigeria, a recent review estimated that approximately 15.75% of hospitalized patients in Nigeria acquire nosocomial infection (Onwuliri et al., 2025). Kesah et al., 2004 reported that incidence rates of nosocomial infections range between 4.7% and 45.8% in surgical wards of Lagos University Teaching Hospital. Similarly, a study at University College Hospital (UCH), Ibadan, recorded 596 cases of nosocomial infection out of 22,941 admissions, corresponding to a prevalence of 2.6% (Ige et al., 2011).

The public health burden of nosocomial infections statistics, combined with the growing threat of antimicrobial resistance, underscore the urgent need to investigate the transmission dynamics of nosocomial infections through mathematical modeling and other analytic approaches.

### 1.2 Statement of Problem

Nosocomial infections continue to pose a critical challenge in healthcare management worldwide, leading to prolonged hospital stays, increased treatment costs, and elevated morbidity and mortality rates (Sandu et al., 2025). In Nigeria, several studies (Kesah et al., 2004; Ige et al., 2011; and Onwuliri et al., 2025) have reported significant incidences of these infections, reflecting their considerable public health and economic burden. Despite sustained efforts at prevention, transmission remains difficult to control due to the complexity of interactions within healthcare facilities (Ilori et al., 2024).

Mathematical models have been widely employed to understand the dynamics of nosocomial infections and to guide intervention strategies (Cooper et al., 1999, McBryde et al., 2004, and Wang and Ruan, 2017). However, most existing models have primarily focused on patient-healthcare worker interactions, while overlooking an important group that plays a substantial role in Nigerian hospital settings, the patients' family caregivers. Several surveillance studies (Park et al., 2020; Lee et al., 2022; Zahradnik et al., 2024 and Clavel et al., 2025) have highlighted the role of family caregivers in infection prevention and control (IPC). In particular, Lee et al. (2022) emphasized that family caregivers may act as vectors of hospital-acquired infections and stressed

the importance of extending IPC efforts beyond healthcare workers to include informal caregivers as well.

Unlike in many developed healthcare systems, where professional staff are solely responsible for direct patient support, Nigerian hospitals frequently rely on family caregivers, who may exceed one per patient and are deeply involved in day-to-day care. These responsibilities include feeding, assisting with bathing and hygiene, running pharmacy errands, handling hospital documentation, and providing bedside support. Through these activities, family caregivers interact not only with patients but also with multiple healthcare workers and high-touch environmental surfaces that are often contaminated.

These create multiple overlooked pathways for transmission. When attending to a colonized patient, caregivers face a high risk of acquiring pathogens through direct contact. Conversely, if a caregiver acquires contamination from the hospital environment or healthcare workers, poor compliance with hand hygiene (often close to zero among non-professional caregivers) makes them potential vectors of infection to uncolonized patients. Thus, caregivers can function both as recipients and transmitters of pathogens, significantly amplifying the risk of hospital-acquired infections.

With the rising threat of antimicrobial resistance, particularly methicillin-resistant *Staphylococcus aureus* (MRSA), the absence of family caregivers in current modeling frameworks represents a critical gap in nosocomial infection research. Incorporating this group into mathematical models is essential for accurately characterizing transmission dynamics, identifying high-risk routes of spread, and designing effective, context-specific interventions. A robust model that explicitly accounts for the role of family caregivers will provide new insights into the persistence and control of nosocomial infections in Nigerian healthcare settings, with potential applications for other low- and middle-income countries facing similar challenges.

### 1.3 Aim and Objectives of the Study

This study aims to develop and analyze deterministic and stochastic models of nosocomial infection transmission that explicitly incorporate patients' family caregivers, with particular focus on MRSA transmission in Nigerian healthcare settings.

The objectives are to:

(i) develop deterministic and stochastic models that explicitly incorporate patients' family caregivers as a distinct transmission pathway

(ii) derive and interpret the basic reproduction number ($R_0$) for nosocomial infections in the presence of patients' family caregivers.

(iii) analyze the dynamics of both deterministic and stochastic models under varying levels of caregiver–patient interaction.

(iv) evaluate the impact of key infection control strategies (e.g., hand hygiene), in the presence of caregivers.

(v) provide theoretical insights and practical recommendations for hospital policies aimed at reducing nosocomial infection prevalence.

## 1.4 Definition of Terms

### 1.4.1 Burden of an Infection

This is the cost and stress an infection poses to public health management. For nosocomial infections it ranges from elongation of hospital stay, exhaustion of hospital bed space, increased cost of treatment, morbidity and mortality in extreme cases. Also a sustained increase in the prevalence of the disease leads to increase in its incidence which further creates addition tension to public health management.

### 1.4.2 Deterministic Model

A deterministic model is a mathematical model whose outcome is determined by the initial conditions and parameter values with no role of randomness. For a given set of inputs, the model will always produce the same output. In modeling of infectious diseases, deterministic models are commonly expressed as system of ordinary differential equations that describe the average behavior of populations' overtime.

### 1.4.3 Stochastic Model

A stochastic model in the other hand is a mathematical model that incorporates the role of randomness in its structure. Stochastic models capture random fluctuations associated with real-

world processes unlike deterministic models, especially in small populations. In modeling of infectious diseases, stochastic models depict disease transmission as a probabilistic process and allow for variability in outcomes such as disease extinction or outbreak even when the initial conditions are same.

### 1.4.4 Basic Reproduction Number

The basic reproduction number denoted as $\boldsymbol{R_0}$ is the expected number of secondary infections generated by a single infectious individual introduced into a completely susceptible population. It is used as a threshold to ascertain whether an infection will persist (if $\boldsymbol{R_0 > 1}$) or dies out (if $\boldsymbol{R_0 < 1}$).

### 1.4.5 Colonized Patients

In epidemiology a colonized patients are patients who harbor microorganisms (like bacteria) on their body, commonly on the skin, without showing signs or symptoms of infection. The patient may not show any symptom but can transmit the organism to others.

### 1.4.6 Uncolonized Patients

Uncolonized patients are patients who do not carry a particular microorganism on or in thier body. They are the susceptible population that can be colonized if exposed.

## 1.5 Outline of the Thesis

This thesis has five chapters. In chapter one, we gave the background of the study, statement of problem, aim and objectives of the study and definition of some basic terms. In chapter two, a literature review on the burden and etiology of nosocomial infections were given together with models of nosocomial infections from other authors. In chapter three, we presented the formulation of a deterministic model for the spread of MRSA, the positivity and boundedness of the developed model and an explicit expression for the basic reproduction number. In chapter four we formulated an equivalent stochastic model for the spread of MRSA based the principles of Continuous Time Markov Chains (CTMC) and obtained the transmission probabilities, Kolmogorov equation and the drift and diffusion terms of the model. Chapter five gave the

analysis of both the deterministic and the stochastic models using plausible parameter values, the results and discussion. Finally in Chapter six the conclusion and recommendations are presented.

# CHAPTER TWO

# LITERATURE REVIEW

## 2.1 Introduction

Nosocomial infections are infections contracted within a healthcare setting. They remain a major public health challenge worldwide leading to increase in morbidity, mortality, length of hospital stay and healthcare costs. The hospital environment remains the major reservoir for these infections due to high patient turnover, frequent invasive procedures, close patient-to-patient contact through healthcare workers (HCWs), patients' family caregivers, and high contact environmental surfaces. The prevalence of these infections in both developed and developing countries highlights gaps in infection control practices, surveillance programs and sensitivity of diagnosis in hospitals. The situation is more severe in low-income and middle-income countries due to overcrowding, insufficient staff, limited resources and poor adherence to infection prevention and control policies.

Mathematical modeling has been used to model the transmission dynamics of nosocomial infections based majorly on the sporadic contacts between patients and HCWs. This has helped in identifying key parameters responsible for the spread of nosocomial infections and also helps in evaluating the impact of intervention procedures like hand hygiene, isolation etc. In doing this both deterministic and stochastic methods have been applied in order to capture the complexities of infection pathways and random events in small populations.

In this chapter we review existing literature on nosocomial infections with emphasis on the burden of the infection, the etiology of MRSA, and deterministic and stochastic models developed by other authors to describe the transmission.

## 2.2 Burden of Nosocomial Infections

Globally, nosocomial infections are a major cause of morbidity and mortality among hospitalized patients (Sandu, 2025). World Health Organization Report (WHO, 2024) reported that nearly 3.5 million people will lose their lives due to nosocomial infections every year up to 2050. This

corresponds to 4.4 times the number of global deaths in 2021 due to human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) and sexually transmitted diseases combined. A global surveillance study across 204 countries and territories in 2019 reported that 4.95 million deaths were associated with various forms of nosocomial infections. The study further revealed that Western Sub-Saharan Africa had the highest mortality rate at 27.3 deaths per 100,000, while Australia recorded the lowest with 6.5 deaths per 100,000 (Antimicrobial Resistance Collaborators, 2022).

In Europe, nosocomial infections were estimated to contribute to an additional 110,000 deaths annually, with associated direct healthcare costs of nearly 7 billion Euros per year (ECDC, 2008). In Belgium, approximately 900 hospital beds are occupied yearly by patients with at least one episode of nosocomial infection (Gordts et al., 2007). In the United States, nearly 2 million patients acquire infections during hospital stays each year, with an estimated 99,000 attributable deaths in 2002 with a corresponding annual economic burden is projected at 6.4 billion USD (Klevens et al., 2007).

In Africa, relatively few surveillance studies have been conducted, but available reports highlight significant prevalence rates and underscore the need for effective intervention measures. Nejad et al. (2011) estimated the prevalence of nosocomial infections in sub-Saharan Africa to range between 2.5% and 14%. Specific studies reported prevalence rates of 2.5–14.8% in Algeria (Atif et al., 2006), Burkina Faso (Lamarque, 2003), and Senegal (Dia et al., 2008). In Zambia, Mukomena et al. (2023) examined 841 clinical specimens from two large tertiary hospitals and identified infections in 69.9% (588) of cases, which resulted in prolonged hospital stays and increased treatment costs. Similarly, Alemu et al. (2020), through a systematic review of 18 studies in Ethiopia, reported a pooled prevalence of 16.96% (2,344/13,821 patients), with point prevalence estimates ranging between 3.5–12% in developed countries and 5.7–19.1% in middle-income countries.

In Nigeria, a recent review estimated that approximately 15.75% of hospitalized patients in Nigeria acquire nosocomial infection (Onwuliri et al., 2025). Kesah et al. (2004) reported incidence rates ranging from 4.7% to 45.8% in the surgical wards of Lagos State University Teaching Hospital. At the University College Hospital (UCH), Ibadan, Ige et al. (2011) observed

596 cases of nosocomial infections out of 22,941 admissions, corresponding to a prevalence of 2.6%. Ameh et al. (2007), in a study of 322 pediatric surgical patients at the National Hospital, Abuja, found that 23.6% (76 patients) developed surgical site infections (SSIs). Also, Abubakar (2020) conducted a point-prevalence survey across three acute care hospitals in Northern Nigeria, reporting 50 cases of HAIs among 321 patients, with an overall prevalence of 14.3%.

In Edo State, evidence remains limited. However, Oshoma et al. (2016) conducted a microbial survey in the Radiological Unit of the University of Benin Teaching Hospital (UBTH), identifying Staphylococcus aureus as the most frequently isolated pathogen from contaminated equipment. Additionally, Obasuyi (2021) assessed knowledge of nosocomial infections among healthcare workers in UBTH, Central Hospital, and Primary Health Centre Okada. While the study revealed satisfactory awareness levels among doctors and nurses, it emphasized the need for stricter adherence to infection control measures.

This growing body of evidence underscores the significant health and economic burden posed by nosocomial infections, as well as the urgent need for further investigation into their transmission pathways. Understanding these dynamics is critical for developing effective interventions and control strategies.

### 2.3 Etiology of Methicillin-Resistant Staphylococcus Aureus (MRSA)

Staphylococcus aureus is the leading cause of various nosocomial infections and the most commonly studied pathogen in the transmission dynamics of nosocomial infections. MRSA in particular, has been reported to contribute significantly to high morbidity and mortality among hospitalized patients (Engemann et al., 2003). Infections caused by MRSA are associated with prolonged hospital stays and increased healthcare costs when compared with those caused by Methicillin-Sensitive Staphylococcus aureus (MSSA) (Capitano et al., 2003). The proportion of *S. aureus* isolates resistant to methicillin has continued to rise globally, and Nigeria is no exception (Ige et al., 2011, Oshoma et al., 2016).

Staphylococcus aureus is a Gram-positive coccus, commonly carried asymptomatically on the skin or in the anterior nares of about 20–30% of the population, with higher prevalence in individuals with eczematous skin (Wertheim et al., 2005). People requiring frequent injections

(such as insulin-dependent diabetics, intravenous drug users, and dialysis patients) are especially vulnerable to *S. aureus* infections.

When penicillin was introduced for clinical use in 1941, S. aureus strains were initially highly sensitive. However, resistance emerged rapidly, and by the 1950s, more than 40% of isolates produced penicillinase enzymes capable of hydrolyzing the β-lactam ring, rendering the antibiotic ineffective (Chambers, 2001).

In response to the growing problem of penicillin resistance, semisynthetic β-lactam antibiotics (such as methicillin, flucloxacillin, dicloxacillin, and cephalothin) were developed and initially proved effective against penicillin-resistant strains. Unfortunately, within just a few years of their introduction, methicillin-resistant Staphylococcus aureus (MRSA) was reported, with the first clinical isolate described in 1961 (Jevons, 1961). MRSA emerged through acquisition of the mecA gene, which encodes a penicillin-binding protein with markedly reduced affinity for β-lactam antibiotics.

Although MRSA can persist as a harmless colonizer, its carriage remains clinically significant (Kluytmans et al., 1997; Wertheim et al., 2005). The median duration of MRSA carriage has been estimated at approximately 8.5 months (Scanvic et al., 2001), and longitudinal studies have shown that between 30–60% of healthcare-associated MRSA colonizations can progress to invasive disease (von Eiff et al., 2001; Wertheim et al., 2005)

Transmission of MRSA occurs primarily through direct physical contact, especially via the hands of healthcare workers. Colonization is often transient and can be eliminated through effective hand hygiene practices. Cooper et al. (2003) established that MRSA spread occurs mainly through cross-transmission of existing clones rather than the spontaneous emergence of new resistant strains. Colonization usually precedes infection and may persist for weeks or months. Earlier studies demonstrated that MRSA can survive on healthcare workers' hands for up to 3 hours, though it can be eradicated by proper hand washing and sanitization (Peacock et al., 1980; Thompson et al., 1982). The hospital environment has also been identified as a reservoir, with surfaces and equipment contributing to MRSA contamination (Boyce et al., 1997; Wang and Ruan, 2017).

Understanding the etiology and transmission pathways of MRSA highlights the complex dynamics underlying hospital-acquired infections. To capture these dynamics and evaluate potential intervention strategies, researchers have increasingly turned to mathematical models. Such models (both deterministic and stochastic) provide valuable tools for analyzing infection spread within healthcare settings and for guiding effective control policies.

### 2.4 Modeling the Spread of Nosocomial Infections

Given the complex pathways through which MRSA and other nosocomial pathogens spread within hospitals, it becomes essential not only to understand their etiology but also to quantify and predict their transmission dynamics. Mathematical modeling provides a useful framework for this, enabling researchers to describe patterns of spread, evaluate control strategies, and estimate the potential impact of interventions.

The use of mathematical models in infectious disease epidemiology dates back centuries. Bernoulli (1760) and Farr (1840) applied empirical methods to evaluate smallpox vaccination and mortality data. Following the acceptance of the germ theory of disease, Hamer (1906) introduced the principle of mass action, which was further developed by Ross (1916) and Ross and Hudson (1916) into continuous-time epidemic equations. Building on these foundations, Kermack and McKendrick (1927) proposed the compartmental SIR (Susceptible–Infectious–Recovered) model, which has since become the classical epidemic framework.

Despite these advances, traditional models do not directly address the unique dynamics of nosocomial transmission within hospital environments. To bridge this gap, Ross (1911) and Macdonald (1957) originally developed the host-vector model for malaria, where transmission occurs through a vector, in this case, the Anopheles mosquito. This framework has since been adapted to describe hospital-acquired infections, with healthcare workers (HCWs) serving as transient “vectors” of transmission between patients.

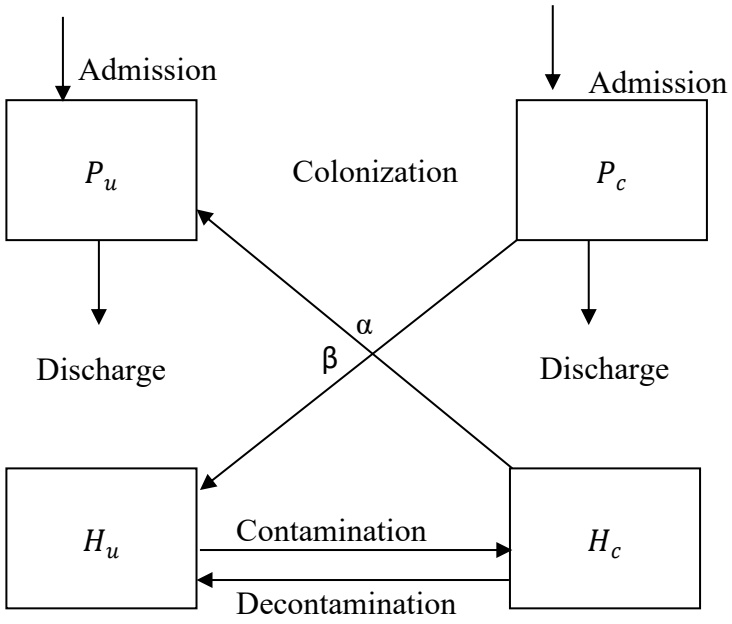



**Figure 2.1**: Basic transmission model for nosocomial infections (McBryde et al.,2004).

In the nosocomial context, pathogens are assumed not to spread directly from patient to patient but through the contaminated hands of HCWs. Transmission occurs when a contaminated healthcare worker $(H_c)$ comes in contact with an uncolonized patient$(P_u)$, or when a colonized patient $(P_c)$ interacts with an uncontaminated healthcare worker$(H_u)$. Decontamination of $H_c$ back to $H_u$ takes place through intervention measures such as proper hand washing compliance.

The key adjustment in Figure 2.1, compared with the Ross–Macdonald host–vector model, is the inclusion of patient flow, that is, the admission and discharge of both colonized and uncolonized patients. This framework forms the foundation for developing more detailed models of nosocomial infection transmission, which we now proceed to review.

### 2.4.1 Deterministic and Stochastic Models on the Spread of Hand-borne Nosocomial Pathogens

Cooper et al. (1999) developed a mathematical model to describe the spread of hand-borne nosocomial pathogens, such as Staphylococcus aureus, within a general medical–surgical ward. Unlike earlier models, their work introduced a stochastic framework for studying nosocomial transmission.

The basic model consisted of colonized patients $(y)$, uncolonized patients $(x)$, contaminated healthcare workers $(y')$, and uncontaminated healthcare workers $(x')$. From this deterministic structure, they derived a stochastic equivalent by converting rates into discrete variables with continuous time.

Analysis of the stochastic model revealed that even small changes in pathogen transmissibility led to substantial differences in introduction rates, ward-level prevalence, and the number of colonized patient-days. Importantly, the study showed that modest improvements in the frequency of effective hand hygiene were sufficient to bring endemic organisms under control. In addition, reducing the admission of colonized patients was highlighted as another effective control measure.

They emphasized that while deterministic models can capture the non-linear interactions between a limited set of processes, the small population sizes typical of hospital wards make a stochastic approach essential for accurately representing nosocomial transmission dynamics.

The deterministic model is as follows:

$$\frac{dx}{dt} = (1-\sigma)(\mu x + \mu y + \gamma y) - \beta x\frac{y'}{n'} + (1-\sigma)(\mu+\gamma)y$$

$$\frac{dy}{dt} = \sigma(\mu x + \mu y + \gamma y) + \beta x\frac{y'}{n'} - (1-\sigma)(\mu+\gamma)y$$

$$\frac{dx'}{dt} = -\beta' y\frac{x'}{n'} + \mu' y' \qquad (2.1)$$

$$\frac{dy'}{dt} = \beta' y\frac{x'}{n'} - \mu' y'$$

The equivalent stochastic process is,

$$\Pr\left\{\left[Y(t+\Delta t), Y'(t+\Delta t)\right] = [i+1, j] \parallel \left[Y(t), Y'(t)\right] = [i,j]\right\} = \frac{\beta(n-i)j\Delta t}{n'} + \sigma(\mu n + \gamma i)\Delta t + o(\Delta t)$$

$$\Pr\left\{\left[Y(t+\Delta t), Y'(t+\Delta t)\right] = [i, j+1] \parallel \left[Y(t), Y'(t)\right] = [i,j]\right\} = \frac{\beta' i(n'-j)\Delta t}{n'} + o(\Delta t) \qquad (2.2)$$

$$\Pr\left\{\left[Y(t+\Delta t), Y'(t+\Delta t)\right] = [i-1, j] \parallel \left[Y(t), Y'(t)\right] = [i,j]\right\} = (1-\sigma)(\mu+\gamma)i\Delta t + o(\Delta t)$$

$$\Pr\left\{\left[Y(t+\Delta t), Y'(t+\Delta t)\right] = [i, j-1] \parallel \left[Y(t), Y'(t)\right] = [i,j]\right\} = \mu' j\Delta t + o(\Delta t)$$

**Table 2.1:** Model Parameters and their Descriptions

| Parameters | Description |
|---|---|
| $n$ | Number of patients |
| $n^{'}$ | Number of health care workers (HCWs) |
| $\mu$ | Patient removal rate |
| $\mu^{'}$ | Hand washing rate |
| $\gamma$ | Detection rate of colonized patients |
| $\sigma$ | Proportion of admissions already colonized |
| $c$ | Patient-carer contact rate |
| $p$ | Carer-patient transmission probability |
| $p^{'}$ | Patient-carer transmission probability |
| $\beta$ | Carer-patient transmission rate |
| $\beta^{'}$ | Patient-carer transmission rate |

### 2.4.2 Model on the Effect of Antimicrobial Cycling on the Spread of Nosocomial Infections

Bergstrom et al. (2004) studied the effect of antimicrobial cycling, on the spread of nosocomial infections. That is, when two or more antibiotic classes are alternated within a period of months to years to checkmate the spread of nosocomial infections in the hospital. They developed a mathematical model consisting of four compartments X, the uncolonized patients, S, the colonized patients, $R_1$, patients colonized by the strains resistant to drug1 , and $R_2$ , patients colonized by strains resistant to drug2.

The model is as follows,

$$\frac{dS}{dt} = (m - S)\mu - (\tau_1 + \tau_2 + \gamma)S + \beta SX + \sigma\beta(c_1R_1 + c_2R_2)S$$

$$\frac{dR_1}{dt} = (m_1 - R_1)\mu - (\tau_2 + \gamma)R_1 + \beta(1 - c_1)R_1X - \sigma\beta(c_1S + (c_1 - c_2)R_2)R_1$$

$$\frac{dR_2}{dt} = (m_2 - R_2)\mu - (\tau_1 + \gamma)R_2 + \beta(1 - c_2)R_2X - \sigma\beta(c_2S + (c_2 - c_1)R_1)R_2 \quad (2.3)$$

$$\frac{dX}{dt} = (1 - m - m_1 - c_1 - X)\mu + (\tau_1 + \tau_2 + \gamma)S + (\tau_2 + \gamma)R_1 + (\tau_1 + \gamma)R_2 - \beta X(S + (1 - c_1)R_1 + (1 - c_2)R_2)$$

**Table 2.2:** Model Parameters and their Descriptions

| Parameter | Definition |
|---|---|
| $\mu$ | The rate of patient turnover in the hospital |
| $\sigma$ | The rate of secondary colonization relative to that of primary colonization |
| $c_1$ | Fitness cost by a bacterium for being resistant in the absence of drug1 |
| $c_2$ | Fitness cost by a bacterium for being resistant in the absence of drug2 |
| $m$ | Proportion of individuals who are colonized |
| $m_1$ | Proportion of individuals who are colonized by strains resistant to drug1 |
| $m_2$ | Proportion of individuals who are colonized by strains resistant to drug2 |
| $\alpha$ | Physician compliance with the cycling program. |
| $\tau_1$ | Rate of use of drug1 |
| $\tau_2$ | Rate of use of drug2 |
| $\beta$ | Rate of colonization |
| $\gamma$ | Rate of decolonization or recovery from colonization |

They concluded that cycling is unlikely to reduce either the incidence or spread of nosocomial infections but noticed that other strategies like mixing were each patient receives one of the drug classes simultaneously in the hospital yields better result.

### 2.4.3 Model Linking Hospital and Community Reservoirs of MRSA Colonization

Cooper et al. (2004) considered both hospital and community reservoirs of MRSA colonization. They used mathematical models to describe the dynamics of MRSA in seven compartments, the colonized patients in the hospital $(y)$ , the uncolonized patients in the hospital $(x)$, the isolated patients in the hospital $(z)$ , the colonized patients in the community with high readmission rate $(y_c)$ , the uncolonised patients in the community with high readmission rate $(x_c)$ , the colonized patients in the community with low readmission rate $(y_c^{'})$ , and the uncolonized patients in the community with low readmission rate $(x_c^{'})$ .

They showed that prompt and effective patient isolation can contribute to control by reducing transmission. However because the isolation rate decreases when isolation capacity is exceeded, for a wide range of parameters, high-level persistence can occur even though the control measures could have prevented such a high level from becoming established. That is, control measures can repeatedly prevent outbreaks in the short-term but may result in long-term control failure resulting from gradual increases in the community reservoir. If resources do not scale with MRSA prevalence, isolation policies can fail catastrophically.

The model schematic diagram, system of differential equations and parameter values are as below.

$$\frac{dy}{dt} = \beta xy - \lambda y + \nu y_c + \xi y_c^{'} - \mu y - \Phi(y,z)$$

$$\frac{dx}{dt} = -\beta xy + \lambda y + \nu x_c + \xi x_c^{'}$$

$$\frac{dz}{dt} = \Phi(y,z) - pz$$

$$\frac{dy_c}{dt} = \mu y + p(1-\pi)z - (\nu + \lambda + \gamma)y_c \qquad (2.4)$$

$$\frac{dx_c}{dt} = \mu x + \lambda y_c + p\pi z - (\nu + \gamma)x_c$$

$$\frac{dy_c^{'}}{dt} = \gamma y_c - (\xi + \lambda)y_c^{'}$$

$$\frac{dx_c^{'}}{dt} = \gamma x_c + \lambda y_c^{'} - (\xi + \lambda)x_c^{'}$$

**Table 2.3:** Model Parameters and their Description

| Parameters | Description |
|---|---|
| $\beta$ | Transmission rate |
| $\Phi$ | Isolation rate per day |
| $n_i$ | Number of beds in isolation unit |
| N | Number of beds in hospital |
| $N_c$ | Community population size |
| $\frac{1}{\lambda}$ | Mean duration of carriage, days |
| $\frac{1}{\mu}$ | Mean length of stay, days |
| $v$ | Readmission rate (High) per day |
| $\xi$ | Readmission rate (Low) per day |
| $\gamma$ | Rate of change from high to low readmission rate per day |
| $\frac{1}{p}$ | Mean length of stay in isolation, days |
| $\pi$ | Proportion of isolated patients cleared of MRSA |

### 2.4.4 A Stochastic Model on the Estimation of the Transmission Rate of MRSA in an Intensive Care Unit (ICU)

McBryde et al. (2007a) developed a stochastic model to estimate the transmission rate of MRSA in an intensive care unit (ICU). They formulated a mathematical method consisting of four compartments, the colonized patients $(Y_p)$, uncolonized patients $(X_p)$, contaminated HCWs $(Y_h)$ and uncontaminated HCWs $(X_h)$.

The hand hygiene compliance was dictated to be the most effective intervention method. Declonization was predicted to be somewhat infective and increasing the number of HCWs was seen to increase the transmission of MRSA, in the absence of patient cohorting. This implies that increasing staff strength does not necessarily lead to reduction in transmission of nosocomial

pathogens. The predictions of the stochastic model differed from that of the deterministic model, as it gives lower levels of colonizations.

The model is as follows,

$$\frac{dX_p}{dt} = (1-\sigma)\Omega + dY_p - cp_{hp}X_pY_h - \mu X_p$$

$$\frac{dY_p}{dt} = \sigma\Omega + cp_{hp}X_pY_h - \mu' Y_p - dY_p \qquad (2.5)$$

$$\frac{dX_h}{dt} = -cp_{ph}X_hY_p + \kappa Y_h$$

$$\frac{dY_h}{dt} = cp_{ph}X_hY_p - \kappa Y_h$$

The stochastic model constructed as,

$$\Pr\left(Y_p(t+\delta) = i+1 \middle| Y_p(t) = i\right) = cp_{hp}(n_p - i)\overline{Y_h}\delta + \mu\sigma(n_p - i)\delta + o(\delta)$$

$$\Pr\left(Y_p(t+\delta) = i-1 \middle| Y_p(t) = i\right) = \left(d + \mu'(1-\sigma)\right)i\delta + o(\delta) \qquad (2.6)$$

$$\Pr\left(Y_p(t+\delta) = i \middle| Y_p(t) = i\right) = 1 - cp_{hp}(n_p - i)\overline{Y_h}\delta - \mu\sigma(n_p - i)\delta - \left(d + \mu'(1-\sigma)\right)i\delta + o(\delta),$$

which are the probabilities during a small time interval($\delta$) of transiting from one state to another.

**Table 2.4:** Model Parameters and their Description

| **Parameters** | **Description** |
|---|---|
| $c$ | Contact rate |
| $d$ | Decolonization rate |
| $\sigma$ | Admission prevalence |
| $\Omega$ | Admission rate |
| $\mu'$ | Discharge rate of colonized patients |
| $\mu$ | Discharge rate of uncolonized patients |
| $p_{ph}$ | Transmission rate from patients to HCWs |
| $p_{hp}$ | Transmission rate from HCWs to patients |
| $\kappa$ | Hand hygiene rate per HCW |

### 2.4.5 A Deterministic Discrete-Time Markov Chain Model for the Dynamics of Antibiotic Resistant Bacteria (MRSA) in ICU

Boldin et al. (2007) formulated a deterministic and a discrete time Markov chain model to describe the dynamics of antibiotic resistant bacteria (MRSA) in ICUs. They demonstrated that precautions through topical antibiotics application of nonabsorbable antibiotics, with the aim of reducing antibiotic resistance at the population level, can only be effective when (i) a high percentage of newly admitted patients are colonized and (ii) cross-transmission rates in the ward are low. Their findings claim to represent a firm theoretical argument against the routine use of topical antimicrobial prophylaxis for infection control.

They described three different sites of colonization, that is, the skin (S), the gut (G) and the lungs (L). Hence they classified each patient in the ICU with these eight different labels: 0, G, S, L, GS, GL, SL and GSL, leading to eight-compartmental model. ˙

$$
\begin{aligned}
\dot{x}_0 &= \mu p_0 - (\sigma \mathrm{I} + \mu) x_0 \\
\dot{x}_G &= \mu p_G - (\sigma \mathrm{I} + \alpha_{GS} + \mu) x_G \\
\dot{x}_S &= \mu p_S + \sigma \mathrm{I} x_0 - (\alpha_{SG} + \alpha_{SL} + \mu) x_S \\
\dot{x}_L &= \mu p_L - (\sigma \mathrm{I} + \alpha_{LS} + \mu) x_L \qquad (2.7) \\
\dot{x}_{GS} &= \mu p_{GS} + (\sigma \mathrm{I} + \alpha_{GS}) x_G + \alpha_{SG} x_S - (\alpha_{SL} + \mu) x_{GS} \\
\dot{x}_{GL} &= \mu p_{GL} - (\sigma \mathrm{I} + \alpha_{GS} + \alpha_{LS} + \mu) x_{GL} \\
\dot{x}_{SL} &= \mu p_{SL} + (\sigma \mathrm{I} + \alpha_{LS}) x_L + \alpha_{SL} x_S - (\alpha_{SG} + \mu) x_{SL} \\
\dot{x}_{GSL} &= \mu p_{GSL} + (\sigma \mathrm{I} + \alpha_{LS} + \alpha_{GS}) x_{GL} + \alpha_{SL} x_{GS} + \alpha_{SG} x_{SL} - \mu x_{GSL}
\end{aligned}
$$

**Table 2.5:** Model Parameters and their Description

| Parameters | Description |
|---|---|
| M | Constant probability per unit time of been removed from the unit |
| $p_0$ | The probability that the three body parts, skin, gut and lungs are not colonized on admission. |
| $p_G$ | The probability that the gut is colonized on admission. |
| $p_S$ | The probability that the skin is colonized on admission. |
| $p_L$ | The probability that the lungs are colonized on admission. |
| $p_{GS}$ | The probability that the gut and skin are colonized on admission. |
| $p_{GL}$ | The probability that the gut and lungs are colonized on admission. |
| $p_{SL}$ | The probability that the skin and lungs are colonized on admission. |
| $p_{GSL}$ | The probability that the three body parts, skin, gut and lungs are colonized on admission. |
| $\alpha_{GS}$ | The transmission rate from gut to skin colonization. |
| $\alpha_{SG}$ | The transmission rate from skin to gut colonization. |
| $\alpha_{SL}$ | The transmission rate from skin to lungs colonization. |
| $\alpha_{LS}$ | The transmission rate from lungs to skin colonization. |
| Σ | The cross transmission rate (skin to skin transmission through the contaminated hands of HCWs) |

### 2.4.6 A Structured Continuous-Time Hidden Markov Chain Model on the Acquisition of Nosocomial Pathogens

McBryde et. al. (2007b) used a structured continuous-time hidden markov chain to model the acquisition of nosocomial pathogens and compared their results with that obtained from genotyping. They found that hidden markov models can be applied to serial prevalence data to estimate the characteristics of acquisition of nosocomial pathogens and distinguished between

epidemic and sporadic acquisition. This model was able to estimate transmission parameters despite imperfect detection of the organism.

$$\frac{d(N-C)}{dt} = \mu C - \beta C(N-C) - \nu(N-C)$$
$$\frac{dC}{dt} = \beta C(N-C) + \nu(N-C) - \mu C \quad (2.8)$$

To apply the HMM they constructed an equivalent stochastic model as

$$\Pr[C(t+h) = i+1 | C(t) = i] = \beta i(N-i)h + \nu(N-i)h$$
$$\Pr[C(t+h) = i-1 | C(t) = i] = \mu i h \quad (2.9)$$
$$\Pr[C(t+h) = i | C(t) = i] = 1 - \beta i(N-i)h + \nu(N-i)h - \mu i h$$
$$\Pr[C(t+h) = j(j \neq i, i+1, i-1) | C(t) = i] = 0$$

**Table 2.6:** Model Parameters and their Description

| Parameters | Description |
|---|---|
| $N$ | Number of patients |
| $C$ | Number of colonized patients |
| $\mu$ | Removal rate of colonized patients |
| $\beta$ | Transmission rate |
| $\nu$ | Sporadic colonization rate (external sources) |

### 2.4.7 A Model on the Impact of Semi-Professional Volunteer Workers on the Transmission of MRSA in a Tertiary Hospital in China

Wang et al. (2011) considered the impact of semi-professional volunteer workers on the transmission of MRSA in a tertiary hospital in China. They developed a compartmental model to describe the transmission of MRSA. The model has six compartments, that is, colonized patients ($P_c$) and uncolonized patients ($P_u$) , contaminated HCWs ($H_c$) and uncontaminated HCWs ($H_u$),

and contaminated volunteers ($V_c$) and uncontaminated volunteers ($V_u$). Analysis of the model showed that increase in the handwashing compliance of both HCWs and volunteers will reduce transmission of MRSA drastically. Also, since volunteers care for patients on one-to-one basics, they showed that replacing volunteers with HCWs will increase the transmission of MRSA.

The model is as follows

$$\frac{dP_u}{dt} = \lambda(1-\phi) - [\frac{(1-\eta)}{N}\beta_{PH}H_c(t) + \frac{(1-\xi)}{N}\beta_{PV}V_c(t)]P_u(t) - \delta_u P_u(t)$$

$$\frac{dP_c}{dt} = \lambda\phi + [\frac{(1-\eta)}{N}\beta_{PH}H_c(t) + \frac{(1-\xi)}{N}\beta_{PV}V_c(t)]P_u(t) - \delta_c P_c(t)$$

$$\frac{dH_u}{dt} = -\frac{(1-\eta)}{N}\beta_{PH}P_c(t)H_u(t) + \gamma_H H_c(t) \qquad (2.10)$$

$$\frac{dH_c}{dt} = \frac{(1-\eta)}{N}\beta_{PH}P_c(t)H_u(t) - \gamma_H H_c(t)$$

$$\frac{dV_u}{dt} = -\frac{(1-\xi)}{N}\beta_{PV}P_c(t)V_u(t) + \gamma_V V_c(t)$$

$$\frac{dV_c}{dt} = \frac{(1-\xi)}{N}\beta_{PV}P_c(t)V_u(t) - \gamma_V V_c(t)$$

The parameter values are given in Table 2.7 below.

**Table 2.7:** Model Parameters and their Description

| Parameters | Description |
|---|---|
| $N$ | Total number of beds |
| $\phi$ | Fraction of admission of colonized patients |
| $1/\delta_u$ | Length of stay of uncolonized patients |
| $1/\delta_c$ | Length of stay of colonized patients |
| $\eta$ | Hand hygiene compliance of HCWs |
| $\xi$ | Hand hygiene compliance of volunteers |
| $\beta_{PH}$ | Transmission rate from colonized patients to HCWs |
| $\beta_{PV}$ | Transmission rate from colonized patients to volunteers |
| $1/\gamma_H$ | Duration of contamination HCWs |
| $1/\gamma_V$ | Duration of contamination of volunteers |

### 2.4.8 A Model on the Transmission of MRSA in a Nursing Home for the Elderly

Chamchod and Ruan (2012) considered the transmission of MRSA in nursing home for the elderly. They constructed a deterministic model consisting of four different compartments; colonized (C) and uncolonized (U) residents, and contaminated ( $H_c$ ) and uncontaminated (H) healthcare workers. They also developed an equivalent stochastic model to elucidate the behavior of the model by understanding the prevalence of MRSA, its persistence and possible control measures for the pathogen in the nursing home.

They concluded that MRSA may persist without strict screening and decolonization at admission. Control strategies include resident decolonization, better hand hygiene, reducing HCW contamination time, and lowering resident–staff ratios. Colonization risk increases with more colonized admissions, longer colonization, and higher contact rates. Notably, a colonized resident is far more likely to trigger an outbreak than a contaminated HCW.

The deterministic model is:

$$\dot{U} = (1-\lambda)\Lambda + \omega C - \frac{\beta_r}{N_r} UC - \frac{\beta_h}{N_h} UH_c - \gamma_u U$$

$$\dot{C} = \lambda\Lambda + \frac{\beta_r}{N_r} UC + \frac{\beta_h}{N_h} UH_c - (\omega + \gamma_c) C \qquad (2.11)$$

$$\dot{H} = -\frac{\alpha_h}{N} HC + \mu H_c$$

$$\dot{H}_c = \frac{\alpha_h}{N} HC - \mu H_c$$

Similarly the equivalent stochastic model stating the transition probabilities of various events occurring in (t+dt) is as follows:

$$P(H_c, 1) = \lambda[\gamma_u N_r - (\gamma_u - \gamma_c) C]dt \qquad C \to C + 1$$

$$P(H_c, 1) = \frac{\beta_r}{N_r}(N_r - C) C dt \qquad C \to C + 1$$

$$P(H_c, 1) = \frac{\beta_h}{N_h}(N_r - C) H_c dt \qquad C \to C + 1$$

$$P(H_c, -1) = \omega C dt \qquad C \to C - 1 \qquad (2.12)$$

$$P(H_c, -1) = \gamma_c C dt \qquad C \to C - 1$$

$$P(1, C) = \frac{\alpha_h}{N_h}(N_h - H_c) C dt \qquad H_c \to H_c + 1$$

$$P(-1, C) = \mu H_c dt \qquad H_c \to H_c - 1$$

**Table 2.8:** Model Parameters and their Descriptions

| Parameters | Description |
|---|---|
| $N_r$ | The total number of residents |
| $N_r/N_h$ | Number of residents per number of HCWs |
| $\lambda$ | Probability of admission of colonized patients |
| $1/\omega$ | Average duration of colonization |
| $1/\gamma_u$ | Average length of stay of uncolonized residents (days) |
| $1/\gamma_c$ | Average length of stay of colonized residents (days) |
| $\beta_r$ | Resident-resident transmission rate |
| $\beta_h$ | HCW-resident transmission rate |
| $\alpha_h$ | Resident-HCW transmission rate |
| $1/\mu$ | Average duration of contamination (hours) |

### 2.4.9 Deterministic and Stochastic Models on the Impact of Environmental Contamination and Presence of Volunteers in the Transmission of MRSA

Wang et al. (2012) formulated deterministic and stochastic mathematical models to investigate the impact of environmental contamination and presence of volunteers in the transmission of MRSA. The model comprises of susceptible HCWs ($H^s$), contaminated HCWs ($H^c$), susceptible patients ($P^s$), infectious patients ($P^c$), the density of bacteria in the ward ($W$), and the number of volunteers ($V$).

The analysis of the models showed that the magnitude of treat posed by environmental contamination is high and free-living bacteria in hospital environment enhances the transmission of the infection and may initiate an outbreak even when the HCWs and patients are all free from infection. This indicates that contaminated environment contributes substantially to MRSA transmission in hospital setting. The analysis showed also the presence of semi-skilled volunteers

contributes to transmission of MRSA through contact with patients. Due to complexity the volunteers were modeled implicitly in the susceptible patients, infectious patients and environmental contamination compartments.

They stated that intervention methods like hand hygiene compliance of volunteers and cleaning of hospital environments are effective in reducing colonization of patients than isolation of newly admitted patients. They however, concluded that given a sufficiently clean environment, isolation of newly admitted MRSA-positive patients could be a dominant intervention approach in reducing MRSA prevalence.

The model,

$$\frac{dH^s}{dt} = -(\beta_1 P^c + v_1 W)H^s + \gamma H^c$$

$$\frac{dH^c}{dt} = (\beta_1 P^c + v_1 W)H^s - \gamma H^c$$

$$\frac{dP^s}{dt} = (1-\overline{\phi})\Lambda - (1-q)\overline{\beta_2}H^c - ((1-p)\overline{v_2}W)P^s - d_1 P^s \qquad (2.13)$$

$$\frac{dP^c}{dt} = (1-r)\overline{\phi}\Lambda + (1-q)\overline{\beta_2}H^c + \left((1-p)\overline{v_2}W\right)P^s - d_2 P^c$$

$$\frac{dW}{dt} = \lambda P^c - (\mu + \xi V + v_1 H)W$$

The stochastic equivalent was given by stating the transition states and rates (probabilities) at which they occur.

**Table 2.9:** State Transitions and their Rates

| State Transitions | Rates |
|---|---|
| $(H^s, H^c, P^s, P^c, W) \rightarrow (H^s - 1, H^c + 1, P^s, P^c, W)$ | $\beta_1 P^c H^s$ |
| $(H^s, H^c, P^s, P^c, W) \rightarrow (H^s - 1, H^c + 1, P^s, P^c, W - 1)$ | $v_1 W H^s$ |
| $(H^s, H^c, P^s, P^c, W) \rightarrow (H^s + 1, H^c - 1, P^s, P^c, W)$ | $\gamma H^c$ |
| $(H^s, H^c, P^s, P^c, W) \rightarrow (H^s, H^c, P^s + 1, P^c, W)$ | $(1 - \overline{\phi})\Lambda$ |
| $(H^s, H^c, P^s, P^c, W) \rightarrow (H^s, H^c, P^s, P^c + 1, W)$ | $\phi\Lambda$ |
| $(H^s, H^c, P^s, P^c, W) \rightarrow (H^s, H^c, P^s - 1, P^c + 1, W)$ | $\beta_2 H^c P^s$ |
| $(H^s, H^c, P^s, P^c, W) \rightarrow (H^s, H^c, P^s - 1, P^c + 1, W - 1)$ | $v_2 W P^s$ |
| $(H^s, H^c, P^s, P^c, W) \rightarrow (H^s, H^c, P^s - 1, P^c, W)$ | $d_1 P^s$ |
| $(H^s, H^c, P^s, P^c, W) \rightarrow (H^s, H^c, P^s, P^c - 1, W)$ | $d_2 P^c$ |
| $(H^s, H^c, P^s, P^c, W) \rightarrow (H^s, H^c, P^s, P^c, W + 1)$ | $\lambda P^c$ |
| $(H^s, H^c, P^s, P^c, W) \rightarrow (H^s, H^c, P^s, P^c, W - 1)$ | $\mu W$ |

**Table 2.10:** Model Parameters and their Description

| Parameters | Description |
|---|---|
| $H$ | Number of HCWs |
| $\beta_1$ | Transmission rate from patients to HCWs (/person/day) |
| $\overline{\beta_2}$ | Transmission rate from HCWs to patients (/person/day) |
| $v_1$ | Indirect transmission rate between HCWs and the environment via volunteers (/CFUs/day) |
| $\overline{v_2}$ | Indirect transmission rate between patient's and the environment via volunteers (/CFUs/day) |
| $\Lambda$ | Inflow rate of patient's to hospital (/day) |
| $\overline{\phi}$ | Proportion of admissions already colonized when being hospitalized |
| $\lambda$ | Shedding rate of patients (CFUs/day) |
| $d_1$ | Outflow of uninfected patients (/day) |
| $d_2$ | Outflow of infected patients (/day) |
| $\gamma$ | Recovery rate of infectious HCWs (/HCW/day) |
| $\mu$ | Clearance rate of bacteria from the environment (/day) |

| | |
|---|---|
| $\xi$ | Indirect transmission rate between volunteers and the environment via free-living bacteria (/CFU/day) |
| $p$ | Hand hygiene rate of volunteers |
| $q$ | Hand hygiene rate of HCWs |
| $r$ | Isolation rate of colonized admissions |
| $\beta_2 = (1-q)\overline{\beta_2}$ | Transmission coefficient of HCWs |
| $v_2 = (1-p)\overline{v_2}$ | Transmission coefficient of volunteers |
| $\phi = (1-r)\overline{\phi}$ | Proportion of patients already colonized when admitted into the ward |

### 2.4.10 A Model on the Effect of Environmental Factor in the Transmission Dynamics of Nosocomial Infections

Browne and Webb (2015) studied the additional effect of environmental factor in the transmission dynamics of nosocomial infections. They cited the case of an outbreak of Klebsiella pneumoniae carbapenemase (KPC) infections in the Clinical Center at the National Institute of Health in Bethesda Maryland (CCNIH) USA. This was to show in addition the importance of the inclusion of environmental effect in the transmission of Nosocomial infections. As such, they classified two levels of room contaminations, level 0 (uncontaminated or contaminated at low levels) and level 1 (contaminated at significantly high level).

They described the model using six compartments, that is, the uninfected patients susceptible to acquiring the infection in level 0 contaminated rooms $(S_0)$, uninfected patients susceptible to acquiring the infection in level 1 contaminated rooms $(S_1)$, infected patients in level 0 contaminated rooms $(I_0)$, infected patients in level 1 contaminated rooms $(I_1)$, uncontaminated HCWs $(H_u)$, and contaminated HCWs $(H_c)$.

Their model showed the importance of small ward populations and transfer structures (movement between wards) in the transmission and persistence of nosocomial infections.

$$\frac{dS_0(t)}{dt} = \frac{1-\alpha_0}{T_0} I_0(t) + \frac{1-\alpha_1}{T_1} I_1(t) - \frac{\pi_0 \rho}{T_v} H_c(t) S_0(t) + v_1 S_1(t)$$

$$\frac{dS_1(t)}{dt} = \frac{\alpha_0}{T_0} I_0(t) + \frac{\alpha_1}{T_1} I_1(t) - \frac{\pi_1 \rho}{T_v} H_c(t) S_1(t) - t_1 S_1(t) + v_1 S_1(t)$$

$$\frac{dI_0(t)}{dt} = \frac{-1}{T_0} I_0(t) + \frac{\pi_0 \rho}{T_v} H_c(t) S_0(t) + \delta_1 I_1(t) - \delta_0 I_0(t) \quad (2.14)$$

$$\frac{dI_1(t)}{dt} = \frac{-1}{T_1} I_1(t) + \frac{\pi_1 \rho}{T_v} H_c(t) S_1(t) + \epsilon_1 S_1(t) - \delta_1 I_1(t) + \delta_0 I_0(t)$$

$$\frac{dH_u(t)}{dt} = \frac{1}{T_v} H_c(t) - \frac{1}{T_v} (\omega_0 I_0(t) + \omega_1 I_1(t) + \xi_1 S_1(t)) H_u(t)$$

$$\frac{dH_c(t)}{dt} = -\frac{1}{T_v} H_c(t) + \frac{1}{T_v} (\omega_0 I_0(t) + \omega_1 I_1(t) + \xi_1 S_1(t)) H_u(t)$$

**Table 2.11:** Model Parameters and their Descriptions

| Parameters | Description |
|---|---|
| $T_0$ | Average length of stay in level 0 |
| $T_1$ | Average length of stay in level 1 |
| $t_1$ | Mean duration of infection in level 1 patients |
| $\alpha_0$ | Fraction of infected patients transferred from level 0 to level 1 |
| $\alpha_1$ | Fraction of infected patients transferred from level 1 to level 0 |
| $\pi_0$ | Probability of infection per HCW–patient contact in level 0 |
| $\pi_1$ | Probability of infection per HCW–patient contact in level 1 |
| $\rho$ | Average number of patient contacts per HCW per unit time |
| $T_v$ | Average duration of HCW contamination |
| $\delta_0$ | Transfer rate of patients from level 0 to level 1 |
| $\delta_1$ | Transfer rate of patients from level 1 to level 0 |
| $\epsilon_1$ | Rate of environmental contamination by infected patients |
| $\xi_1$ | Clearance rate of environmental contamination |
| $v_1$ | Recovery or decontamination rate of infected patients |
| $\omega_0$ | HCW contact rate with patients in level 0 |
| $\omega_1$ | HCW contact rate with patients in level 1 |

They only defined parameters qualitatively and then analyzed outcomes under different symbolic conditions.

### 2.4.11 Deterministic and Stochastic Models on the Impact of Bacteria Load within the Hospital Environment on the Transmission of MRSA

Wang and Ruan (2017) considered the impact of bacteria load within the hospital environment in the transmission of MRSA. They developed a deterministic model of five compartments, that is, colonized patients, the uncolonized patients, the contaminated HCWs, the uncontaminated HCWs and the bacteria load in the hospital environment. They also developed an equivalent stochastic model using a Continuous Time Markov Chain (CTMC) approach, to better understand the model behavior.

The analysis of both the deterministic and stochastic models gave some key control measures, such as increasing the hand hygiene compliance of HCWs, enhancing environmental disinfection, and lowering transmission between patients, HCWs, and the environment.

The model is,

$$\frac{dP_u(t)}{dt} = (1-\theta)[\gamma_u P_u(t) + \gamma_c P_c(t)] - \alpha_p \beta_p (1-\eta) P_u(t) H_c(t) - k_p P_u(t) B_e(t) - \gamma_u P_u(t)$$

$$\frac{dP_c(t)}{dt} = \theta[\gamma_u P_u(t) + \gamma_c P_c(t)] + \alpha_p \beta_p (1-\eta) P_u(t) H_c(t) + k_p P_u(t) B_e(t) - \gamma_c P_c(t)$$

$$\frac{dH_u(t)}{dt} = -\alpha_p \beta_h (1-\eta) P_c(t) H_u(t) + \mu_c H_c(t) - k_h H_u(t) B_e(t) \qquad (2.15)$$

$$\frac{dH_c(t)}{dt} = \alpha_p \beta_h (1-\eta) P_c(t) H_u(t) - \mu_c H_c(t) + k_h H_u(t) B_e(t)$$

$$\frac{dB_e(t)}{dt} = \nu_p P_c(t) + \nu_h H_c(t) - \gamma_b B_e(t)$$

To construct the equivalent stochastic model, they adopted the continuous time markov chain process (CTMC) and stated that since, $P_c(t) + P_u(t) = N_p \; and \; H_c(t) + H_u(t) = N_h$ , then $P_u(t) = N_p - P_c(t) \; and \; H_u(t) = N_h - H_c(t) \; \forall \; t \geq 0$ making the process trivariate. These three variables have a joint probability given by

$p_{(s,j,k)}(t) = Prob\{P_c(t) = s, H_c(t) = j, B_e(t) = k\}$, where $s = 0,1, \ldots, N_p$; $j = 0,1, \ldots, N_h$; $and\ k \geq 0$

The transition probabilities are written as follows:

$$p_{(s+i_1,j+i_2,k+i_3);(s,j,k)}(\Delta t) = Prob(\Delta P_c, \Delta H_c, \Delta B_e) = (i_1, i_2, i_3) | (P_c(t), H_c(t), B_e(t)) = (s, j, k)$$

where, $\Delta P_c = P_c(t + \Delta t) - P_c(t)\ and\ i_1, i_2, i_3 \in \{-1,0,1\}$ .

Hence,

$p_{(s+i_1,j+i_2,k+i_3);(s,j,k)}(\Delta t) =$

$$\begin{cases} [\theta[\gamma_u(N_p - s) + \gamma_c s] + \alpha_p \beta_p (1-\eta)(N_p - s)j + k_p(N_p - s)k]\Delta t & (i_1, i_2, i_3) = (1,0,0) \\ \gamma_c s \Delta t & (i_1, i_2, i_3) = (-1,0,0) \\ [\alpha_p \beta_h (1-\eta) s(N_h - j) + k_h(N_h - j)k]\Delta t & (i_1, i_2, i_3) = (0,1,0) \\ \mu_c j \Delta t & (i_1, i_2, i_3) = (0,-1,0) \\ [\nu_p s + \nu_h j]\Delta t & (i_1, i_2, i_3) = (0,0,1) \\ \gamma_b k \Delta t & (i_1, i_2, i_3) = (0,0,-1) \\ 1 - [\theta[\gamma_u(N_p - s) + \gamma_c s] + \alpha_p \beta_p (1-\eta)(N_p - s)j + k_p(N_p - s)k]\Delta t & \\ -\gamma_c s \Delta t - [\alpha_p \beta_h (1-\eta) s(N_h - j) + k_h(N_h - j)k]\Delta t - \mu_c j \Delta t & \\ -[\nu_p s + \nu_h j]\Delta t - \gamma_b k \Delta t & (i_1, i_2, i_3) = (0,0,0) \\ 0 & elsewhere \end{cases} \quad (2.16)$$

**Table 2.12:** Model Parameters and their Description

| Parameters | Description |
|---|---|
| $\theta$ | Proportion of colonized patients admitted in hospital (1/day) |
| $N_p$ | Number of patients |
| $N_h$ | Number of HCWs |
| $\alpha_p$ | Contact rate (1/day) |

| | |
|---|---|
| $\gamma_u$ | Discharge rate of uncolonized patients (1/day) |
| $\gamma_c$ | Discharge rate of uncolonized patients (1/day) |
| $\gamma_b$ | Cleaning/disinfection rate of environment (1/day) |
| $k_P$ | Colonization rate from environment of uncolonized patients (CFU's/day) |
| $k_P$ | Colonization rate from environment of uncontaminated HCWs (CFU's/day) |
| $\eta$ | Hand hygiene compliance of HCWs |
| $\mu_c$ | Decontamination rate of HCWs (1/day) |
| $\upsilon_P$ | Contamination rate to environment by colonized patients (CFU's/day) |
| $\upsilon_h$ | Contamination rate to environment by contaminated HCWs (CFU's/day) |

### 2.4.12 Modeling the Spread of Covid-19 as a Nosocomial Infection by considering its Transmission within a Hospital Setting

Masandawa et al. (2022) modeled the spread of Covid-19 as a nosocomial infection by considering its transmission within a healthcare setting. They identified asymptomatic and super-spreaders as the major transmission agents of the infection within a healthcare setting and studied the role of personal protective equipment in the model. To achieve this, a five compartmental model was constructed comprising of, susceptible individuals ($S$), exposed individuals ($E$), infected individuals ($I$), hospitalized individuals ($H$) and recovered individuals ($R$). The analysis of the model showed that the personal protective equipment can minimize the spread of nosocomial infection of covid-19 within a healthcare setting.

The model is,

$$\frac{dS}{dt} = \Lambda + \rho R - [\mu + (1-\theta)(\beta_1 I + \beta_2 H)]S$$

$$\frac{dE}{dt} = (1-\theta)(\beta_1 I + \beta_2 H)S - (\alpha + \mu + \varepsilon)E$$

$$\frac{dI}{dt} = \alpha E - (\delta + v + d + \mu)I \qquad (2.17)$$

$$\frac{dH}{dt} = \varepsilon E + vI - (d + \mu + \omega)H$$

$$\frac{dR}{dt} = \delta I + \omega H - (\mu + \rho)R$$

**Table 2.13:** Model Parameters and their Description

| Parameters | Description |
|---|---|
| $\Lambda$ | Recruitment rate |
| $\beta_1$ | Contact rate |
| $\beta_2$ | Contact rate of hospitalized patients |
| $\theta$ | The rate of wearing personal protective equipment |
| $\varepsilon$ | Rate at which exposed individuals are isolated in hospitals |
| $d$ | Disease induced death rate |
| $\mu$ | Removal rate |
| $\omega$ | Recovery rate of hospitalized population |
| $\alpha$ | Rate at which exposed individuals become infected |
| $\delta$ | Rate of recovery of infected individuals |
| $v$ | Rate at which infected individuals are hospitalized |

### 2.4.13 Modeling Community-Acquired MRSA and Hospital-Acquired MRSA and Assessing the Effect of some Intervention Methods

Gokbulut et al. (2024) considered a community-acquired MRSA and hospital-acquired MRSA using eight-compartmental model and assessed the effect of some intervention methods in preventing the spread of the disease. Their work suggested an increase in the level of awareness concerning the transmission of MRSA is extremely significant in preventing the further spread of both CA-MRSA and HA-MRSA.

The eight compartments consists of susceptible individuals $(S)$, individuals who are infected with CA-s.aureus $(C_c)$, individuals who are infected with CA-MRSA $(C_I)$, individuals who are infected with HA- s.aureus $(H_c)$, individuals who are infected with HA-MRSA $(H_I)$, antibiotic group Oxazolidinones $(O)$,antibiotic group Glycopeptides $(G)$, antibiotic group Trimethoprim-derivatives $(T)$ as below:

$$\frac{dS}{dt} = \Lambda(1 - k_1 - k_2 - k_3 - k_4) - \beta_1 C_c S - \beta_2 C_I S - \beta_3 H_c S - \beta_4 H_I S + \gamma_1 O + \gamma_2 G + \gamma_3 T + a\delta_1 C_c + b\delta_3 H_c - \mu S$$

$$\frac{dC_c}{dt} = \Lambda k_1 + \beta_1 C_c S - [a\delta_1 + (1-a)\delta_2]C_c - \mu C_c$$

$$\frac{dC_I}{dt} = \Lambda k_2 + \beta_2 C_I S + (1-a)\delta_2 C_c - (o_1 + g_1 + r_1)C_I - \mu C_I$$

$$\frac{dH_c}{dt} = \Lambda k_3 + \beta_3 H_c S - [b\delta_3 + (1-b)\delta_4]H_c - \mu H_c \qquad (2.18)$$

$$\frac{dH_I}{dt} = \Lambda k_4 + \beta_4 H_I S + (1-b)\delta_4 H_c - (o_2 + g_2 + r_2)H_I - (\mu + d)H_I$$

$$\frac{dO}{dt} = o_1 C_I + o_2 H_I - \gamma_1 O$$

$$\frac{dG}{dt} = g_1 C_I + g_2 H_I - \gamma_2 G$$

$$\frac{dT}{dt} = r_1 C_I + r_2 H_I - \gamma_3 T$$

**Table 2.14:** Model Parameters and their Description

| Parameters | Description |
|---|---|
| $\Lambda$ | Admissions to the hospital laboratory |
| $k_1$ | The rate of patients admitted as $C_c$ |
| $k_2$ | The rate of patients admitted as $C_I$ |
| $k_3$ | The rate of patients admitted as $H_c$ |
| $k_4$ | The rate of patients admitted as $H_I$ |
| $\beta_1$ | Transmission rate from $S\ to\ C_c$ |
| $\beta_2$ | Transmission rate from $S\ to\ C_I$ |
| $\beta_3$ | Transmission rate from $S\ to\ H_c$ |
| $\beta_4$ | Transmission rate from $S\ to\ H_I$ |
| $\gamma_1$ | Recovery rate when treated with oxazolidinones |
| $\gamma_2$ | Recovery rate when treated with glycopeptides |
| $\gamma_3$ | Recovery rate when treated with trimethoprim-derivatives |
| $\delta_1$ | Transmission rate from $C_c\ to\ S$ |

| | |
|---|---|
| $\delta_2$ | Transmission rate from $C_c\ to\ C_I$ |
| $\delta_3$ | Transmission rate from $H_c\ to\ S$ |
| $\delta_4$ | Transmission rate from $H_c\ to\ H_I$ |
| $a$ | Cure rate of $C_c$ |
| $b$ | Cure rate of $H_c$ |
| $d$ | Hospital discharge rate |
| $\mu$ | Natural death rate |

### 2.4.14 A Model on the Effect of Environmental Contamination on the Spread of MRSA in Hospitals using Caputo Fractional Derivative

Ozturk (2025), gave a compartmental mathematical model to investigate the effect of environmental contamination on the spread of MRSA in hospitals, using Caputo fractional derivative. He created a fractional counterpart of the Wang and Ruan (2017) model, in order to model the memory-dependent behaviour of the system, using the Caputo fractional derivative operator. The model examined has five compartments, the uncolonized patients Pu(t), the colonized patients Pc(t), the uncontaminated healthcare workers Hu(t), the contaminated healthcare workers Hc(t), and the bacteria load in the environment B(t). The Caputo fractional derivative is denoted as ${}_C D^{\chi}\omega(t)$ and defined as, ${}_C D^{\chi}\omega(t) = \frac{1}{\Gamma(1-\chi)}\int_0^t \frac{\omega'(\tau)}{(t-\tau)}d\tau$ .

He gave the system of fractional derivative as,

$${}_C D^{\chi}P_u(t) = (1-\alpha^{\chi})[\beta_u^{\chi}P_u(t) + \beta_c^{\chi}P_c(t)] - \gamma_p^{\chi}\kappa_p^{\chi}(1-\theta^{\chi})P_u(t)H_c(t) - \sigma_p^{\chi}P_u(t)B(t) - \beta_u^{\chi}P_u(t)$$

$${}_C D^{\chi}P_c(t) = \alpha^{\chi}[\beta_u^{\chi}P_u(t) + \beta_c^{\chi}P_c(t)] + \gamma_p^{\chi}\kappa_p^{\chi}(1-\theta^{\chi})P_u(t)H_c(t) + \sigma_p^{\chi}P_u(t)B(t) - \beta_c^{\chi}P_c(t)$$

$${}_C D^{\chi}H_u(t) = -\gamma_p^{\chi}\kappa_h^{\chi}(1-\theta^{\chi})P_c(t)H_u(t) + \nu_c^{\chi}H_c(t) - \sigma_h^{\chi}H_u(t)B(t)$$

$${}_C D^{\chi}H_c(t) = \gamma_p^{\chi}\kappa_h^{\chi}(1-\theta^{\chi})P_c(t)H_u(t) - \nu_c^{\chi}H_c(t) + \sigma_h^{\chi}H_u(t)B(t)$$

$${}_C D^{\chi}B(t) = \mu_p^{\chi}P_c(t) + \mu_h^{\chi}H_c(t) - \beta_b^{\chi}B(t)$$

He observed that Caputo fractional derivative can change the course of spread of MRSA by understanding the model system in depth and examining the effects of different parameters in making predictions about the system behavior. This offers a comprehensive analysis in predicting and comparing infection control methods.

**Table 2.15:** Definition of model parameters

| Parameters | Description |
|---|---|
| $\theta$ | Proportion of colonized patients admitted in hospital (1/day) |
| $N_p$ | Number of patients |
| $N_h$ | Number of HCWs |
| $\alpha_p$ | Contact rate (1/day) |
| $\gamma_u$ | Discharge rate of uncolonized patients (1/day) |
| $\gamma_c$ | Discharge rate of uncolonized patients (1/day) |
| $\gamma_b$ | Cleaning/disinfection rate of environment (1/day) |
| $k_P$ | Colonization rate from environment of uncolonized patients (CFUs/day) |
| $k_P$ | Colonization rate from environment of uncontaminated HCWs (CFUs/day) |
| $\eta$ | Hand hygiene compliance of HCWs |
| $\mu_c$ | Decontamination rate of HCWs (1/day) |
| $\upsilon_P$ | Contamination rate to environment by colonized patients (CFUs/day) |

| | |
|---|---|
| $\upsilon_h$ | Contamination rate to environment by contaminated HCWs (CFUs/day) |

# CHAPTER THREE

# METHODOLOGY

## 3.1 Introduction

A deterministic model for the transmission of MRSA in the presence patients' family caregivers is formulated using two compartments each for patients, HCWs and caregivers. The model structure is derived from established epidemiological modeling frameworks (Hethcote, 2000; Brauer and Castillo-Chavez, 2012; Diekmann et al., 2013) and adapted to reflect hospital-specific interactions.

Also, we construct a stochastic version of our deterministic model using the continuous-time Markov chain (CTMC) framework to capture the inherent randomness in the transmission dynamics of MRSA in the presence of patients' family caregivers within the hospital. This approach is particularly suitable for hospital settings, where the population size is relatively small and chance events can significantly influence outcomes. According to Wang and Ruan (2017), stochastic formulations often provide deeper insights into epidemic behavior in small populations compared to purely deterministic models.

In general, stochastic epidemic models are developed as probabilistic counterparts of their deterministic analogues, by defining the rates at which transitions (or "jumps") occur between compartments over infinitesimally small time intervals, Δt (Allen, 2008; Allen, 2017). Assuming continuous time and discrete state variables, we represent the MRSA transmission process as a CTMC. To formulate the stochastic epidemic model, we specify the probabilities of changes in the state variables, the infinitesimal mean and variance and the drift and diffusion terms of the stochastic model.

### 3.2 Formulation of the proposed Deterministic model

#### 3.2.1 Description of Compartments

- The susceptible patients are referred to as uncolonized patients and denoted as $P_u(t)$.
- The infectious patients are referred to as colonized patients and denoted as $P_c(t)$.
- The uncontaminated HCWs who are susceptible to contamination and denoted as $H_u(t)$.
- The contaminated HCWs who are infectious and denoted as the $H_c(t)$.
- The susceptible caregiver's compartment referred to as uncontaminated caregivers is denoted as $G_u(t)$.
- The contaminated caregivers who are infectious and denoted as $G_c(t)$.

It is assumed that patients are admitted into the hospital at a rate $\Lambda_a$ and a fraction σ, are colonized with MRSA on admission.

The discharge rates for colonized and uncolonized patients are denoted as $\delta_c$ and $\delta_u$ respectively.

The hand wash compliances for HCWs and caregivers are given as η and ξ respectively. The hand wash compliance of caregivers was assumed to be very small compared to HCWs as they are not professionals and are untrained.

$\beta_{ph}$ and $\beta_{pg}$ are the transmission rates between patients and HCWs and between patients and caregivers respectively.

The rate of decontamination of contaminated HCWs is given by $\mu_c$ and that of contaminated caregivers is $\alpha_c$.

The inflow of uncontaminated caregivers is $\Lambda_b$ and $\phi$ is the outflow. The outflow is assumed to be the same for both contaminated and uncontaminated caregivers.

The number of HCWs is a constant $N_h$ and, it is also assumed that basically, there is adequate interaction of the compartments with the hospital environment.

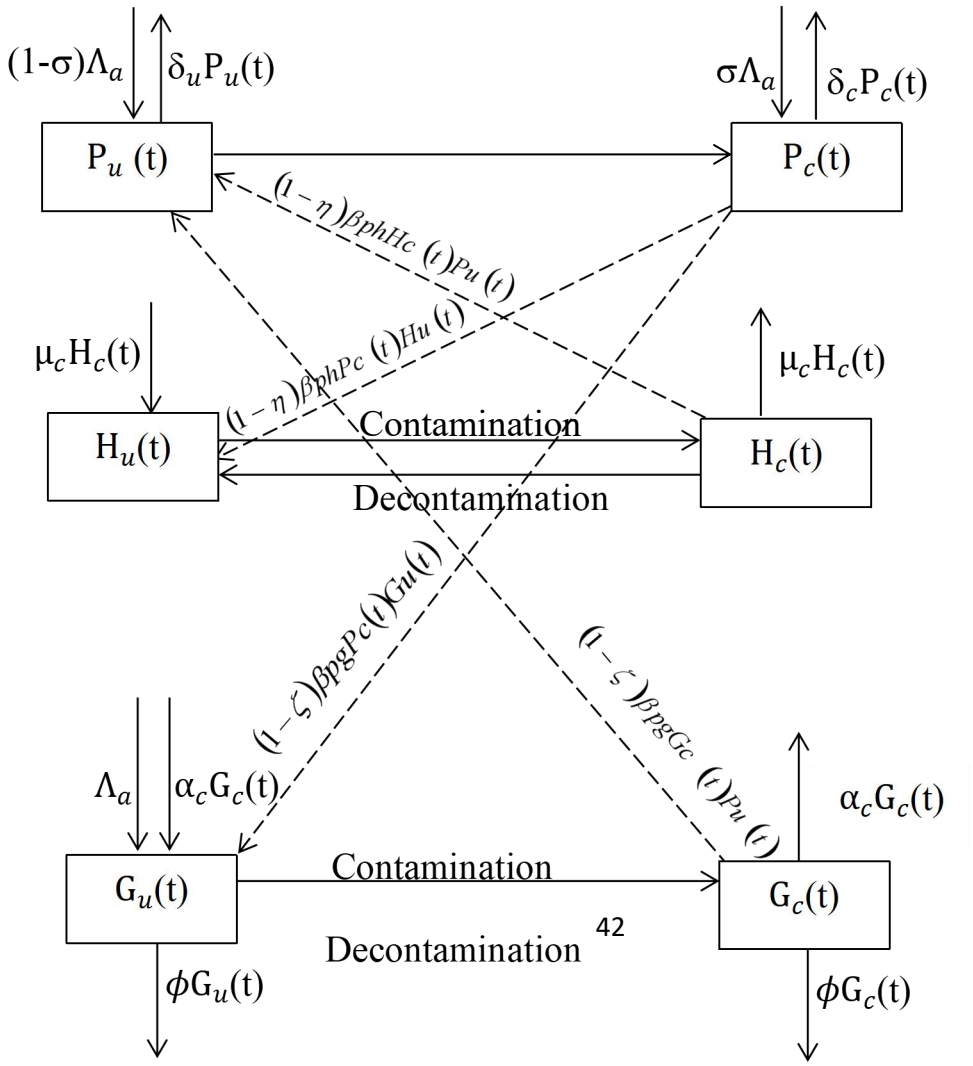
### 3.2.2 Basic Assumptions:

1. The number of HCWs is a constant
2. All the compartments mix effectively with the hospital environment
3. The outflow of contaminated and uncontaminated caregivers is the same.
4. The caregivers are assumed to be uncontaminated before arrival.

**Table 3.1:** Variables and Parameters Description

| **Variables/ Parameters** | **Description** |
|---|---|
| $P_u$ | Uncolonized patients |
| $P_c$ | Colonized patients |
| $H_u$ | Uncontaminated HCWs |
| $H_c$ | Contaminated HCWs |
| $G_u$ | Uncontaminated caregivers |
| $G_c$ | Contaminated caregivers |
| $\Lambda_a$ | Inflow of patients |
| $\sigma$ | Proportion of patients colonized on arrival |
| $\beta_{ph}$ | Transmission rate between patients and HCWs |
| $\beta_{pg}$ | Transmission rate between patients and caregivers |
| $\delta_u$ | Discharge rate of uncolonized patients |
| $\delta_c$ | Discharge rate of colonized patients |

| | |
|---|---|
| $N_h$ | Constant number of HCWs |
| $\Lambda_b$ | Inflow of caregivers |
| $\phi$ | Outflow of caregivers |
| $\eta$ | Handwashing compliance of HCWs |
| $\xi$ | Handwashing compliance of caregivers |
| $\mu_c$ | Decontamination rate of contaminated HCWs |
| $\alpha_c$ | Decontamination rate of contaminated caregivers |



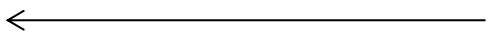


**Figure 3.1:** The Schematic Model Transmission Diagram

Figure 3.1, shows the model diagram for the developed model. The dynamics of the six classes of humans in the six compartments are clearly shown. The tick arrows indicate a movement in and out of compartments or between compartments, while the perforated arrows indicate the force of infection. The colonization of uncolonized patients is as a result of the resultant force of colonization through contact with the contaminated HCWs and caregivers. The contamination of uncontaminated HCWs and caregivers are both through contact with colonized patients.

The decontamination of HCWs and caregivers are mainly through handwashing which is almost zero for caregivers because they are not professionals and lack any form of training.

### 3.2.3 Transmission Pathways

Uncolonized patients can become colonized through contact with contaminated HCWs and contaminated caregivers, that is

$$\frac{dP_u(t)}{dt} = (1-\sigma)\Lambda_a - \left[(1-\eta)\beta_{ph}H_c(t) + (1-\xi)\beta_{pg}G_c(t)\right]P_u(t) - \delta_u P_u(t) \tag{3.1}$$

Uncontaminated HCWs can become contaminated through contact with colonized patients, that is,

$$\frac{dH_u(t)}{dt} = -(1-\eta)\beta_{ph}P_c(t)H_u(t) + \mu_c H_c(t) \tag{3.2}$$

Also, uncontaminated caregivers can become contaminated through contact with colonized patients, that is,

$$\frac{dG_u(t)}{dt} = -(1-\xi)\beta_{pg}P_c(t)G_u(t) + \Lambda_b - \phi G_u(t) + \alpha_c G_c(t) \tag{3.3}$$

The infectious classes are:

$$\frac{dP_c(t)}{dt} = \sigma\Lambda_a + \left[(1-\eta)\beta_{ph}H_c(t) + (1-\xi)\beta_{pg}G_c(t)\right]P_u(t) - \delta_c P_c(t) \quad (3.4)$$

$$\frac{dH_c(t)}{dt} = (1-\eta)\beta_{ph}P_c(t)H_u(t) - \mu_c H_c(t) \quad (3.5)$$

and,

$$\frac{dG_c(t)}{dt} = (1-\xi)\beta_{pg}P_c(t)G_u(t) - \phi G_c(t) - \alpha_c G_c(t) \quad (3.6)$$

Adding up equations (3.1- 3.6) together with assumptions made we have the system of differential equations as:

$$\left.\begin{aligned}
\frac{dP_u(t)}{dt} &= (1-\sigma)\Lambda_a - \left[(1-\eta)\beta_{ph}H_c(t) + (1-\xi)\beta_{pg}G_c(t)\right]P_u(t) - \delta_u P_u(t)\\
\frac{dP_c(t)}{dt} &= \sigma\Lambda_a + \left[(1-\eta)\beta_{ph}H_c(t) + (1-\xi)\beta_{pg}G_c(t)\right]P_u(t) - \delta_c P_c(t)\\
\frac{dH_u(t)}{dt} &= -(1-\eta)\beta_{ph}P_c(t)H_u(t) + \mu_c H_c(t)\\
\frac{dH_c(t)}{dt} &= (1-\eta)\beta_{ph}P_c(t)H_u(t) - \mu_c H_c(t)\\
\frac{dG_u(t)}{dt} &= -(1-\xi)\beta_{pg}P_c(t)G_u(t) + \Lambda_b - \phi G_u(t) + \alpha_c G_c(t)\\
\frac{dG_c(t)}{dt} &= (1-\xi)\beta_{pg}P_c(t)G_u(t) - \phi G_c(t) - \alpha_c G_c(t)
\end{aligned}\right\} \quad (3.7)$$

### 3.3 Positivity of Solutions

Following standard results in epidemic modeling the variables in modeling of human infectious diseases should be positive in order to have public health relevance (Brauer and Castillo-Chavez 2012, and Hethcote, 2020).The following theorems are used to establish that all the variables considered in our model are positive having positive solutions.

**Theorem 3.1:** Let the initial values for the model parameter be $P_u(0) > 0$ , $P_c(0) > 0$ , $H_u(0) > 0$ , $H_c(0) > 0$, $G_u(0) > 0$, $G_c(0) > 0$, then the solutions ($P_u(t)$ , $P_c(t)$ , $H_u(t)$ , $H_c(t)$, $G_u(t)$, $G_c(t)$) of the model, with positive initial data values, will remain positive for all time $t > 0$ .

**Proof**

Let $t_1 = \sup\{t > 0: P_u(t) > 0\ , P_c(t) > 0\ , H_u(t) > 0\ , H_c(t) > 0, G_u(t) > 0,\ G_c(t) > 0\} > 0$ .
To prove the theorem, we choose an arbitrary equation from (3.7), say the first equation, that is,

$$\frac{dP_u(t)}{dt} = (1-\sigma)\Lambda_a - \left[(1-\eta)\beta_{ph}H_c(t) + (1-\xi)\beta_{pg}G_c(t)\right]P_u(t) - \delta_u P_u(t) \qquad (3.8)$$

This ordinary differential equation in (3.8) can be solved for $P_u$ by the method of integrating factor (I.F.).

Let $\lambda(t) = (1-\eta)\beta_{ph}H_c(t) + (1-\xi)\beta_{pg}G_c(t)$

Then (3.8) can be written,

$$\frac{dP_u(t)}{dt} = (1-\sigma)\Lambda_a - \lambda(t)P_u(t) - \delta_u P_u(t) \qquad (3.9)$$

Then,

$$\frac{dP_u(t)}{dt} = (1-\sigma)\Lambda_a - (\lambda(t) + \delta_u)P_u(t)$$

$$\frac{dP_u(t)}{dt} + (\lambda(t) + \delta_u)P_u(t) = (1-\sigma)\Lambda_a$$

I.F. $= exp\left[\int_o^t (\lambda(s) + \delta_u)ds\right]$, then

$$P_u(t)\left(exp\left[\int_o^t (\lambda(s) + \delta_u)ds\right]\right) = \int\left((1-\sigma)\Lambda_a\, exp\left[\int_o^t (\lambda(s) + \delta_u)ds\right]\right)$$

Differentiating both sides,

$$\frac{d}{dt}P_u(t)\left[exp\left(\int_0^t (\lambda(s) + \delta_u)ds\right)\right] = \frac{d}{dt}\int\left((1-\sigma)\Lambda_a\, exp\left[\int_0^t (\lambda(s) + \delta_u)ds\right]\right)dt$$

$$\frac{d}{dt}P_u(t)\left[exp\left(\int_0^t (\lambda(s) + \delta_u)ds\right)\right] = (1-\sigma)\Lambda_a\, exp\left[\int_0^t (\lambda(s) + \delta_u)ds\right]$$

Integration from $t = 0\ to\ t = t_1$, we have,

$$\int_0^{t_1} \frac{d}{dt}P_u(t)\left[exp\left(\int_0^t (\lambda(s) + \delta_u)ds\right)\right]dt = \int_0^{t_1}(1-\sigma)\Lambda_a\, exp\left[\int_0^t (\lambda(s) + \delta_u)ds\right]dt$$

$$P_u(t)\,exp\left(\int_0^t(\lambda(s)+\delta_u)ds\right)\Big|_0^{t_1} = \int_0^{t_1}(1-\sigma)\Lambda_a\,exp\left[\int_0^t(\lambda(s)+\delta_u)ds\right]dt$$

$$P_u(t_1)\,exp\left(\int_o^{t_1}(\lambda(s)+\delta_u)ds\right) - P_u(0)\,exp\left(\int_0^t(\lambda(s)+\delta_u)ds\right) = \int_0^{t_1}(1-\sigma)\Lambda_a\,exp\left[\int_0^t(\lambda(s)+\delta_u)ds\right]dt\;at\;t=0$$

see that, $exp\left(\int_0^{t_1}(\lambda(s)+\delta_u)ds\right)=1\;at\;t=0$, therefore,

$$P_u(t_1)\,exp\left(\int_o^{t_1}(\lambda(s)+\delta_u)ds\right) - P_u(0) = \int_0^{t_1}(1-\sigma)\Lambda_a\,exp\left[\int_o^t(\lambda(s)+\delta_u)ds\right]dt$$

$$P_u(t_1)\,exp\left(\int_o^{t_1}(\lambda(s)+\delta_u)ds\right) = P_u(0) + \int_0^{t_1}(1-\sigma)\Lambda_a\,exp\left[\int_o^t(\lambda(s)+\delta_u)ds\right]dt\,.$$

Hence,

$$P_u(t_1) = exp-\left(\int_o^{t_1}(\lambda(s)+\delta_u)ds\right)\left(P_u(0)+\int_0^{t_1}(1-\sigma)\Lambda_a\,exp\left[\int_o^t(\lambda(s)+\delta_u)ds\right]dt\right)>0 \qquad (3.10)$$

That is, $P_u(t_1)>0$ as required.

Following the same procedure, it can be shown that $P_c(t)$, $H_u(t)$, $H_c(t)$, $G_u(t)$, $G_c(t)$ are all greater than zero. Hence the model variables have positive solutions.

### 3.4 Invariant Set (Boundedness)

**Theorem 3.2:** The closed set $\mathcal{D}_1=\left\{P_u\le\frac{(1-\sigma)\Lambda_a}{\delta_u}\right\}$ in the uncolonized patients is positively invariant and attracts all solutions of the model.

**Proof:** For the uncolonized patients as in equation (3.7),

$$\frac{dP_u(t)}{dt} = (1-\sigma)\Lambda_a - \left[(1-\eta)\beta_{ph}H_c(t)+(1-\xi)\beta_{pg}G_c(t)\right]P_u(t)-\delta_u P_u(t)$$

Let $\lambda(t)=(1-\eta)\beta_{ph}H_c(t)+(1-\xi)\beta_{pg}G_c(t)$

Then, $\frac{dP_u(t)}{dt} = (1-\sigma)\Lambda_a - \lambda(t)P_u(t) - \delta_u P_u(t)$

See that $\frac{dP_u(t)}{dt} \leq (1-\sigma)\Lambda_a - \delta_u P_u(t)$ , since $\lambda(t) \geq 0$

$\Rightarrow \frac{dP_u(t)}{dt} + \delta_u P_u(t) \leq (1-\sigma)\Lambda_a$ (3.11)

Solving by integrating factor method we have, I.F.$= e^{\int \delta_u dt} = e^{\delta_u t}$

Then, $e^{\delta_u t}P_u(t) \leq (1-\sigma)\Lambda_a \int e^{\delta_u t}dt$

$e^{\delta_u t}P_u(t) \leq (1-\sigma)\Lambda_a \delta_u^{-1} e^{\delta_u t} + A$

$P_u(t) \leq (1-\sigma)\Lambda_a \delta_u^{-1} + Ae^{-\delta_u t}$

At $t = 0$, $P_u(0) \leq (1-\sigma)\Lambda_a \delta_u^{-1} + A$

$P_u(0) - (1-\sigma)\Lambda_a \delta_u^{-1} \leq A$

$\therefore P_u(t) \leq (1-\sigma)\Lambda_a \delta_u^{-1} + [P_u(0) - (1-\sigma)\Lambda_a \delta_u^{-1}]e^{-\delta_u t}$ (3.12)

From (3.12), if $P_u(0) \leq (1-\sigma)\Lambda_a \delta_u^{-1}$ , $P_u(t) \leq (1-\sigma)\Lambda_a \delta_u^{-1}$ , $\forall\, t > 0$. Hence, $\mathcal{D}_1$ is positively invariant and attracts all solutions within its bound.

**Theorem 3.3:** The closed set $\mathcal{D}_2 = \left\{P_c \leq \frac{\Lambda_a \sigma}{\delta_c}\right\}$ in the colonized patients is positively invariant and attracts all solutions of the model.

**Proof:** For the colonized patients as in equation (3.7),

$\frac{dP_c(t)}{dt} = \sigma\Lambda_a + \left[(1-\eta)\beta_{ph}H_c(t) + (1-\xi)\beta_{pg}G_c(t)\right]P_u(t) - \delta_c P_c(t)$

But, $\lambda(t) = (1-\eta)\beta_{ph}H_c(t) + (1-\xi)\beta_{pg}G_c(t)$ and

$P_u(t) \leq (1-\sigma)\Lambda_a \delta_u^{-1} + [P_u(0) - (1-\sigma)\Lambda_a \delta_u^{-1}]e^{-\delta_u t}$

Then,

$$\frac{dP_c(t)}{dt} \leq \sigma\Lambda_a + \lambda(t)((1-\sigma)\Lambda_a\delta_u^{-1} + [P_u(0) - (1-\sigma)\Lambda_a\delta_u^{-1}]e^{-\delta_u t}) - \delta_c P_c(t)$$

$$\frac{dP_c(t)}{dt} + \delta_c P_c(t) \leq \sigma\Lambda_a + \lambda(t)((1-\sigma)\Lambda_a\delta_u^{-1} + [P_u(0) - (1-\sigma)\Lambda_a\delta_u^{-1}]\, e^{-\delta_u t}) \quad (3.13)$$

I.F. $= e^{\int \delta_c dt} = e^{\delta_c t}$

Then,

$$P_c(t)e^{\delta_c t} \leq \int \sigma\Lambda_a e^{\delta_c t}\, dt + \int e^{\delta_c t}\lambda(t)((1-\sigma)\Lambda_a\delta_u^{-1} + [P_u(0) - (1-\sigma)\Lambda_a\delta_u^{-1}]\, e^{-\delta_u t})\, dt$$

$$P_c(t)e^{\delta_c t} \leq \Lambda_a\sigma\delta_c^{-1}e^{\delta_c t} + \int e^{\delta_c t}\lambda(t)((1-\sigma)\Lambda_a\delta_u^{-1} + [P_u(0) - (1-\sigma)\Lambda_a\delta_u^{-1}]\, e^{-\delta_u t})\, dt$$

$$P_c(t) \leq \Lambda_a\sigma\delta_c^{-1} + e^{-\delta_c t}\int e^{\delta_c t}\lambda(t)((1-\sigma)\Lambda_a\delta_u^{-1} + [P_u(0) - (1-\sigma)\Lambda_a\delta_u^{-1}]\, e^{-\delta_u t})\, dt \quad (3.14)$$

If $P_c(t) > \Lambda_a\sigma\delta_c^{-1}$, then in (3.14), $\frac{dP_c(t)}{dt} < 0$. Hence, $P_c(t) \leq \Lambda_a\sigma\delta_c^{-1}$, $\forall\, t > 0$ and $\mathcal{D}_2$ is positively invariant and attracts all solutions within its bound.

**Theorem 3.4:** Given, $G = G_u + G_c$, the closed set $\mathcal{D}_3 = \left\{G \leq \frac{\Lambda_b}{\phi}\right\}$ in the caregivers is positively invariant and attracts all solutions of the model.

**Proof:** For caregivers $G = G_u + G_c$ and from equation, (3.7),

$$\frac{dG_u(t)}{dt} = -(1-\xi)\beta_{pg}P_c(t)G_u(t) + \Lambda_b - \phi G_u(t) + \alpha_c G_c(t) \text{ and,}$$

$$\frac{dG_c(t)}{dt} = (1-\xi)\beta_{pg}P_c(t)G_u(t) - \phi G_c(t) - \alpha_c G_c(t)$$

then

$$\frac{d(G_u(t)+G_c(t))}{dt} = \Lambda_b - \phi G_u(t) - \phi G_c(t)$$

$$\frac{d(G_u(t)+G_c(t))}{dt} + \phi(G_u(t) + G_c(t)) = \Lambda_b$$

But, $G_u(t) + G_c(t) = G(t)$,

$\therefore \frac{dG(t)}{dt} + \phi G(t) = \Lambda_b$ (3.15)

I.F. $= e^{\int \phi dt} = e^{\phi t}$

$\therefore e^{\phi t} G(t) = \Lambda_b \int e^{\phi t}\, dt$

$e^{\phi t} G(t) = \Lambda_b \phi^{-1} e^{\phi t} + A$, where A is an arbitrary constant.

At $t = 0$, $G(0) = \Lambda_b \phi^{-1} + A \Rightarrow A = G(0) - \Lambda_b \phi^{-1}$

Hence, $e^{\phi t} G(t) = \Lambda_b \phi^{-1} e^{\phi t} + G(0) - \Lambda_b \phi^{-1}$, then

$G(t) = \Lambda_b \phi^{-1} + [G(0) - \Lambda_b \phi^{-1}] e^{-\phi t}$ (3.16)

If $G(t) > \Lambda_b \phi^{-1}$, then in (3.15), $\frac{dG(t)}{dt} < 0$. Hence, we have that if $(0) < \Lambda_b \phi^{-1}$ in (3.16), then $G(t) \leq \Lambda_b \phi^{-1}$, $\forall\, t > 0$. If $G(0) > \Lambda_b \phi^{-1}$, then either the solution enters $\mathcal{D}_3$ in finite time or $G(t)$ approaches $\Lambda_b \phi^{-1}$ as $t \to \infty$. Hence, $\mathcal{D}_3$ is positively invariant and attracts all solutions within its bound.

**NOTE:** The number of HCWs is a constant and hence bounded. That is from equation (3.7),

$\frac{dH_u(t)}{dt} = -(1-\eta)\beta_{ph} P_c(t) H_u(t) + \mu_c H_c(t)$ ,

$\frac{dH_c(t)}{dt} = (1-\eta)\beta_{ph} P_c(t) H_u(t) - \mu_c H_c(t)$

$\frac{d(H_u(t)+H_c(t))}{dt} = 0$ . Integrating both sides, we have,

$\therefore H_u(t) + H_c(t) =$ c, where $c = N_h$ is a constant.

### 3.5 Equilibrium Points and Reproduction Number

#### 3.5.1 Disease Free Equilibrium

Disease-free equilibrium (DFE) is obtained by setting all the equations in the noninfectious classes of the model to zero. Here the infected classes are neglected since we are interested in a situation where the hospital is free from infections (Hethcote, 2000; van den Driessche and Watmough, 2002; Diekmann et al., 2013).

From equation (7),

$$\frac{dP_u(t)}{dt} = (1-\sigma)\Lambda_a - \left[(1-\eta)\beta_{ph}H_c(t) + (1-\xi)\beta_{pg}G_c(t)\right]P_u(t) - \delta_u P_u(t)$$

Here, $H_c(t)$ , $G_c(t)$ and $\sigma$ are zeros, hence

$$0 = \Lambda_a - \delta_u P_u(t) \Rightarrow\ P_u(t) = \frac{\Lambda_a}{\delta_u}$$

Also, $\frac{dH_u(t)}{dt} = -\ (1-\eta)\beta_{ph}P_c(t)H_u(t) + \mu_c H_c(t)$

$H_u(t) = N_h$ . $N_h$ is the assumed constant number of HCWs .

Finally, $\frac{dG_u(t)}{dt} = -\ (1-\xi)\beta_{pg}P_c(t)G_u(t) + \Lambda_b - \phi G_u(t) + \alpha_c G_c(t)$

Here, $P_c(t)$ and $G_c(t)$ are zeros, hence

$$0 = \Lambda_b - \phi G_u(t) \Rightarrow\ G_u(t) = \frac{\Lambda_b}{\phi}$$

Therefore, the disease-free equilibrium is

$$E_0 = (P_u^*, P_c^*, H_u^*, H_c^*, G_u^*, G_c^*) = \left(\frac{\Lambda_a}{\delta_u}, 0, \mathrm{N}_h, 0, \frac{\Lambda_b}{\phi}, 0\right) \qquad (3.17)$$

### 3.5.2 Reproduction Number

The reproduction number or basic reproductive rate is the average number of secondary infections produced when one infectious person is introduced into a host population of susceptible persons. Mathematically, it is defined as the dominant eigenvalue of the positive linear operator (Chiyaka et al., 2008).

To determine the reproduction number for the six-class model developed in this work as in (3.7), we make use of only the disease-free equilibrium in (3.17) and rearrange the model equations in (3.7) to include infectious classes before the susceptible classes.

That is,

$$\frac{dP_c(t)}{dt} = \sigma\Lambda_a + \left[(1-\eta)\beta_{ph}H_c(t) + (1-\xi)\beta_{pg}G_c(t)\right]P_u(t) - \delta_c P_c(t)$$

$$\frac{dH_c(t)}{dt} = (1-\eta)\beta_{ph}P_c(t)H_u(t) - \mu_c H_c(t)$$

$$\frac{dG_c(t)}{dt} = (1-\xi)\beta_{pg}P_c(t)G_u(t) - \phi G_c(t) - \alpha_c G_c(t) \qquad (3.18)$$

$$\frac{dP_u(t)}{dt} = (1-\sigma)\Lambda_a - \left[(1-\eta)\beta_{ph}H_c(t) + (1-\xi)\beta_{pg}G_c(t)\right]P_u(t) - \delta_u P_u(t)$$

$$\frac{dH_u(t)}{dt} = -(1-\eta)\beta_{ph}P_c(t)H_u(t) + \mu_c H_c(t)$$

$$\frac{dG_u(t)}{dt} = -(1-\xi)\beta_{pg}P_c(t)G_u(t) + \Lambda_b - \phi G_u(t) + \alpha_c G_c(t)$$

At the disease free equilibrium when $\sigma = 0$, then,

$$E_0 = (P_u^*, P_c^*, H_u^*, H_c^*, G_u^*, G_c^*) = \left(\frac{\Lambda_a}{\delta_u}, 0, \mathrm{N}_h, 0, \frac{\Lambda_b}{\phi}, 0\right) \qquad (3.19)$$

Where $\mathrm{N}_h$ is a constant equal to the number of HCWs.

Let $\mathcal{F}$ be the rate of appearance of new infections in the infectious compartments and $\mathcal{V}$ be the difference between the transfer rate of individuals out of the compartments by all other means and the transfer rate of individuals into the compartments by all other means.

Hence,

$$\mathcal{F} = \begin{pmatrix} (1-\eta)\beta_{ph}H_c(t)P_u(t) + (1-\xi)\beta_{pg}G_c(t)P_u(t) \\ (1-\eta)\beta_{ph}P_c(t)H_u(t) \\ (1-\xi)\beta_{pg}P_c(t)G_u(t) \end{pmatrix} \tag{3.20}$$

$$\mathcal{V} = \begin{pmatrix} \delta_c P_c(t) - \sigma\Lambda_a \\ \mu_c H_c(t) \\ \phi G_c(t) + \alpha_c G_c(t) \end{pmatrix} \tag{3.21}$$

The partial derivatives of $\mathcal{F}$ and $\mathcal{V}$ with respect to the infected classes evaluated at the DFE gives a non-negative matrix F and a non-singular M-matrix V respectively. That is,

$F = \left[\frac{\partial \mathcal{F}_i}{\partial x_i}(x_0)\right]$ and $V = \left[\frac{\partial \mathcal{V}_i}{\partial x_i}(x_0)\right]$, $1 \leq i, j \leq 3$, j, being the number of infected classes. Then taking the partial derivative of each element in the column vector in (3.20) w.r.t. the infectious classes we have,

$$\frac{\partial \mathcal{F}}{\partial P_c(t)}\left((1-\eta)\beta_{ph}H_c(t)P_u(t) + (1-\xi)\beta_{pg}G_c(t)P_u(t)\right) = 0$$

$$\frac{\partial \mathcal{F}}{\partial H_c(t)}\left((1-\eta)\beta_{ph}H_c(t)P_u(t) + (1-\xi)\beta_{pg}G_c(t)P_u(t)\right) = (1-\eta)\beta_{ph}P_u(t)$$

$$\frac{\partial \mathcal{F}}{\partial G_c(t)}\left((1-\eta)\beta_{ph}H_c(t)P_u(t) + (1-\xi)\beta_{pg}G_c(t)P_u(t)\right) = (1-\xi)\beta_{pg}P_u(t)$$

$$\frac{\partial \mathcal{F}}{\partial P_c(t)}\left((1-\eta)\beta_{ph}P_c(t)H_u(t)\right) = (1-\eta)\beta_{ph}H_u(t)$$

$$\frac{\partial \mathcal{F}}{\partial H_c(t)}\left((1-\eta)\beta_{ph}P_c(t)H_u(t)\right) = 0$$

$$\frac{\partial \mathcal{F}}{\partial G_c(t)}\left((1-\eta)\beta_{ph}P_c(t)H_u(t)\right) = 0$$

$$\frac{\partial \mathcal{F}}{\partial P_c(t)}\big((1-\xi)\beta_{pg}P_c(t)G_u(t)\big) = (1-\xi)\beta_{pg}G_u(t)$$

$$\frac{\partial \mathcal{F}}{\partial H_c(t)}\big((1-\xi)\beta_{pg}P_c(t)G_u(t)\big) = 0$$

$$\frac{\partial \mathcal{F}}{\partial G_c(t)}\big((1-\xi)\beta_{pg}P_c(t)G_u(t)\big) = 0$$

Therefore,

$$F = \begin{pmatrix} 0 & (1-\eta)\beta_{ph}P_u(t) & (1-\xi)\beta_{pg}P_u(t) \\ (1-\eta)\beta_{ph}H_u(t) & 0 & 0 \\ (1-\xi)\beta_{pg}G_u(t) & 0 & 0 \end{pmatrix} \tag{3.22}$$

Similarly, taking the partial derivative of each element in the column vector in (3.20) w.r.t. the infectious classes we have,

$$\frac{\partial \mathcal{V}}{\partial P_c(t)}(\delta_c P_c(t) - \sigma\Lambda_a) = \delta_c$$

$$\frac{\partial \mathcal{V}}{\partial H_c(t)}(\delta_c P_c(t) - \sigma\Lambda_a) = 0$$

$$\frac{\partial \mathcal{V}}{\partial G_c(t)}(\delta_c P_c(t) - \sigma\Lambda_a) = 0$$

$$\frac{\partial \mathcal{V}}{\partial P_c(t)}\big(\mu_c H_c(t)\big) = 0$$

$$\frac{\partial \mathcal{V}}{\partial H_c(t)}\big(\mu_c H_c(t)\big) = \mu_c$$

$$\frac{\partial \mathcal{V}}{\partial G_c(t)}\big(\mu_c H_c(t)\big) = 0$$

$$\frac{\partial \mathcal{V}}{\partial P_c(t)}\big(\phi G_c(t) + \alpha_c G_c(t)\big) = 0$$

$$\frac{\partial \mathcal{V}}{\partial H_c(t)}\left(\phi G_c(t) + \alpha_c G_c(t)\right) = 0$$

$$\frac{\partial \mathcal{V}}{\partial G_c(t)}\left(\phi G_c(t) + \alpha_c G_c(t)\right) = \phi + \alpha_c$$

Hence,

$$V = \begin{pmatrix} \delta_c & 0 & 0 \\ 0 & \mu_c & 0 \\ 0 & 0 & \phi + \alpha_c \end{pmatrix} \tag{3.23}$$

Evaluating F in (3.22) and V in (3.23) at the DFE in (3.19), we have,

$$F = \begin{pmatrix} 0 & \frac{(1-\eta)\beta_{ph}\Lambda_a}{\delta_u} & \frac{(1-\xi)\beta_{pg}\Lambda_a}{\delta_u} \\ (1-\eta)\beta_{ph}N_h & 0 & 0 \\ \frac{(1-\xi)\beta_{pg}\Lambda_b}{\phi} & 0 & 0 \end{pmatrix} \tag{3.24}$$

$$V = \begin{pmatrix} \delta_c & 0 & 0 \\ 0 & \mu_c & 0 \\ 0 & 0 & \phi + \alpha_c \end{pmatrix} \tag{3.25}$$

Then the reproduction number is obtained as the spectral radius ($\rho$) of the matrix,

$$R_0 = \rho F V^{-1} \tag{3.26}$$

Where, $V^{-1} = \begin{pmatrix} \frac{1}{\delta_c} & 0 & 0 \\ 0 & \frac{1}{\mu_c} & 0 \\ 0 & 0 & \frac{1}{\phi+\alpha_c} \end{pmatrix}$

and,

$$FV^{-1} = \begin{pmatrix} 0 & \frac{(1-\eta)\beta_{\mathrm{ph}}\Lambda_a}{\delta_u\mu_c} & \frac{(1-\xi)\beta_{\mathrm{pg}}\Lambda_a}{(\phi+\alpha_c)\delta_u} \\ \frac{(1-\eta)N_h\beta_{\mathrm{ph}}}{\delta_c} & 0 & 0 \\ \frac{(1-\xi)\beta_{\mathrm{pg}}\Lambda_b}{\phi\delta_c} & 0 & 0 \end{pmatrix}$$ with eigenvalues

$$\left(0, -\frac{\sqrt{(1-\eta)^2\phi N_h(\phi+\alpha_c)\beta_{\text{ph}}^2\Lambda_a+(1-\xi)^2\beta_{\text{pg}}^2\Lambda_b\Lambda_a\mu_c}}{\sqrt{\phi\delta_c\delta_u\mu_c(\phi+\alpha_c)}}, \frac{\sqrt{(1-\eta)^2\phi N_h(\phi+\alpha_c)\beta_{\text{ph}}^2\Lambda_a+(1-\xi)^2\beta_{\text{pg}}^2\Lambda_b\Lambda_a\mu_c}}{\sqrt{\phi\delta_c\delta_u\mu_c(\phi+\alpha_c)}}\right)$$

Hence,

$$R_0 = \rho FV^{-1} = \sqrt{\frac{(1-\eta)^2\phi N_h(\phi+\alpha_c)\beta_{\text{ph}}^2\Lambda_a+(1-\xi)^2\beta_{\text{pg}}^2\Lambda_b\Lambda_a\mu_c}{\phi\delta_c\delta_u\mu_c(\phi+\alpha_c)}} \tag{3.27}$$

### 3.5.3 Endemic Equilibrium Point

An infection that persists in the population or community is said to be endemic. Endemic equilibrium point, on the other hand, gives the values the state variables will assume before an infection becomes endemic. This unique point occurs since we have earlier shown in Theorem 1, that our state variables are all nonnegative (Hethcote, 2000; van den Driessche and Watmough, 2002; Diekmann et al., 2013). To obtain this equilibrium point the following procedures are followed. From the system of equations (3.7),

$$\frac{dP_u(t)}{dt} = (1-\sigma)\Lambda_a - \left[(1-\eta)\beta_{ph}H_c(t) + (1-\xi)\beta_{pg}G_c(t)\right]P_u(t) - \delta_u P_u(t)$$

Let $\lambda_1 = (1-\eta)\beta_{ph}H_c(t) + (1-\xi)\beta_{pg}G_c(t)$, then,

$$\frac{dP_u(t)}{dt} = (1-\sigma)\Lambda_a - \lambda_1 P_u(t) - \delta_u P_u(t)$$

$$0 = (1-\sigma)\Lambda_a - \lambda_1 P_u(t) - \delta_u P_u(t) = (1-\sigma)\Lambda_a - (\lambda_1+\delta_u)P_u(t)$$

Then, $P_u(t) = \frac{(1-\sigma)\Lambda_a}{(\lambda_1+\delta_u)}$ (3.28)

Also, $\frac{dP_c(t)}{dt} = \sigma\Lambda_a + \left[(1-\eta)\beta_{ph}H_c(t) + (1-\xi)\beta_{pg}G_c(t)\right]P_u(t) - \delta_c P_c(t)$

$0 = \sigma\Lambda_a + \lambda_1 P_u(t) - \delta_c P_c(t)$ , $P_c(t) = \frac{\sigma\Lambda_a + \lambda_1 P_u(t)}{\delta_c} = \frac{\sigma\Lambda_a + \lambda_1 \left[\frac{(1-\sigma)\Lambda_a}{(\lambda_1+\delta_u)}\right]}{\delta_c}$

$P_c(t) = \frac{\sigma\Lambda_a(\lambda_1+\delta_u)+\lambda_1(1-\sigma)\Lambda_a}{\delta_c(\lambda_1+\delta_u)} = \frac{\sigma\Lambda_a\lambda_1+\sigma\Lambda_a\delta_u+\Lambda_a\lambda_1-\sigma\Lambda_a\lambda_1}{\delta_c(\lambda_1+\delta_u)} = \frac{\sigma\Lambda_a\delta_u+\Lambda_a\lambda_1}{\delta_c(\lambda_1+\delta_u)}$

Hence, $P_c(t) = \frac{\Lambda_a(\sigma\delta_u+\lambda_1)}{\delta_c(\lambda_1+\delta_u)}$ (3.29)

From equation (3.7), $\frac{dG_u(t)}{dt} = -(1-\xi)\beta_{pg}P_c(t)G_u(t) + \Lambda_b - \phi G_u(t) + \alpha_c G_c(t)$

Let $\lambda_2 = (1-\xi)\beta_{pg}P_c(t)$, then,

$0 = -\lambda_2 G_u(t) + \Lambda_b - \phi G_u(t) + \alpha_c G_c(t) = -(\lambda_2 + \phi)G_u(t) + \Lambda_b + \alpha_c G_c(t)$

Simplifying, $G_u(t) = \frac{(\Lambda_b + \alpha_c G_c(t))}{(\lambda_2+\phi)}$ (3.30)

and, $\frac{dG_c(t)}{dt} = (1-\xi)\beta_{pg}P_c(t)G_u(t) - \phi G_c(t) - \alpha_c G_c(t)$

$0 = \lambda_2 G_u(t) - \phi G_c(t) - \alpha_c G_c(t) = \lambda_2 G_u(t) - (\phi + \alpha_c)G_c(t)$

$G_c(t) = \frac{\lambda_2 G_u(t)}{(\phi+\alpha_c)} = \frac{\lambda_2\left[\frac{(\Lambda_b+\alpha_c G_c(t))}{(\lambda_2+\phi)}\right]}{(\phi+\alpha_c)} = \frac{\lambda_2(\Lambda_b+\alpha_c G_c(t))}{(\lambda_2+\phi)(\phi+\alpha_c)} = \frac{\lambda_2\Lambda_b+\lambda_2\alpha_c G_c(t)}{(\lambda_2+\phi)(\phi+\alpha_c)}$, then

$G_c(t)[(\lambda_2 + \phi)(\phi + \alpha_c)] = \lambda_2\Lambda_b + \lambda_2\alpha_c G_c(t)$

$\lambda_2\phi G_c(t) + \lambda_2\alpha_c G_c(t) + \phi^2 G_c(t) + \phi\alpha_c G_c(t) - \lambda_2\alpha_c G_c(t) = \lambda_2\Lambda_b$

$(\lambda_2\phi + \phi^2 + \phi\alpha_c)G_c(t) = \lambda_2\Lambda_b$, evaluating we have, $G_c(t) = \frac{\lambda_2\Lambda_b}{\phi(\lambda_2+\phi+\alpha_c)}$ (3.31)

Then (3.30) becomes,

$G_u(t) = \frac{(\Lambda_b+\alpha_c G_c(t))}{(\lambda_2+\phi)} = \frac{\Lambda_b+\alpha_c\left[\frac{\lambda_2\Lambda_b}{\phi(\lambda_2+\phi+\alpha_c)}\right]}{(\lambda_2+\phi)} = \frac{\Lambda_b\phi(\lambda_2+\phi+\alpha_c)+\alpha_c\lambda_2\Lambda_b}{\phi(\lambda_2+\phi)(\lambda_2+\phi+\alpha_c)}$ (3.32)

Then from equations 3.28, 3.29, 3.31 and 3.32, and with the assumption of the constant number of HCWs, we have the endemic equilibrium as

$$E_1 = (P_u^{**}, P_c^{**}, H_u^{**}, H_c^{**}, G_u^{**}, G_c^{**}) = \left(\frac{(1-\sigma)\Lambda_a}{(\lambda_1+\delta_u)}, \frac{\Lambda_a(\sigma\delta_u+\lambda_1)}{\delta_c(\lambda_1+\delta_u)}, \mathrm{c}_1, \mathrm{c}_2, \frac{\Lambda_b\phi(\lambda_2+\phi+\alpha_c)+\alpha_c\lambda_2\Lambda_b}{\phi(\lambda_2+\phi)(\lambda_2+\phi+\alpha_c)}, \frac{\lambda_2\Lambda_b}{\phi(\lambda_2+\phi+\alpha_c)}\right) \quad ,$$

$\mathrm{c}_1 + \mathrm{c}_2 = \mathrm{N}_h$ . (3.33)

### 3.6 Formulation of the Proposed Stochastic Model

From the deterministic model developed earlier in (3.7),

$$\left.\begin{aligned}
\frac{dP_u(t)}{dt} &= (1-\sigma)\Lambda_a - \left[(1-\eta)\beta_{ph}H_c(t) + (1-\xi)\beta_{pg}G_c(t)\right]P_u(t) - \delta_u P_u(t)\\
\frac{dP_c(t)}{dt} &= \sigma\Lambda_a + \left[(1-\eta)\beta_{ph}H_c(t) + (1-\xi)\beta_{pg}G_c(t)\right]P_u(t) - \delta_c P_c(t)\\
\frac{dH_u(t)}{dt} &= -(1-\eta)\beta_{ph}P_c(t)H_u(t) + \mu_c H_c(t)\\
\frac{dH_c(t)}{dt} &= (1-\eta)\beta_{ph}P_c(t)H_u(t) - \mu_c H_c(t)\\
\frac{dG_u(t)}{dt} &= -(1-\xi)\beta_{pg}P_c(t)G_u(t) + \Lambda_b - \phi G_u(t) + \alpha_c G_c(t)\\
\frac{dG_c(t)}{dt} &= (1-\xi)\beta_{pg}P_c(t)G_u(t) - \phi G_c(t) - \alpha_c G_c(t)
\end{aligned}\right\}$$

and the steady state expression, we have that $P_u(t) + P_c(t) = N_p \Rightarrow P_u(t) = N_p - P_c(t)$ , where $N_p = \frac{\Lambda_a}{\delta_u}$ , $G_u(t) + G_c(t) = N_g \Rightarrow G_u(t) = N_g - G_c(t)$ , where $N_g = \frac{\Lambda_b}{\phi}$ , and $H_u(t) + H_c(t) = N_h \Rightarrow H_u(t) = N_h - H_c(t)$ , where $N_h$ is a constant. Hence we have a model embedded in $\mathcal{R}^3$. We can write the joint probability of the state variables as

$$p_{(i,j,k)}(t) = Prob[P_c(t) = i, H_c(t) = j, G_c(t) = k], \quad (3.34)$$

where $i = 1(1)N_p, j = 1(1)N_h, and\ k = 1(1)N_g$.

### 3.6.1 Transition Probabilities

To determine the transition probabilities we consider a sufficiently small change in time $\Delta t$, such that at most only one change in the state variable occurs during a time step $\Delta t$. That is, we can only have a new colonization or decolonization of a patient, or a new contamination or decontamination of a HCW, or a new contamination or decontamination of a caregiver. From the deterministic model in (3.7), we have the change in state and transition probabilities as,

**Table 3.2: Transition Rates**

| **Description of state change** | **Change in state** | **Transition rates** |
|---|---|---|
| Admission of colonized patients | $(P_c, H_c, G_c) \rightarrow (P_c + 1, H_c, G_c)$ | $\sigma\Lambda_a$ |
| Discharge of colonized patients | $(P_c, H_c, G_c) \rightarrow (P_c - 1, H_c, G_c)$ | $\delta_c P_c$ |
| Contamination of uncolonized patient by HCW | $(P_c, H_c, G_c) \rightarrow (P_c + 1, H_c, G_c)$ | $[(1-\eta)\beta_{ph} H_c](N_p - P_c)$ |
| Contamination of uncolonized patient by caregiver | $(P_c, H_c, G_c) \rightarrow (P_c + 1, H_c, G_c)$ | $[(1-\xi)\beta_{pg} G_c]\,(N_p - P_c)$ |
| Contamination of uncontaminated HCW by patient | $(P_c, H_c, G_c) \rightarrow (P_c, H_c + 1, G_c)$ | $[(1-\eta)\beta_{ph} P_c](N_h - H_c)$ |
| Decontamination of contaminated HCW by hand washing | $(P_c, H_c, G_c) \rightarrow (P_c, H_c - 1, G_c)$ | $\mu_c H_c$ |
| Contamination of uncontaminated caregiver by patient | $(P_c, H_c, G_c) \rightarrow (P_c, H_c, G_c + 1)$ | $[(1-\xi)\beta_{pg} P_c]\,(N_g - G_c)$ |

| | | |
|---|---|---|
| Decontamination of contaminated caregiver by hand washing | $(P_c, H_c, G_c) \rightarrow (P_c, H_c, G_c - 1)$ | $\alpha_c G_c$ |
| Outflow of caregivers | $(P_c, H_c, G_c) \rightarrow (P_c, H_c, G_c - 1)$ | $\phi(N_g - G_c)$ |

$Where,\ N_p = \frac{\Lambda_a}{\delta_u} and\ N_g = \frac{\Lambda_b}{\phi}$

From equation (3.34), and the event jumps $V = (v_1, v_2, v_3)\epsilon(-1,0,1)$ we write the transition probabilities as

$$p_{(i+v_1,j+v_2,k+v_3);(i,j,k)}(\Delta t) = Prob[\Delta P_c, \Delta H_c, \Delta G_c] = (i, j, k)$$

Where $\Delta P_c = P_c(t + \Delta t) - P_c(t)$

$$p_{(i+v_1,j+v_2,k+v_3);(i,j,k)}(\Delta t) = \begin{cases} \left(\sigma\Lambda_a + \left[(1-\eta)\beta_{ph}j\right]\left(N_p - i\right) + \left[(1-\xi)\beta_{pg}k\right]\left(N_p - i\right)\right)\Delta t & (v_1, v_2, v_3) = (1,0,0) \\ \delta_c i \Delta t & (v_1, v_2, v_3) = (-1,0,0) \\ [(1-\eta)\beta_{ph}i](N_h - j)\Delta t & (v_1, v_2, v_3) = (0,1,0) \\ \mu_c j \Delta t & (v_1, v_2, v_3) = (0,-1,0) \\ [(1-\xi)\beta_{pg}i]\,(N_g - k)\Delta t & (v_1, v_2, v_3) = (0,0,1) \\ \left(\alpha_c k + \phi(N_g - k)\right)\Delta t & (v_1, v_2, v_3) = (0,0,-1) \\ 1 - (q_1 + q_2 + q_3 + q_4 + q_5 + q_6) & (v_1, v_2, v_3) = (0,0,0) \\ 0 & elsewhere \end{cases} \quad (3.35)$$

Where,

$$q_1 = \left(\sigma\Lambda_a + \left[(1-\eta)\beta_{ph}j\right]\left(N_p - i\right) + \left[(1-\xi)\beta_{pg}k\right]\left(N_p - i\right)\right)\Delta t$$

$$q_2 = \delta_c i \Delta t$$

$$q_3 = [(1-\eta)\beta_{ph}i](N_h - j)\Delta t$$

$$q_4 = \mu_c j \Delta t$$

$$q_5 = [(1-\xi)\beta_{pg}i]\,(N_g - k)\Delta t$$

$$q_6 = \big(\alpha_c k + \phi(N_g - k)\big)\Delta\mathrm{t}$$

Using the Markov property, we can write $p_{(i,j,k)}(\mathrm{t} + \Delta t)$ as

$$\begin{aligned}
p_{(i,j,k)}(\mathrm{t} + \Delta t) = {} & p_{(i-1,j,k)}(\mathrm{t})\Big(\sigma\Lambda_a + \big[(1-\eta)\beta_{ph} j\big]\big(N_p - i + 1\big) \\
& + \big[(1-\xi)\beta_{pg} k\big]\big(N_p - i + 1\big)\Big)\Delta\mathrm{t} + p_{(i+1,j,k)}(\mathrm{t})\delta_c(i+1)\Delta\mathrm{t} \\
& + p_{(i,j-1,k)}(\mathrm{t})\big[(1-\eta)\beta_{ph} i\big](N_h - j + 1)\Delta\mathrm{t} + p_{(i,j+1,k)}(\mathrm{t})\mu_c(j+1)\Delta\mathrm{t} \\
& + p_{(i,j,k-1)}(\mathrm{t})\big[(1-\xi)\beta_{pg} i\big]\big(N_g - k + 1\big)\Delta\mathrm{t} \\
& + p_{(i,j,k+1)}(\mathrm{t})\big(\alpha_c(k+1) + \phi(N_g - k - 1)\big)\Delta\mathrm{t} \\
& + p_{(i,j,k)}(\mathrm{t})\Big\{1 - \Big\{p_{(i-1,j,k)}(\mathrm{t})\Big(\sigma\Lambda_a + \big[(1-\eta)\beta_{ph} j\big]\big(N_p - i + 1\big) \\
& + \big[(1-\xi)\beta_{pg} k\big]\big(N_p - i + 1\big)\Big) + p_{(i+1,j,k)}(\mathrm{t})\delta_c(i+1) \\
& + p_{(i,j-1,k)}(\mathrm{t})\big[(1-\eta)\beta_{ph} i\big](N_h - j + 1) + p_{(i,j+1,k)}(\mathrm{t})\mu_c(j+1) \\
& + p_{(i,j,k-1)}(\mathrm{t})\big[(1-\xi)\beta_{pg} i\big]\big(N_g - k + 1\big) \\
& + p_{(i,j,k+1)}(\mathrm{t})\big(\alpha_c(k+1) + \phi(N_g - k - 1)\big)\Big\}\Big\}\Delta\mathrm{t}
\end{aligned} \tag{3.36}$$

### 3.6.2 System of Kolmogorov Equation

The system of forward Kolmogorov equation can now be written as,

$$\begin{aligned}
&\frac{d}{dt}p_{(i,j,k)}(\mathrm{t}+\Delta t)\\
&\quad= p_{(i-1,j,k)}(\mathrm{t})\left(\sigma\Lambda_a+\left[(1-\eta)\beta_{ph}j\right]\left(N_p-i+1\right)+\left[(1-\xi)\beta_{pg}k\right]\left(N_p-i+1\right)\right)\\
&\quad+p_{(i+1,j,k)}(\mathrm{t})\delta_c(i+1)+p_{(i,j-1,k)}(\mathrm{t})\left[(1-\eta)\beta_{ph}i\right](N_h-j+1)\\
&\quad+p_{(i,j+1,k)}(\mathrm{t})\mu_c(j+1)\ +p_{(i,j,k-1)}(\mathrm{t})\left[(1-\xi)\beta_{pg}i\right]\left(N_g-k+1\right)\\
&\quad+p_{(i,j,k+1)}(\mathrm{t})\left(\alpha_c(k+1)+\phi\left(N_g-k-1\right)\right) \qquad (3.37)\\
&\quad+p_{(i,j,k)}(\mathrm{t})\Big\{1-\Big\{p_{(i-1,j,k)}(\mathrm{t})\left(\sigma\Lambda_a+\left[(1-\eta)\beta_{ph}j\right]\left(N_p-i+1\right)\right.\\
&\quad+\left.\left[(1-\xi)\beta_{pg}k\right]\left(N_p-i+1\right)\right)+p_{(i+1,j,k)}(\mathrm{t})\delta_c(i+1)\\
&\quad+p_{(i,j-1,k)}(\mathrm{t})\left[(1-\eta)\beta_{ph}i\right](N_h-j+1)+p_{(i,j+1,k)}(\mathrm{t})\mu_c(j+1)\\
&\quad+p_{(i,j,k-1)}(\mathrm{t})\left[(1-\xi)\beta_{pg}i\right]\left(N_g-k+1\right)\\
&\quad+p_{(i,j,k+1)}(\mathrm{t})\left(\alpha_c(k+1)+\phi(N_g-k-1)\right)\Big\}\Big\}
\end{aligned}$$

### 3.7 Drift and Diffusion Terms of the System

Let the CTMC model be defined as having a state $X(t)\in\mathcal{R}^n$ and the list of possible jumps (events) indexed by r. Then given a jump vector $v_r\in\mathcal{R}^n$ (change in state when event r occurs) and rate $\lambda_r(X)$ when the process is in state X, the infinitesimal mean (drift) vector $f(X)$ per unit time and infinitesimal covariance (diffusion term) $\sum(X)$ per unit time are:

$f(X)=\sum_r v_r\lambda_r(X)$ and $\sum(X)=\sum_r v_r v_r^T\lambda_r(X)$.

Considering the proposed model,

$p_{(i,j,k)}(t)=Prob[P_c(t)=i,H_c(t)=j,G_c(t)=k]$ , where $i=1(1)N_p, j=1(1)N_h, and\ k=1(1)N_g$ with transition probabilities given in (3.35), $X(t)=\left(P_c(t),H_c(t),G_c(t)\right)$ with infinitesimal $\Delta X(t)=\left(\Delta P_c(t),\Delta H_c(t),\Delta G_c(t)\right)$. Then, the infinitesimal mean matrix $f(X(t),t)$ can be written as

$$E\big(\Delta X(t)\big|X(t)\big) = \begin{pmatrix} \mathrm{u}_p \\ \mathrm{u}_h \\ \mathrm{u}_g \end{pmatrix}.\Delta(\mathrm{t}) = f(X(t),t).\Delta(\mathrm{t}) \tag{3.38}$$

Where,

$$\mathrm{u}_p = \sigma\Lambda_a + \big[(1-\eta)\beta_{ph}H_c\big]\big(N_p - P_c\big) + \big[(1-\xi)\beta_{pg}G_c\big]\big(N_p - P_c\big) - \delta_c P_c$$

$$\mathrm{u}_h = \big[(1-\eta)\beta_{ph}P_c\big](N_h - H_c) - \mu_c H_c \text{ and}$$

$$\mathrm{u}_g = [(1-\xi)\beta_{pg}P_c]\,(N_g - G_c) - \big(\alpha_c k + \phi(N_g - G_c)\big)$$

Similarly, the infinitesimal variance-covariance matrix $\sum(X(t),t)$ is given as,

$$E\left(\Delta X(t)\big(\Delta X(t)\big)^T\middle|X(t)\right) = \begin{pmatrix} \omega_p & 0 & 0 \\ 0 & \omega_h & 0 \\ 0 & 0 & \omega_g \end{pmatrix}.\Delta(\mathrm{t}) = \sum(X(t),t)\,.\Delta(\mathrm{t}) \tag{3.39}$$

Where,

$$\omega_p = \sigma\Lambda_a + \big[(1-\eta)\beta_{ph}H_c\big]\big(N_p - P_c\big) + \big[(1-\xi)\beta_{pg}G_c\big]\big(N_p - P_c\big) + \delta_c P_c$$

$$\omega_h = \big[(1-\eta)\beta_{ph}P_c\big](N_h - H_c) + \mu_c H_c \text{ and}$$

$$\omega_g = \big[(1-\xi)\beta_{pg}P_c\big]\big(N_g - G_c\big) + \big(\alpha_c k + \phi(N_g - G_c)\big)$$

# CHAPTER FOUR

# MODEL SOLUTIONS, ANALYSIS AND DISCUSSION

## 4.1 Numerical Solution of the Deterministic Model

Here, we provide the numerical simulation of the deterministic MRSA transmission model, which captures the transmission dynamics of Methicillin Resistant Staphylococcus Aureus in hospital wards involving three interacting populations: patients, healthcare workers and family caregiver's. The simulations were carried out using baseline parameter values as in Table 4.1. These parameter values were selected based on empirical data from surveillance studies in Nigerian hospitals, and plausible assumptions that represent realistic hospital operational conditions as below.

**Table 4.1: Baseline Parameter Values**

| Parameters | Description | Baseline value | Units | Source |
|---|---|---|---|---|
| $\Lambda_a$ | Inflow of patients | 3/day | patients / day | Assumed |
| $\sigma$ | Proportion of patients colonized on arrival | 0.12 | Proportion | Abdullahi et al. (2022) |
| $\beta_{ph}$ | Transmission rate between patients and HCWs | 0.003387 | per (patient-HCW)day | Estimated |
| $\beta_{pg}$ | Transmission rate between patients and caregivers | 0.002902 | per (patient-caregiver)day | Estimated |
| $\delta_u$ | Discharge rate of uncolonized patients | 0.083 | $day^{-1}$ | Somotun et al. (2017) |
| $\delta_c$ | Discharge rate of colonized patients | 0.071 | $day^{-1}$ | Assumed |
| $N_h$ | Constant number of HCWs | 20 | Persons | Assumed |
| $\Lambda_b$ | Inflow of caregivers | 3/day | caregivers/day | Assumed |
| $\phi$ | Outflow of caregivers | 0.077 | $day^{-1}$ | Estimated |
| $\eta$ | Handwashing compliance of HCWs | 0.31 | Proportion | Onyedibe et al. (2020) |
| $\xi$ | Handwashing compliance of caregivers | 0.15 | Proportion | Assumed |
| $\mu_c$ | Decontamination rate of contaminated HCWs | 0.0658 | $day^{-1}$ | Wang and Ruan (2017) |
| $\alpha_c$ | Decontamination rate of contaminated caregivers | 0.0658 | $day^{-1}$ | Assumed |

### 4.1.1 Solution of the Proposed Deterministic System of Ordinary Differential Equations

The proposed deterministic system of ordinary differential equations was integrated over a 365-day time horizon using an adaptive ODE solver in MATLAB. The resulting time-dependent trajectories illustrate how each compartment evolves over time and approaches a steady state determined by the balance between transmission, decontamination, inflow, and discharge processes.

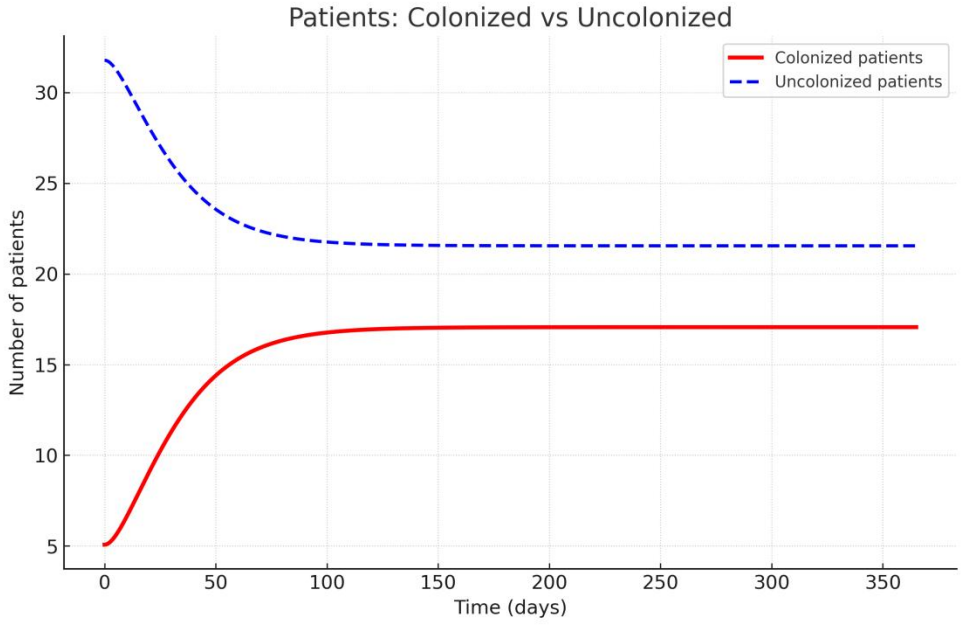



**Figure 4.1**: Solution of the colonized and uncolonized patients of the deterministic epidemic model.

Figure 4.1 illustrates the evolution of colonized and uncolonized patient populations. Initially, the number of colonized patients increases due to admission of colonized individuals and cross-transmission from contaminated HCWs and caregivers. As time progresses, the system stabilizes as discharge and reduced transmission balance the inflow of new colonization events.

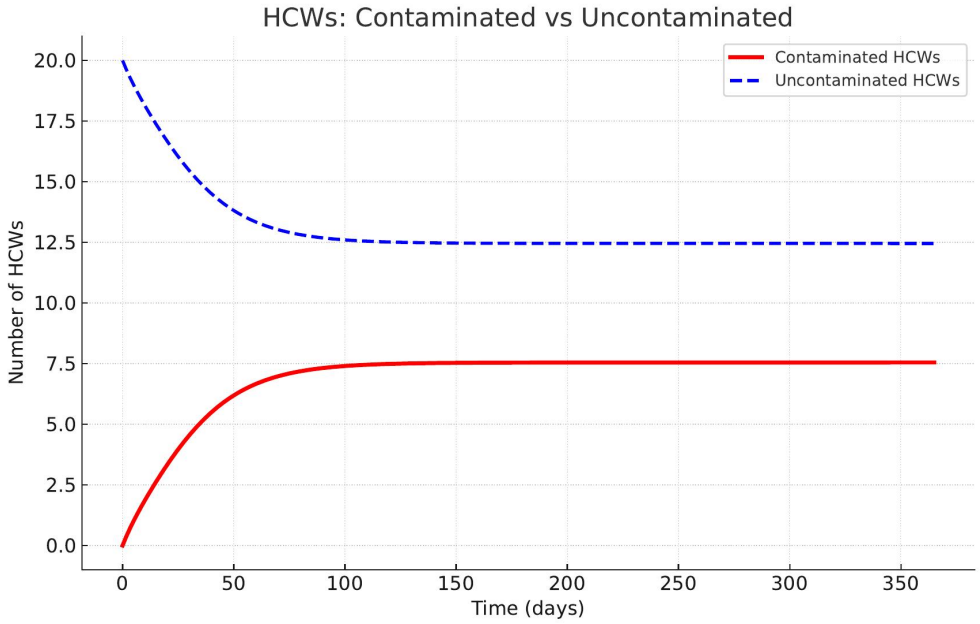



**Figure 4.2**: Solution of the contaminated and uncontaminated HCWs of the deterministic epidemic model.

Figure 4.2 shows the dynamics of contaminated and uncontaminated HCWs. Their contamination levels rise early in the simulation due to frequent contact with colonized patients but eventually approach equilibrium as the decontamination rate halts ongoing transmission.

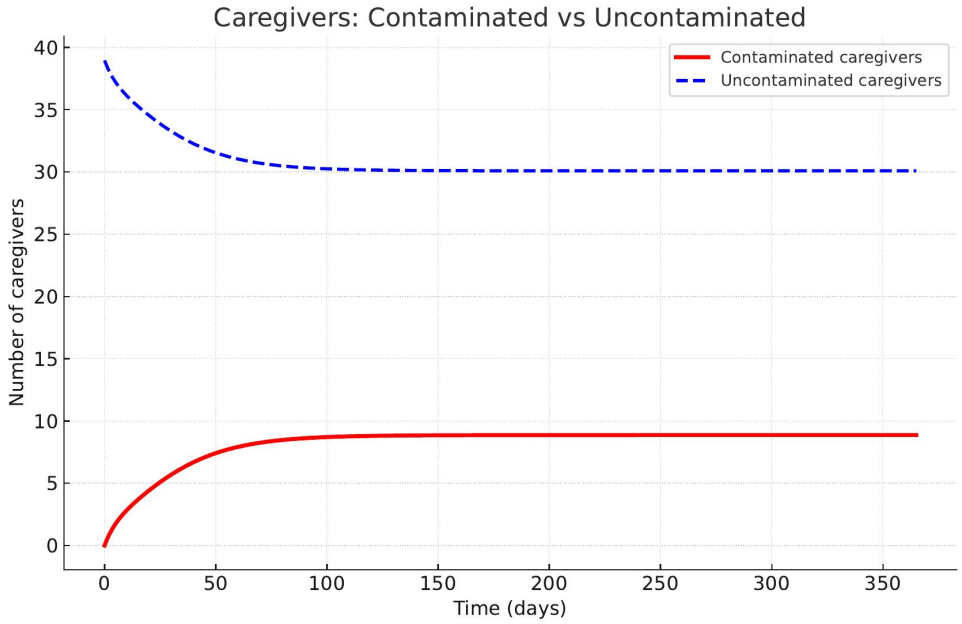



**Figure 4.3**: Solution of the contaminated and uncontaminated caregiver's of the deterministic epidemic model.

From Figure 4.3 we deduce that while the dynamics of uncontaminated and contaminated family caregivers shares similar qualitative behavior with that of healthcare workers, the inclusion of caregivers introduces new pathways into the transmission dynamics of hospital-acquired infections that are not captured by existing patient-HCW models. The time-series behavior of caregivers highlights that even modest levels of caregiver contamination can sustain transmission pressure within the ward, thereby delaying convergence to low-prevalence equilibrium. This reiterates the idea that infection control strategies focusing solely on healthcare workers may be insufficient to adequately control the spread of MRSA.

In summary, the deterministic model provides insights into the average behavior of MRSA transmission under baseline assumptions. It predicts the expected long-term levels of contamination in patients, HCWs, and caregivers and forms the foundation for stochastic analysis.

### 4.1.2 Sensitivity Analysis on the Basic Reproduction Number

The basic reproduction number $(R_0)$ is the number of secondary infections one infectious individual can produce in its infectious period within a susceptible population. The analytic expression for the basic reproduction number was earlier derived in chapter two as,

$$R_0 = \sqrt{\frac{(1-\eta)^2\phi N_h(\phi+\alpha_c)\beta_{\text{ph}}^2\Lambda_a+(1-\xi)^2\beta_{\text{pg}}^2\Lambda_b\Lambda_a\mu_c}{\phi\delta_c\delta_u\mu_c(\phi+\alpha_c)}} \tag{4.1}$$

where an infection persist if $R_0 > 1$ and dies out if $R_0 \leq 1$. Here we performed a sensitivity analysis of $R_0$ (in Matlab) to investigate how variations in key behavioral parameters affect MRSA transmission potential. Specifically, we examined $R_0$ as a function of caregiver hand-hygiene compliance, healthcare-worker hand-hygiene compliance, the HCW decontamination rate and the caregiver decontamination rate. For each parameter, the remaining parameters were held fixed at baseline values. The following plots describe these behaviours.

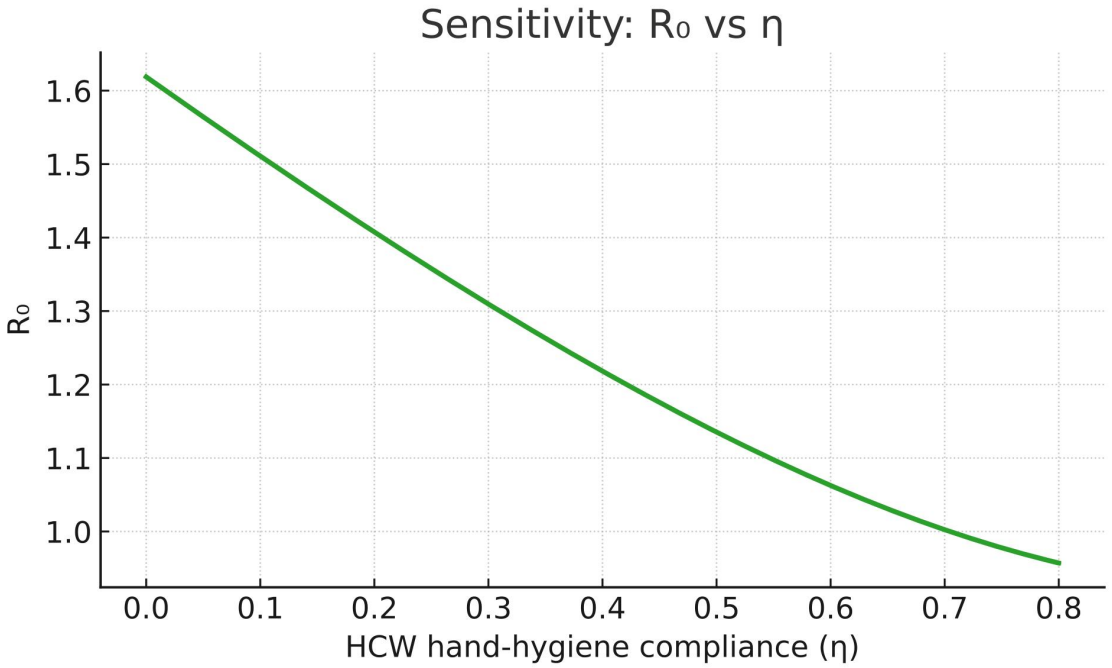



**Figure 4.4**: $R_0$ versus hand-hygiene compliance of HCWs $(\eta)$.

Figure 4.4 illustrates the sensitivity of $R_0$ to variations in HCWs hand-hygiene compliance $(\eta)$, while all other parameters are held at their baseline values. A clear monotonic decline in $R_0$ is

observed as $\eta$ increases, indicating that improved hand hygiene among HCWs substantially reduces the transmission potential of MRSA within the hospital environment.

At low levels of hand hygiene compliance, $R_0$ remains relatively high, reflecting increased opportunity for patient-HCW-patient transmission due to contaminated contacts. As compliance improves, the effective transmission rate between patients and HCWs is reduced by the factor$(1-\eta)$, leading to a progressive decline in $R_0$ .

Despite the downward trend, the figure show that $R_0$ does not immediately fall below unity for moderate values of $\eta$ . This suggests that HCWs hand hygiene as a critical control measure may not be sufficient on its own to eliminate MRSA transmission, particularly in the presence of additional transmission pathways.

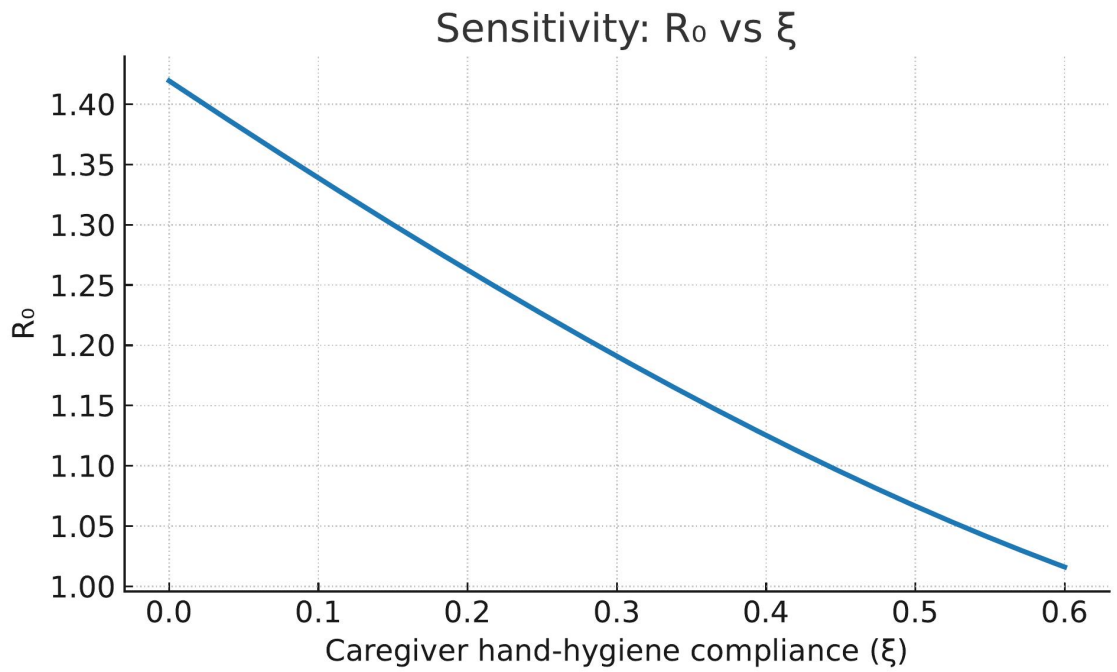



**Figure 4.5**: $R_0$ versus hand-hygiene compliance of caregivers$(\xi)$.

Figure 4.5 illustrates the sensitivity of $R_0$ to variations in caregiver hand-hygiene compliance$(\xi)$, with all other model parameters fixed at their baseline values. A clear decreasing trend in $R_0$ is observed as caregiver compliance improves, demonstrating that family caregivers constitute a non-negligible transmission pathway in the hospital. This result provides strong quantitative

evidence that caregivers can significantly influence the persistence and control of MRSA within healthcare settings.

At low levels of $\xi$, $R_0$ remains elevated, indicating sustained transmission potential driven by frequent patient-caregiver interactions. As reflected in the sensitivity curve, inadequate caregiver hand hygiene can therefore maintain MRSA transmission even when other control measures are in place.

As $\xi$ increases, the contribution of caregiver-induced transmission to $R_0$ diminishes through the factor $(1-\xi)$ in the reproduction number. However, the figure shows that reductions in $R_0$ occur gradually, highlighting the cumulative nature of caregiver effects. This indicates that even moderate non-compliance among caregivers may sustain MRSA circulation, particularly in wards with high caregiver turnover, as predominant in Nigeria and other low-income and middle-income countries.

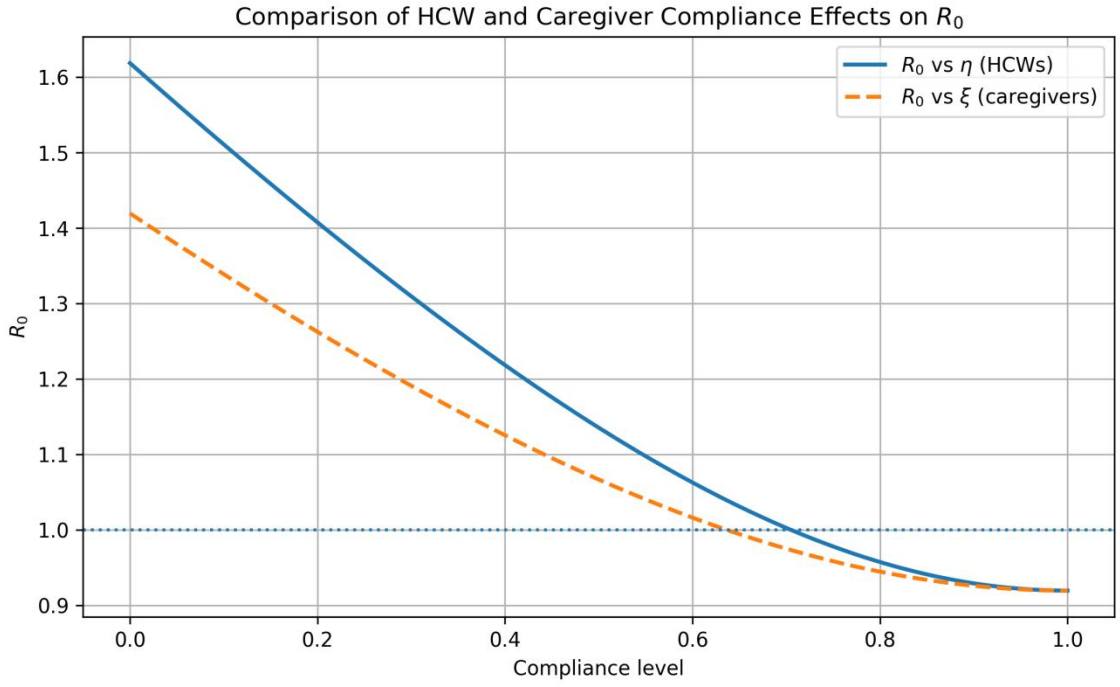



**Figure 4.6**: Comparative impact of HCWs and Caregiver's hand-hygiene compliances on $R_0$.

Figure 4.6 compares the sensitivity of $R_0$ to changes in HCWs hand-hygiene compliance $(\eta)$ and caregiver hand-hygiene compliance $(\xi)$, with all other parameters fixed at their baseline values.

Both curves exhibit a clear decreasing trend, confirming that improvements in hygiene compliance among either group reduce the transmission potential of MRSA in the hospital setting. However, there are important differences in the magnitude of these effects.

The HCWs compliance curve shows a steeper decline in $R_0$ , reflecting the central role of healthcare workers in patient contact networks and the high frequency of patient–HCW interactions. Improvements in HCWs compliance rapidly reduce patient-induced transmission, consistent with the dominant contribution of HCWs in traditional hospital-acquired infection models.

Crucially, the caregiver compliance curve also demonstrates a substantial and systematic reduction in $R_0$ as $\xi$ increases. This result provides quantitative evidence that family caregivers constitute a significant transmission pathway, capable of sustaining MRSA transmission independently of healthcare workers. Although the slope of the caregiver curve is less steep than that of HCWs, the persistence of elevated $R_0$ values at low caregiver compliance highlights the effect of patient-caregiver contact.

The comparison reveals that even when HCWs compliance is improved, inadequate caregiver hand hygiene can keep $R_0$ above the epidemic threshold.

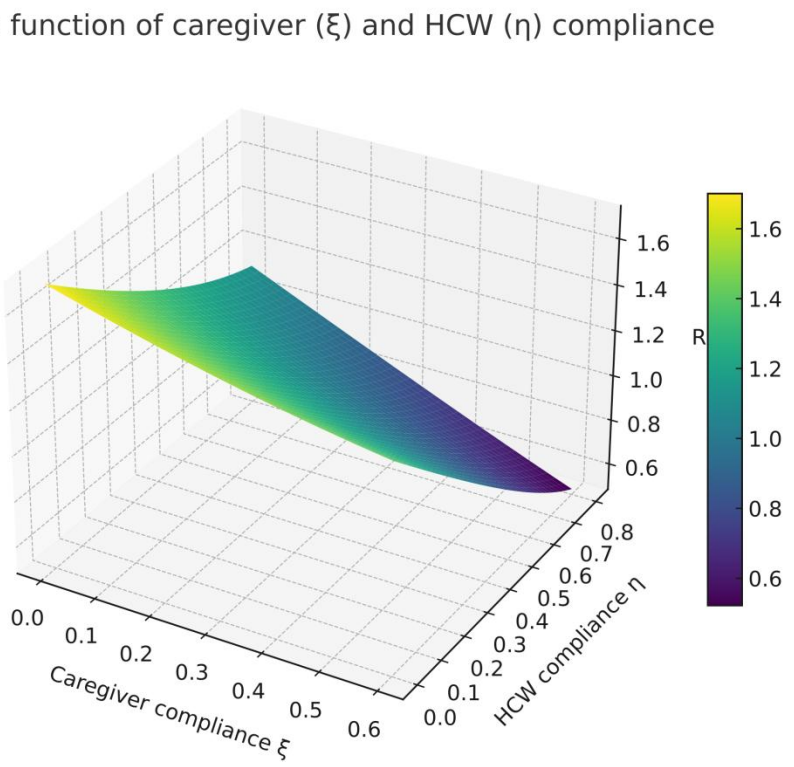



**Figure 4.7**: Joint effect of $\eta$ and $\xi$ on $R_0$.

In Figure 4.7 three-dimensional surface plot of $R_0$ as a joint function of caregiver hand-hygiene compliance and HCWs compliance. Unlike existing hospital-acquired infection models that examine the effect of HCWs compliance alone, this figure explicitly captures the combined influence of both HCWs and non-professional patients' caregivers on the transmission of MRSA.

The surface exhibits a consistent downward trend in $R_0$ as either compliance parameter increases, confirming that improved hygiene practices among both caregivers and HCWs reduce the transmission potential of MRSA. However, the most important insight emerges from the shape of the surface as reductions in $R_0$ are not driven by HCWs compliance alone. Even at moderate to high levels of HCWs compliance, low caregiver's compliance sustains elevated $R_0$ values, indicating persistent transmission risk. Conversely, an improvement in caregiver's compliance substantially lowers $R_0$, particularly when combined with improvements in HCWs hand hygiene.

Importantly, the surface plot reveals that the threshold condition $R_0 < 1$ is achieved most efficiently when both compliance parameters are increased simultaneously.

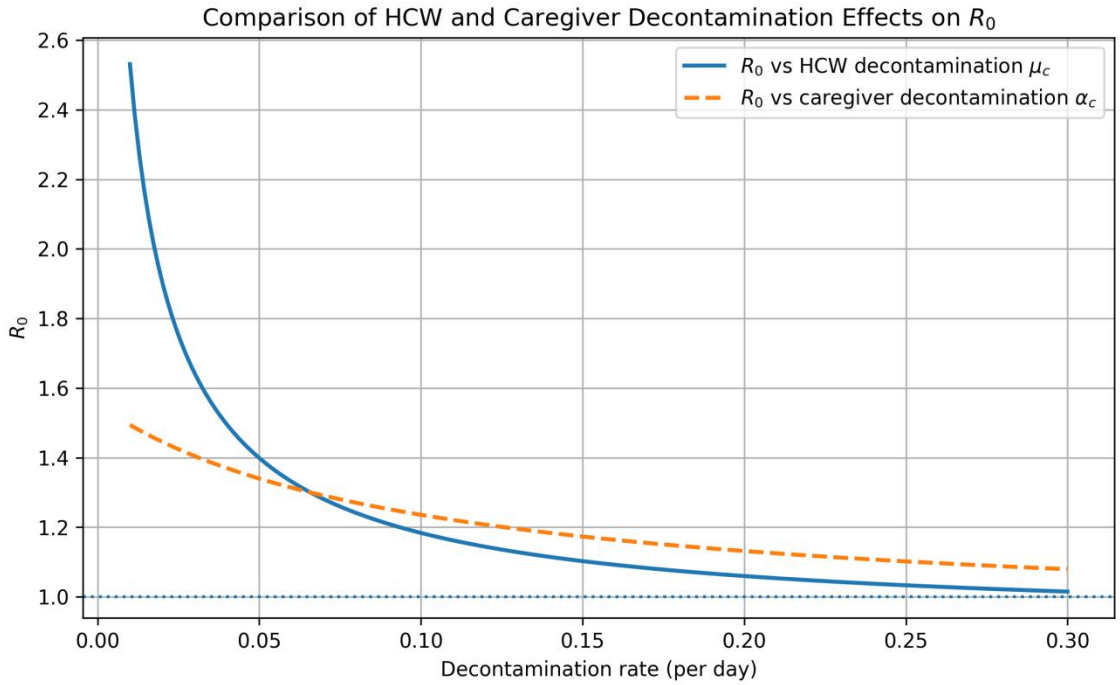



**Figure 4.8**: Comparative effects of HCWs and Caregivers decontamination rates on $R_0$

Figure 4.8 compares the sensitivity of the basic reproduction number $R_0$ to the decontamination rates of healthcare workers $(\mu_c)$ and caregivers $(\alpha_c)$. Both curves display a monotonic decline, indicating that faster decontamination of either group reduces the transmission potential of MRSA by shortening the duration of contamination and limiting the spread.

The curve corresponding to $\mu_c$ shows a steeper reduction in $R_0$, reflecting the role of healthcare workers in hospital, with high frequency of patient-HCWs interactions. Improvements in HCWs decontamination rapidly lower HCW-mediated transmission.

Importantly, the caregiver decontamination curve also exhibits a clear and systematic decline in $R_0$. Although the curve is comparatively less steep, the effect remains substantial, demonstrating that caregivers contribute meaningfully to sustained transmission when decontamination is slow. This result highlights that caregivers impact in the transmission of MRSA is not negligible, as

prolonged contamination among caregivers can maintain $R_0$ above the epidemic threshold even when HCWs decontamination is moderately effective.

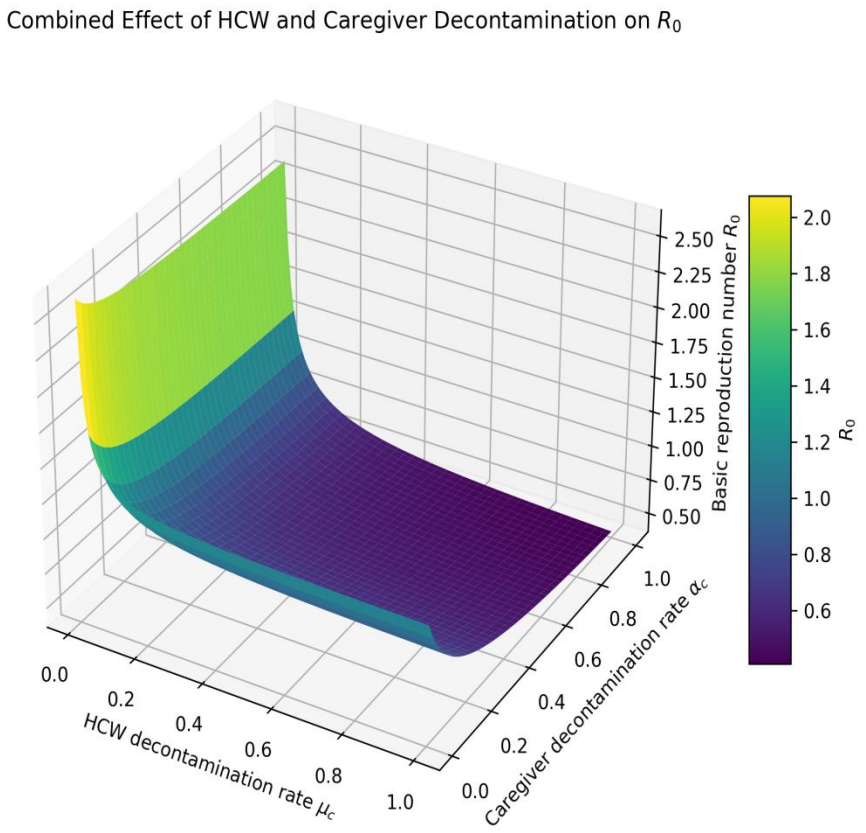



**Figure 4.9**: Combined effect of $\mu_c$ and $\alpha_c$ on $R_0$.

The surface plot in Figure 4.9 illustrates the joint dependence of $R_0$ on the healthcare worker decontamination rate $\mu_c$ and the caregiver decontamination rate $\alpha_c$ . A pronounced downward slope of the surface is observed as either $\mu_c$ or $\alpha_c$ increases, indicating that improvements in decontamination for both groups reduce the transmission potential of MRSA. Importantly, the curvature of the surface reveals that a strong reduction in $R_0$ is achieved by increasing one decontamination rate when the other is also increased. This demonstrates that the combined effect of improving both HCWs and caregiver's decontamination is substantially greater than the effect of varying either parameter in isolation.

When either $\mu_c$ or $\alpha_c$ is low, the surface remains elevated, indicating sustained transmission of MRSA even if the other parameter is increased. This explains why one-

parameter sensitivity analyses may fail to push $R_0$ below the epidemic threshold. In contrast, regions of the surface corresponding to simultaneously high values of $\mu_c$ and $\alpha_c$ show $R_0$ falling below unity, highlighting conditions under which MRSA transmission can be effectively controlled or eliminated.

In summary, we have given the solutions of the deterministic model and the sensitivity and elasticity of the basic reproduction on key parameters of the model. The deterministic analysis elucidates the mean behavior of the system and identifies critical parameters governing transmission and control. However, deterministic models describe only the average trajectory and cannot capture random fluctuations, variability in outbreak size, or the possibility of infection extinction in finite populations.

### 4.2 Stochastic Simulations

While the deterministic model provides valuable insight into the average behavior of MRSA transmission within a hospital ward, it does not account for the inherent randomness present in real hospital environments. In practice, hospital populations are relatively small, contacts occur irregularly, and transmission events are discrete and probabilistic. Under such conditions, chance effects can play a decisive role in determining whether an infection persists or becomes extinct. To capture these features, a stochastic model was formulated as in equation 3.35.

The stochastic model was constructed directly from the deterministic framework by interpreting each term in the system of ordinary differential equations as a possible discrete event occurring in continuous time. Specifically, transitions between epidemiological states, such as patient colonization, contamination of healthcare workers or caregivers, decontamination events, admissions, and discharges, were modeled as random events governed by state-dependent rates. This formulation leads to a continuous-time Markov chain (CTMC), in which the state variables represent integer-valued population counts, while the time is continuous.

Using these transition rates, the system can be simulated numerically using Euler-Maruyama stochastic simulation algorithm, which generates exact sample paths consistent with the underlying CTMC.

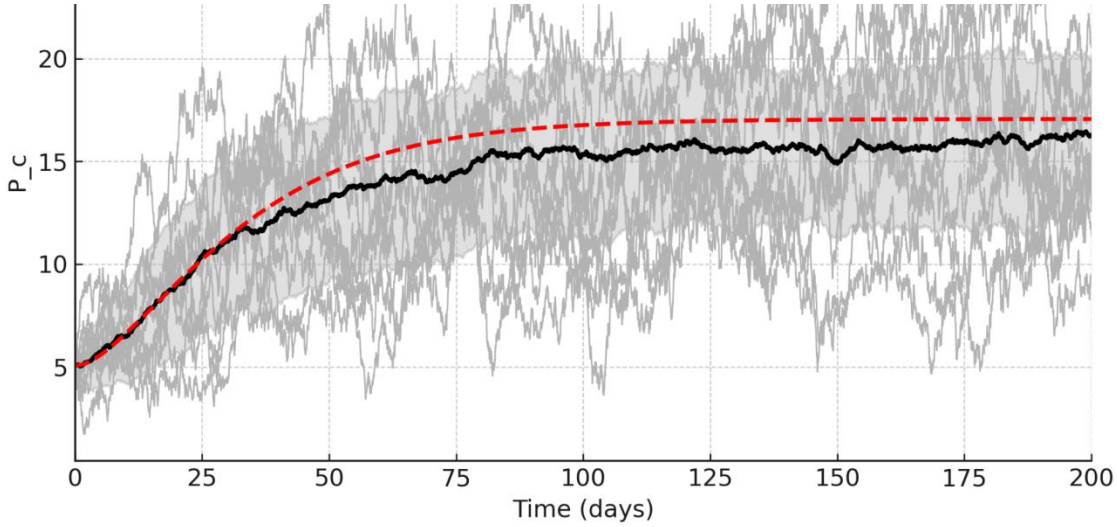



**Figure 4.10**: Stochastic sample paths of the colonized patients ($P_c$) in the MRSA model graphed with the deterministic solution (dashed line).

Figure 4.10 gives the stochastic simulation results for the number of colonized patients ($P_c$) , obtained using a continuous-time Markov chain formulation and the Euler-Maruyama stochastic simulation algorithm. The solid black curve represents the stochastic mean over multiple stochastic realizations, while the shaded region denotes stochastic fluctuations above and below the mean, capturing the inherent variability of the process. The red dashed curve corresponds to the deterministic solution of the model.

The stochastic mean closely follows the deterministic trajectory, particularly during the early and intermediate phases of the epidemic. This agreement confirms that the deterministic model provides a good approximation of the average behavior of the system. However, unlike the deterministic solution, the stochastic simulations exhibit substantial fluctuations around the mean, arising from the discrete and random nature of transmission, recovery, and admission events in a finite hospital population.

The deterministic solution converges smoothly to a steady-state value, implying persistent colonization at the population level. In contrast, the stochastic framework allows for the

possibility of significant deviations from this mean behavior and, in some cases, eventual extinction of colonization.

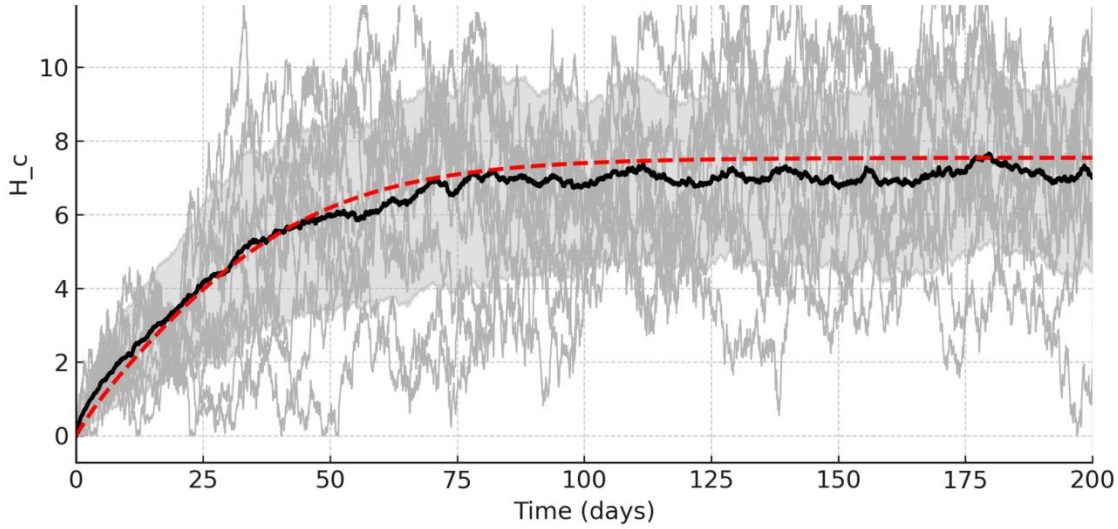



**Figure 4.11**: Stochastic sample paths of the contaminated HCWs ($H_c$) in the MRSA model graphed with the deterministic solution (dashed line).

Figure 4.11 illustrates the temporal evolution of HCWs contamination under stochastic dynamics, together with the deterministic solution. The stochastic realizations fluctuate substantially around the deterministic trajectory, particularly during the early phase when contamination levels are low and individual contact events have a larger relative impact. As time progresses, the mean of the stochastic simulations approaches the deterministic steady state, confirming that the deterministic model provides a good approximation of the average behavior.

However, the persistent variability around the mean highlights the influence of random patient-HCWs interactions and stochastic decontamination events in finite hospital populations. Transient peaks in contamination, which exceed deterministic predictions, indicate periods of heightened transmission risk that would not be noticed using deterministic analysis alone. These results emphasize the role of healthcare workers as a core transmission pathway and demonstrate that stochastic effects can amplify infection risks even when averages appear stable.

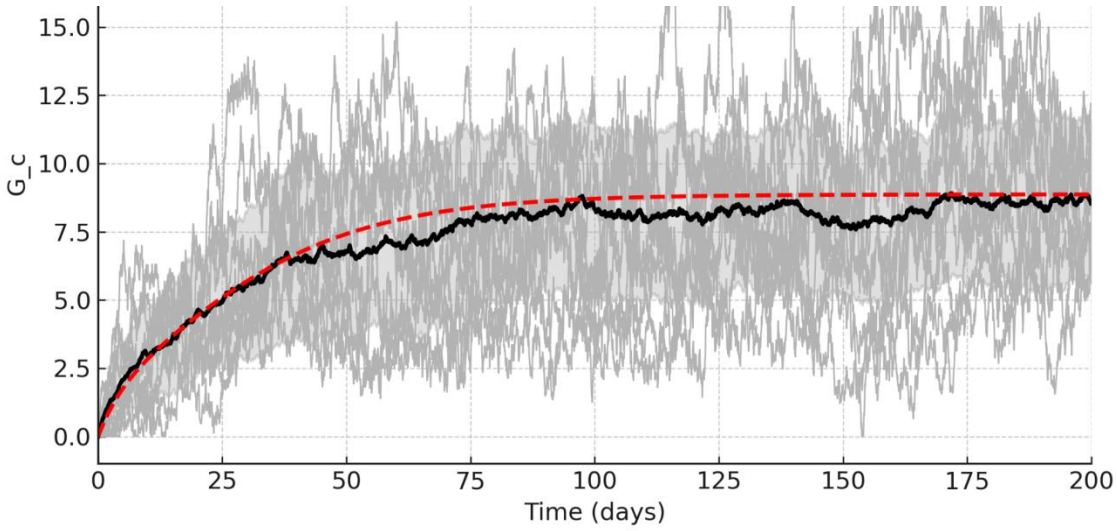



**Figure 4.12**: Stochastic sample paths of the contaminated patients' family caregivers ($G_c$) in the MRSA model graphed with the deterministic solution (dashed line).

In figure 4.12, the stochastic dynamics of contaminated caregiver's exhibit even greater variability than those observed for healthcare workers. This increased variability arises from caregiver inflow and outflow, irregular contact patterns with patients, and stochastic decontamination events. While the deterministic solution captures the mean trend of caregiver contamination, individual stochastic realizations display pronounced fluctuations, including rapid increases and decreases in contamination levels.

Temporary increases in caregiver contamination can elevate the force of infection acting on patients and healthcare workers, thereby sustaining transmission even when average contamination levels remain moderate. Such behavior cannot be captured by deterministic models alone. The stochastic results therefore demonstrate that caregivers act as intermittent but impactful contributors to MRSA transmission, underscoring it's the need for its inclusion in modeling hospital acquired infections.

### 4.3 Estimation of Extinction Probability

Deterministic models describe the average behavior of an epidemic process and predict persistence whenever the basic reproduction number exceeds unity. However, in finite populations such as hospital wards, random fluctuations can cause infection to die out even when deterministic theory predicts persistence. The ratio of the number of stochastic runs where the number of colonized patients touches zero to the total number of runs gives the extinction probability (Allen and Burgin, 2000).

The extinction probability was estimated using repeated stochastic simulations based on the continuous-time Markov chain model implemented via Gillespie's stochastic simulation algorithm (Gillespie, 1977). A large number of independent sample paths were generated from the same initial conditions and baseline parameter values used in the deterministic analysis. For each realization, extinction was defined as the event in which the number of colonized patients reached zero and remained at zero for the remainder of the simulation period (Allen, 2008).

Let $N$ denote the total number of stochastic realizations and $N_e$ the number of realizations that resulted in extinction. The extinction probability was then estimated as

$$\hat{p}_{ext} = \frac{N_e}{N} \tag{4.2}$$

Using the baseline parameter values, the estimated extinction probability was found to be $\hat{p}_{ext} = 0.012$ indicating that approximately 1.2% of stochastic realizations resulted in complete elimination of MRSA colonization during the simulation period, despite the deterministic reproduction number exceeding one.

The non-zero extinction probability highlights an important limitation of deterministic modeling in hospital settings. Although the deterministic model predicts persistence of MRSA due to sustained transmission pathways involving patients, healthcare workers, and caregivers, stochastic effects can still drive the system to extinction through reductions in colonization, particularly during periods of low prevalence.

**4.4 Discussion of Results**

The deterministic analysis provided a baseline to understanding the average behavior of the system. Time-series simulations demonstrated convergence of all state variables to steady-state values, confirming that the model is mathematical well-posed.

Sensitivity and elasticity analyses of the basic reproduction number ($R_0$) revealed that parameters associated with caregivers, particularly caregiver hand-hygiene compliance and decontamination rate, significantly affect transmission potential. Joint sensitivity analyses showed that improvements in healthcare worker compliance alone are insufficient to reduce $R_0$ below unity when caregiver-related transmission remains uncontrolled, hence effective reduction of $R_0$ require interventions targeting both healthcare workers and caregivers. These findings extend existing hospital-acquired infection models by demonstrating that caregiver-induced transmission can sustain MRSA circulation even when traditional control measures focused on healthcare workers are implemented.

While the deterministic model captures mean-field behavior, stochastic simulations revealed important features that are invisible at the deterministic level. Sample-path simulations for colonized patients, contaminated healthcare workers, and contaminated caregivers exhibited substantial variability around the deterministic trajectories. In particular, caregiver contamination dynamics showed pronounced fluctuations due to caregiver inflow, outflow, and irregular contact patterns.

The stochastic results highlight that caregiver involvement introduces additional randomness into hospital transmission dynamics. Transient stochastic peaks in caregiver contamination were observed, which can temporarily amplify the force of infection acting on patients and healthcare workers.

The close agreement between stochastic solutions and deterministic solutions confirms the validity of the deterministic model as an approximation of average behavior. However, the wide dispersion of stochastic realizations emphasizes that relying solely on deterministic predictions may underestimate outbreak variability and possibility of extinction.

A key advantage of the stochastic framework is the ability to quantify extinction probability. Despite deterministic predictions of persistence under baseline parameter values, a non-zero

probability of MRSA extinction was observed in the stochastic simulations. This result underscores the importance of random effects in finite hospital populations, where reductions in colonization or contamination can interrupt transmission chains.

Caregivers play a dual role in this context. On one hand, caregiver-induced transmission can contribute to persistence by introducing additional contacts and contamination pathways. On the other hand, caregiver turnover and stochastic decontamination events can also facilitate extinction by breaking transmission links. This dual effect increases outcome variability and influences extinction probabilities in ways that cannot be captured by models excluding caregivers.

The combined deterministic and stochastic findings strongly support the inclusion of patients' family caregivers in models of hospital-acquired infections. Traditional models that focus exclusively on patients and healthcare workers implicitly assume that caregiver interactions are negligible. The present results challenge this assumption by showing that caregivers can significantly alter both average transmission dynamics and stochastic variability.

From a modeling perspective, excluding caregivers may lead to underestimation of transmission risk, overconfidence in the effectiveness of healthcare worker-centered interventions, and incomplete assessment of outbreak uncertainty. Including caregivers provides a more realistic representation of hospital environments, particularly in settings where family involvement in patient care is common.

The results have important implications for infection prevention and control. Interventions aimed solely at healthcare workers may be insufficient if caregiver compliance and decontamination are neglected. Strategies such as caregiver hand-hygiene education, access to sanitation facilities, and structured caregiver policies could meaningfully reduce MRSA transmission and increase the likelihood of elimination.

# CHAPTER FIVE

# SUMMARY AND CONCLUSION

## 5.1 Summary

This study gave a comprehensive overview of nosocomial infections, with emphasis on their prevalence, etiology and associated burden. A critical review of existing models of nosocomial infection transmission (primarily focusing on MRSA) was conducted consisting of both deterministic and stochastic frameworks. During the review we identified a notable gap in the literature, that is, the exclusion of patients' family caregivers in modeling the transmission dynamics of MRSA.

To address this limitation, this study developed both deterministic and stochastic models for MRSA transmission that explicitly incorporate patients' family caregivers. Simulation results from the deterministic model using surveillance data from Nigeria showed that the caregivers' population plays a significantly role in the spread of the infection. Sensitivity analysis on the basic reproduction number further showed that reductions in the transmission associated with caregivers occur more slowly compared to HCWs, supporting the need to extend infection control interventions to include patients' family caregivers.

Analysis of the stochastic model revealed that the patients' family caregivers can sustain MRSA transmission even under strict adherence to prevention protocols by HCWs. Moreover, the stochastic framework captures inherent variability in the model transmission dynamics, enabling the estimation of extinction probabilities. Notably, the extinction probability was found to be non-zero, indicating the possibility of complete eradication of the infection even when basic reproduction number exceeds unity.

## 5.2 Findings

In this study we found that:

1.under baseline parameter values, the deterministic analysis demonstrates that MRSA transmission dynamics converge to a non-trivial endemic equilibrium. This confirms that the infection can persist within the hospital environment even when HCWs hand hygiene and decontamination measures are present, provided patients' family caregivers are involved in patient care.

2. contaminated caregivers reach a stable positive level comparable in magnitude to contaminated HCWs, as revealed by the time-series simulations. This indicates that caregivers constitute an additional and independent reservoir of MRSA contamination, capable of sustaining transmission even when HCW-induced transmission is being controlled.

3. by sensitivity analysis of the basic reproduction number ($R_0$), both HCWs compliance ($\eta$) and caregiver compliance ($\xi$) significantly reduce $R_0$ . However, reductions in $R_0$ are more pronounced when improvements in both parameters are implemented jointly, rather than targeting HCWs alone.

4. combined sensitivity analysis of decontamination rates of HCWs ($\mu_c$) and caregivers ($\alpha_c$) demonstrates that simultaneous increases in both parameters are required to drive $R_0$ below unity. Isolated increases in HCWs decontamination alone are often insufficient in the presence of caregiver-induced transmission.

5. by extinction probability analysis, MRSA may die out purely due to stochastic effects, even when $R_0$ exceeds unity.

**5.3 Contributions to Knowledge**

The study has contributed to knowledge:

1. by extending classical hospital-acquired infection models by explicitly introducing patients' family caregivers as a distinct epidemiological compartment. This represents a significant advancement over existing models that focus solely on patients, HCWs, and environmental contamination.

2. through analytical derivation of $R_0$ and sensitivity analysis, this work quantifies how caregiver behavior directly influences the persistence and control of MRSA. This provides a theoretical basis for recognizing caregivers as active participants in hospital infection dynamics.

3. by showing that joint compliance and decontamination strategies are more effective than HCWs-only interventions, this work provides new insights into infection control policy, particularly in healthcare systems where family involvement in patient care is substantial.

4. by showing its relevance to hospitals in low-income and middle-income countries, where patients' family caregivers play a prominent role. The model supports the inclusion of caregivers in infection prevention strategies, training programs, and hand hygiene campaigns.

### 5.4 Conclusion

This study investigated the transmission dynamics of Methicillin-Resistant Staphylococcus Aureus (MRSA) in a hospital setting using both deterministic and stochastic modeling frameworks, with explicit inclusion of patients' family caregivers as an additional epidemiological class. The primary objective was to assess whether caregiver-induced interactions meaningfully influence MRSA dynamics and to evaluate the implications of their inclusion for infection persistence, variability, and control.

We gave a brief description of hospital acquired infections, the etiology and the burden, ranging from extending length of stay, increased cost of healthcare, morbidity and mortality in extreme cases. Further we presented a robust review of models on nosocomial infections, both deterministic and stochastic models. It was established that no existing work has included family caregiver's in its model structure. We made effort to give the basics upon which the primary model of nosocomial infection modeling, involving the interaction between patients and healthcare workers, was formulated from malaria model.

The formulation of a new deterministic model for nosocomial infections, incorporating explicitly the impact of patients' family caregivers as a distinct transmission pathway was presented. The nature of the six different compartments in the model was described, together with the definition of the parameters. The positivity of the variables and their boundedness were established indicating that the model is mathematically well-posed. The disease free and endemic equlibria were obtained and the expression for the model reproduction number was explicitly derived. In order to capture the inherent randomness associated with the model variability in small hospital population, we formulated a stochastic model using the deterministic model.

The stochastic model was formulated using the principles of Continuous Time Markov Chain (CTMC), where the state variables are discrete with continuous time. The different transition rates were tabulated enabling us to state the transition probabilities, and the Kolmogorov

equation. The drift (mean) and diffusion (variance) terms of the model were determined; these will enable us run stochastic simulations given baseline parameter values.

The analysis of both the deterministic and stochastic models showed that patients' family caregivers are not passive population but active participants in the transmission dynamics of MRSA. By integrating deterministic analysis, stochastic simulations, and extinction probability estimation, the work provides a comprehensive assessment of caregiver-induced transmission. The findings reinforce the need to broaden the scope of hospital-acquired infection models and interventions to explicitly account for family caregiver's involvement, thereby improving both theoretical understanding and practical disease control measures.

### 5.5 Recommendation for Further Studies

1. Future studies may extend the current framework by explicitly incorporating hospital environmental contamination as an additional compartment, allowing assessment of the role of bacterial load in sustaining transmission.
2. Integrating game-theoretic approaches with the proposed model could provide insights into optimal intervention strategies and decision-making during MRSA outbreaks.

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# APPENDICES

## APPENDIX A

### Algorithms used in the Study

Algorithm 1: (Adaptive ODE Solver)

**Begin**

Step 1: Define the system of ordinary differential equations

$dX/_{dt} = F(t, X, \Theta)$

Step 2: Specify biologically feasible parameter values $(\Theta)$

Step 3: Set initial conditions $X(0)$

Step 4: Define simulation time interval $[0, \mathrm{T}]$

Step 5: Select an adaptive numerical solver (Runge–Kutta method)

Step 6: Numerically integrate the ODE system to obtain $X(t)$

Step 7: Extract compartment trajectories from $X(t)$

Step 8: Plot:

$P_u(t) and\ P_c(t)$

$H_u(t) and\ H_c(t)$

$G_u(t) and\ G_c(t)$

**End**

Algorithm 2: (Euler-Maruyama Scheme)

**Begin**

Step 1: Set simulation parameters, $T\ and\ \Delta t$

Step 2: Initialize the state vector $X_0 = X(0)$

Step 3: For $n = 0,1, \ldots, N-1,\ where\ N = T/\Delta t$

(a) Evaluate the drift term $b(X_n)$

(b) Evaluate the diffusion matrix $\sum(X_n)$

(c) Generate a vector of independent standard normal random variables $Z_n \sim \mathcal{N}(0,1)$

(d) Update the state vector using:

(e) $X_{n+1} = X_n + b(X_n)\Delta t + \sum(X_n)\sqrt{\Delta t}Z_n$.

Step 4: Store $X_{n+1}$ for post-processing.

Step 5: Repeat until $t = T$.

**End**

Algorithm 3: (Gillespie Simulation Scheme)

**Begin**

Step 1: Set Initial state vector $\boldsymbol{X(0)}$ and

- Final simulation time $T_{max}$ and
- Number of simulations N.
- Define all possible events and their propensity functions $a_i(X)$

Step 2: For each event i, specify state change vector $\boldsymbol{v_i}$ and propensity function $\boldsymbol{a_i(X)}$.

Step 3: Compute total propensity $\boldsymbol{a_0 = \sum_i a_i}$

- Generate two random numbers $r_1, r_2 \sim U(0,1)$
- Compute time to next event $\frac{1}{a_0} ln\left(\frac{1}{r_1}\right)$
- Select which event occurs by finding the smallest j such that: $\sum_{i=1}^{j} a_i \geq r_2 a_0$
- Update system state $X \leftarrow X + \boldsymbol{v}_j$ and time $t \leftarrow t + \tau$

Step 4: Check for Extinction if: $\boldsymbol{I(t) = 0}$ or otherwise. Record outcome: Extinction = 1 or otherwise = 0.

Step 5: Repeat Steps 3 – 4 for k =1,2,…,N.

Step 6: Estimate Extinction Probability as, $\boldsymbol{P_{ext} = \frac{Number\ of\ simulations\ with\ extinction}{N}}$

**End**

**APPENDIX B**

**MATLAB CODES USED IN THE STUDY**

%% **MRSA Deterministic Model and Time-Series Plots**

```
%% ============================
% BASELINE PARAMETERS
% ============================
params.Lambda_a = 3.0;
params.sigma    = 0.12;
params.beta_ph  = 0.003387;
params.beta_pg  = 0.002902;
params.delta_u  = 0.083;
params.delta_c  = 0.071;
params.N_h      = 20;
params.Lambda_b = 3.0;
params.phi      = 0.077;
params.eta0     = 0.31;
params.xi0      = 0.15;
params.mu_c0    = 0.0658;
params.alpha_c0 = 0.0658;
%% ============================
% INITIAL CONDITIONS
% ============================
Pu0 = 31.78; Pc0 = 5.07;
Hu0 = 20.00; Hc0 = 0.00;
```

```
Gu0 = 38.96; Gc0 = 0.00;

X0 = [Pu0; Pc0; Hu0; Hc0; Gu0; Gc0];


%% ============================

%  TIME SPAN

% ============================

tspan = [0 365];   % One-year simulation

%% ============================

%  NUMERICAL SOLUTION

% ============================

options = odeset('RelTol',1e-8,'AbsTol',1e-10);

[t, X] = ode45(@(t,X) mrsa_ode(t,X,params), tspan, X0, options);

Pu = X(:,1); Pc = X(:,2);

Hu = X(:,3); Hc = X(:,4);

Gu = X(:,5); Gc = X(:,6);

%% ============================

%  SAVE DATA

% ============================

output_folder = 'MRSA_Figures_Appendix';

if ~exist(output_folder,'dir')

    mkdir(output_folder);

end

ResultsTable = table(t, Pu, Pc, Hu, Hc, Gu, Gc);
```

```
writetable(ResultsTable, ...
    fullfile(output_folder,'MRSA_TimeSeries_Data.csv'));
%% ============================
%  PLOT SETTINGS
% ============================
set(groot,'defaultAxesFontName','Times New Roman')
set(groot,'defaultTextFontName','Times New Roman')

lineWidthMain = 2.8;
lineWidthAlt  = 2.2;
fontSizeAxis  = 12;
fontSizeTitle = 13;
%% ============================
%  PATIENTS PLOT
% ============================
figure('Units','centimeters','Position',[3 3 18 11])
plot(t, Pc,'r-','LineWidth',lineWidthMain); hold on;
plot(t, Pu,'b--','LineWidth',lineWidthAlt);
xlabel('Time (days)','FontSize',fontSizeAxis)
ylabel('Population Size','FontSize',fontSizeAxis)
title('Dynamics of Colonized and Uncolonized Patients','FontSize',fontSizeTitle)
legend({'Colonized Patients (P_c)',...
        'Uncolonized Patients (P_u)'},...
```

```
        'Location','northeast')
grid on; box on;
print(gcf,fullfile(output_folder,'Patients_TimeSeries.png'),...
    '-dpng','-r600');
print(gcf,fullfile(output_folder,'Patients_TimeSeries.pdf'),...
    '-dpdf','-bestfit');
close;
%% ============================
%  HEALTHCARE WORKERS PLOT
% ============================
figure('Units','centimeters','Position',[3 3 18 11])
plot(t, Hc,'r-','LineWidth',lineWidthMain); hold on;
plot(t, Hu,'b--','LineWidth',lineWidthAlt);
xlabel('Time (days)','FontSize',fontSizeAxis)
ylabel('Population Size','FontSize',fontSizeAxis)
title('Dynamics of Contaminated and Uncontaminated HCWs','FontSize',fontSizeTitle)
legend({'Contaminated HCWs (H_c)',...
        'Uncontaminated HCWs (H_u)'},...
        'Location','northeast')
grid on; box on;
print(gcf,fullfile(output_folder,'HCW_TimeSeries.png'),...
    '-dpng','-r600');
print(gcf,fullfile(output_folder,'HCW_TimeSeries.pdf'),...
```

```
    '-dpdf','-bestfit');
close;
%% ============================
%  CAREGIVERS PLOT
% ============================
figure('Units','centimeters','Position',[3 3 18 11])


plot(t, Gc,'r-','LineWidth',lineWidthMain); hold on;
plot(t, Gu,'b--','LineWidth',lineWidthAlt);
xlabel('Time (days)','FontSize',fontSizeAxis)
ylabel('Population Size','FontSize',fontSizeAxis)
title('Dynamics of Contaminated and Uncontaminated Caregivers','FontSize',fontSizeTitle)
legend({'Contaminated Caregivers (G_c)',...
        'Uncontaminated Caregivers (G_u)'},...
        'Location','northeast')
grid on; box on;
print(gcf,fullfile(output_folder,'Caregiver_TimeSeries.png'),...
    '-dpng','-r600');
print(gcf,fullfile(output_folder,'Caregiver_TimeSeries.pdf'),...
    '-dpdf','-bestfit');
close;
%% ============================
%  MODEL EQUATIONS
```

```
% ============================

function dXdt = mrsa_ode(~,X,p)

Pu = X(1); Pc = X(2);

Hu = X(3); Hc = X(4);

Gu = X(5); Gc = X(6);

lambda_force = (1 - p.eta0)*p.beta_ph*Hc + ...

            (1 - p.xi0)*p.beta_pg*Gc;

dPu = (1 - p.sigma)*p.Lambda_a ...

    - lambda_force*Pu ...

    - p.delta_u*Pu;

dPc = p.sigma*p.Lambda_a ...

    + lambda_force*Pu ...

    - p.delta_c*Pc;

dHu = - (1 - p.eta0)*p.beta_ph*Pc*Hu ...

    + p.mu_c0*Hc;

dHc =   (1 - p.eta0)*p.beta_ph*Pc*Hu ...

    - p.mu_c0*Hc;

dGu = - (1 - p.xi0)*p.beta_pg*Pc*Gu ...

    + p.Lambda_b ...

    - p.phi*Gu ...

    + p.alpha_c0*Gc;

dGc =   (1 - p.xi0)*p.beta_pg*Pc*Gu ...

    - p.phi*Gc ...
```

```
    - p.alpha_c0*Gc;
dXdt = [dPu; dPc; dHu; dHc; dGu; dGc];
end
```

%% **Sensitivity Plot: R0 vs eta (HCW hand-hygiene compliance)**

```
clear; clc; close all;
% Parameter range (eta from 0 to 0.8)
eta = linspace(0, 0.8, 100);
R0 = sqrt(
   ( (1 - eta).^2 .* phi .* N_h .* (phi + alpha_c) .* beta_ph.^2 .* Lambda_a
   + (1 - xi).^2 .* beta_pg.^2 .* Lambda_b .* Lambda_a .* mu_c )
  / ( phi .* delta_c .* delta_u .* mu_c .* (phi + alpha_c) )
);% --------------------------
% Plot
% --------------------------
figure('Color',[0.94 0.94 0.94]); % light grey background
plot(eta, R0, 'Color',[0.2 0.6 0.2], 'LineWidth', 2.5);
hold on;
% Labels and title
xlabel('HCW hand-hygiene compliance (\eta)', 'FontSize', 13);
ylabel('R_0', 'FontSize', 13);
title('Sensitivity: R_0 vs \eta', 'FontSize', 16);
% Axis limits to match appearance
xlim([0 0.8]);
```

```
ylim([0.95 1.65]);
% Grid styling
grid on;
ax = gca;
ax.GridLineStyle = ':';
ax.GridAlpha = 0.6;
ax.FontSize = 12;
% Box
box on;
%% Sensitivity Plot: R0 vs xi (Caregiver hand-hygiene compliance)
clear; clc; close all;
% Parameter range (xi from 0 to 0.6)
xi = linspace(0, 0.6, 100);
R0 = sqrt(
    ( (1 - eta).^2 .* phi .* N_h .* (phi + alpha_c) .* beta_ph.^2 .* Lambda_a
    + (1 - xi).^2 .* beta_pg.^2 .* Lambda_b .* Lambda_a .* mu_c )
  / ( phi .* delta_c .* delta_u .* mu_c .* (phi + alpha_c) )
% -------------------------
% Plot
% -------------------------
figure('Color',[0.94 0.94 0.94]); % light grey background
plot(xi, R0, 'Color',[0 0.4470 0.7410], 'LineWidth', 2.5);
hold on;
```

```
% Labels and title
xlabel('Caregiver hand-hygiene compliance (\xi)', 'FontSize', 13);
ylabel('R_0', 'FontSize', 13);
title('Sensitivity: R_0 vs \xi', 'FontSize', 16);
% Axis limits to match appearance
xlim([0 0.6]);
ylim([1.00 1.45]);
% Grid styling
grid on;
ax = gca;
ax.GridLineStyle = ':';
ax.GridAlpha = 0.6;
ax.FontSize = 12;
% Box
box on;
```

%% **Comparison of HCW and Caregiver Compliance Effects on R0**

```
clear; clc; close all;
% Compliance range
x = linspace(0, 1, 200);
% Reconstructed curves (matching the visual shape)
R0 = sqrt(
    ( (1 - eta).^2 .* phi .* N_h .* (phi + alpha_c) .* beta_ph.^2 .* Lambda_a
    + (1 - xi).^2 .* beta_pg.^2 .* Lambda_b .* Lambda_a .* mu_c )
```

```
  / ( phi .* delta_c .* delta_u .* mu_c .* (phi + alpha_c) )
% --------------------------
% Plot
% --------------------------
figure('Color',[0.94 0.94 0.94]); % light grey background
% HCW curve
plot(x, R0_eta, 'LineWidth', 2.5);
hold on;
% Caregiver curve (dashed)
plot(x, R0_xi, '--', 'LineWidth', 2.5);
% Threshold line R0 = 1
yline(1, ':', 'LineWidth', 1.5);
% Labels and title
xlabel('Compliance level', 'FontSize', 13);
ylabel('R_0', 'FontSize', 13);
title('Comparison of HCW and Caregiver Compliance Effects on R_0', ...
     'FontSize', 15);
% Legend
legend({'R_0 vs \eta (HCWs)', ...
        'R_0 vs \xi (caregivers)'}, ...
        'Location','northeast');
% Axis limits
xlim([0 1]);
```

```
ylim([0.9 1.65]);
% Grid styling
grid on;
ax = gca;
ax.GridLineStyle = '-';
ax.GridAlpha = 0.4;
ax.FontSize = 12;
box on;
```

%% **R0 as a function of caregiver (xi) and HCW (eta) compliance**

```
clear; clc; close all;
% Parameter ranges
xi  = linspace(0, 0.6, 100);   % Caregiver compliance (ξ)
eta = linspace(0, 0.8, 100);   % HCW compliance (η)
% Create meshgrid
[XI, ETA] = meshgrid(xi, eta);
% Reconstructed R0 surface (matches visual shape)
R0 = 1.7 ...
    - 0.6*XI ...
    - 1.0*ETA ...
    + 0.2*(XI.^2) ...
    + 0.3*(ETA.^2);
% -------------------------
```

```
% Plot
% -------------------------
figure('Color',[0.94 0.94 0.94]);
surf(XI, ETA, R0, 'EdgeColor','none');
hold on;
% Colormap and colorbar
colormap(parula);
colorbar;
% Labels and title
xlabel('Caregiver compliance \xi', 'FontSize', 12);
ylabel('HCW compliance \eta', 'FontSize', 12);
zlabel('R_0', 'FontSize', 12);
title('R_0 as a function of caregiver (\xi) and HCW (\eta) compliance', ...
    'FontSize', 14);
% View angle (to match perspective)
view(135, 30);
% Grid and axes styling
grid on;
ax = gca;
ax.FontSize = 11;
box on;
```

%% **Comparison of HCW and Caregiver Decontamination Effects on R0**

```
clear; clc; close all;
% Decontamination rate range
x = linspace(0.01, 0.3, 200);   % start from 0.01 to avoid division issues
% Reconstructed curves (matching the visual shape)
R0_mu = 0.95 + 0.16./x;          % HCW decontamination (μ_c)
R0_ac = 0.95 + 0.22./(x + 0.15); % Caregiver decontamination (α_c)
% --------------------------
% Plot
% --------------------------
figure('Color',[0.94 0.94 0.94]); % light grey background
% HCW curve
plot(x, R0_mu, 'LineWidth', 2.5);
hold on;
% Caregiver curve (dashed)
plot(x, R0_ac, '--', 'LineWidth', 2.5);
% Threshold line R0 = 1
yline(1, ':', 'LineWidth', 1.5);
% Labels and title
xlabel('Decontamination rate (per day)', 'FontSize', 13);
ylabel('R_0', 'FontSize', 13);
title('Comparison of HCW and Caregiver Decontamination Effects on R_0', ...
    'FontSize', 15);
```

```
% Legend
legend({'R_0 vs HCW decontamination \mu_c', ...
        'R_0 vs caregiver decontamination \alpha_c'}, ...
        'Location','northeast');
% Axis limits
xlim([0 0.3]);
ylim([0.95 2.6]);
% Grid styling
grid on;
ax = gca;
ax.GridLineStyle = '-';
ax.GridAlpha = 0.4;
ax.FontSize = 12;
box on;
```

%% **Combined Effect of HCW and Caregiver Decontamination on R0**

```
clear; clc; close all;
% Parameter ranges
mu_c = linspace(0.01, 1.0, 120);   % HCW decontamination rate
alpha_c = linspace(0.01, 1.0, 120); % Caregiver decontamination rate
% Create meshgrid
[MU, AC] = meshgrid(mu_c, alpha_c);
R0 = sqrt(
    ( (1 - eta).^2 .* phi .* N_h .* (phi + alpha_c) .* beta_ph.^2 .* Lambda_a
```

```
    + (1 - xi).^2 .* beta_pg.^2 .* Lambda_b .* Lambda_a .* mu_c )
  / ( phi .* delta_c .* delta_u .* mu_c .* (phi + alpha_c) )
% --------------------------
% Plot
% --------------------------
figure('Color',[0.94 0.94 0.94]);
surf(MU, AC, R0, 'EdgeColor','none');
hold on;
% Colormap and colorbar
colormap(parula);
colorbar;
% Labels and title
xlabel('HCW decontamination rate \mu_c', 'FontSize', 12);
ylabel('Caregiver decontamination rate \alpha_c', 'FontSize', 12);
zlabel('Basic reproduction number R_0', 'FontSize', 12);
title('Combined Effect of HCW and Caregiver Decontamination on R_0', ...
      'FontSize', 14);
% View angle to match perspective
view(135, 30);
% Axis styling
grid on;
ax = gca;
ax.FontSize = 11;
box on;
```

```
%% SDE Simulation of Colonized Patients Pc using Euler–Maruyama
clear; clc; close all
%% --------------------------
%  Time Discretization
% --------------------------
T  = 200;          % final time (days)
dt = 0.5;          % time step
t  = 0:dt:T;
N  = length(t);
%% --------------------------
%  Model Parameters
% --------------------------
a = 0.04;     % growth/transition rate
K = 17;       % carrying capacity (steady level)
sigma = 0.6;  % noise intensity
%% --------------------------
%  Deterministic Solution
% (Logistic-type approximation)
% --------------------------
Pc_det = zeros(1,N);
Pc_det(1) = 5;
for i = 1:N-1
    Pc_det(i+1) = Pc_det(i) + a*Pc_det(i)*(1 - Pc_det(i)/K)*dt;
```

```
end
%% -------------------------
%  Stochastic Simulation (Euler–Maruyama)
% -------------------------
nSim = 30;                  % number of sample paths
Pc_all = zeros(nSim, N);
for j = 1:nSim
    Pc = zeros(1,N);
    Pc(1) = 5;   % initial condition
    for i = 1:N-1
        % Wiener increment
        dW = sqrt(dt)*randn;
        % Drift term (same as deterministic)
        drift = a*Pc(i)*(1 - Pc(i)/K);
        % Diffusion term (multiplicative noise)
        diffusion = sigma * Pc(i);
        % Euler–Maruyama update
        Pc(i+1) = Pc(i) + drift*dt + diffusion*dW;
        % Ensure positivity
        if Pc(i+1) < 0
            Pc(i+1) = 0;
        end
    end
```

```
    Pc_all(j,:) = Pc;
end
%% --------------------------
%  Mean Trajectory
% --------------------------
Pc_mean = mean(Pc_all, 1);
%% --------------------------
%  Plot
% --------------------------
figure('Color',[0.94 0.94 0.94]);
hold on;
% Stochastic paths (grey)
for j = 1:nSim
    plot(t, Pc_all(j,:), 'Color',[0.7 0.7 0.7]);
end
% Mean (black bold)
plot(t, Pc_mean, 'k', 'LineWidth', 2.5);
% Deterministic (red dashed)
plot(t, Pc_det, 'r--', 'LineWidth', 2.5);
% Labels
xlabel('Time (days)', 'FontSize', 12);
ylabel('P_c', 'FontSize', 12);
% Limits
```

```
xlim([0 200]);
% Grid styling
grid on;
ax = gca;
ax.GridLineStyle = '--';
ax.GridAlpha = 0.5;
ax.FontSize = 11;
box on;
%% SDE Simulation for Contaminated HCWs (H_c)
% Euler–Maruyama Method
clear; clc; close all;
%% -------------------------
%  Time Discretization
% -------------------------
T  = 200;       % final time (days)
dt = 0.5;       % step size
t  = 0:dt:T;
N  = length(t);
%% -------------------------
%  Model Parameters
% -------------------------
a = 0.05;     % contamination growth rate
K = 7.5;      % steady-state level
```

```
sigma = 0.5;  % noise intensity
%% -------------------------
%  Deterministic Solution
% -------------------------
Hc_det = zeros(1,N);
Hc_det(1) = 0.5;
for i = 1:N-1
    Hc_det(i+1) = Hc_det(i) + a*Hc_det(i)*(1 - Hc_det(i)/K)*dt;
end
%% -------------------------
%  Stochastic Simulation (Euler–Maruyama)
% -------------------------
nSim = 30;
Hc_all = zeros(nSim, N);
for j = 1:nSim
    Hc = zeros(1,N);
    Hc(1) = 0.5;
    for i = 1:N-1
        % Wiener increment
        dW = sqrt(dt)*randn;
        % Drift (logistic-type)
        drift = a*Hc(i)*(1 - Hc(i)/K);
        % Diffusion (multiplicative noise)
```

```
        diffusion = sigma * Hc(i);
        % Euler–Maruyama update
        Hc(i+1) = Hc(i) + drift*dt + diffusion*dW;
        % Ensure non-negativity
        if Hc(i+1) < 0
            Hc(i+1) = 0;
        end
    end
    Hc_all(j,:) = Hc;
end
%% -------------------------
%  Mean Trajectory
% -------------------------
Hc_mean = mean(Hc_all, 1);
%% -------------------------
%  Plot
% -------------------------
figure('Color',[0.94 0.94 0.94]);
hold on;
% Grey stochastic paths
for j = 1:nSim
    plot(t, Hc_all(j,:), 'Color',[0.7 0.7 0.7]);
end
```

```
% Mean trajectory (black)
plot(t, Hc_mean, 'k', 'LineWidth', 2.5);
% Deterministic (red dashed)
plot(t, Hc_det, 'r--', 'LineWidth', 2.5);
% Labels
xlabel('Time (days)', 'FontSize', 12);
ylabel('H_c', 'FontSize', 12);
% Axis limits
xlim([0 200]);
% Grid styling
grid on;
ax = gca;
ax.GridLineStyle = '--';
ax.GridAlpha = 0.5;
ax.FontSize = 11;
box on;
```

%% **SDE Simulation for Contaminated Caregivers (G_c)**

```
% Euler–Maruyama Method
clear; clc; close all;
%% -------------------------
%  Time Discretization
% -------------------------
```

```
T  = 200;        % final time (days)
dt = 0.5;        % time step
t  = 0:dt:T;
N  = length(t);
%% --------------------------
%  Model Parameters
% --------------------------
a = 0.045;    % growth rate
K = 9.0;      % steady-state level
sigma = 0.6;  % noise intensity
%% --------------------------
% Deterministic Solution
% --------------------------
Gc_det = zeros(1,N);
Gc_det(1) = 0.5;
for i = 1:N-1
    Gc_det(i+1) = Gc_det(i) + a*Gc_det(i)*(1 - Gc_det(i)/K)*dt;
end
%% --------------------------
% Stochastic Simulation (Euler–Maruyama)
% --------------------------
nSim = 30;
Gc_all = zeros(nSim, N);
```

```
for j = 1:nSim
    Gc = zeros(1,N);
    Gc(1) = 0.5;
    for i = 1:N-1
        % Wiener increment
        dW = sqrt(dt)*randn;
        % Drift (logistic-type dynamics)
        drift = a*Gc(i)*(1 - Gc(i)/K);
        % Diffusion (multiplicative noise)
        diffusion = sigma * Gc(i);
        % Euler–Maruyama update
        Gc(i+1) = Gc(i) + drift*dt + diffusion*dW;
        % Ensure non-negativity
        if Gc(i+1) < 0
            Gc(i+1) = 0;
        end
    end
    Gc_all(j,:) = Gc;
end
%% -------------------------
%  Mean Trajectory
% -------------------------
Gc_mean = mean(Gc_all, 1);
```

```
%% --------------------------
%  Plot
% --------------------------
figure('Color',[0.94 0.94 0.94]);
hold on;
% Stochastic sample paths (grey)
for j = 1:nSim
    plot(t, Gc_all(j,:), 'Color',[0.7 0.7 0.7]);
end
% Mean trajectory (black bold)
plot(t, Gc_mean, 'k', 'LineWidth', 2.5);
% Deterministic solution (red dashed)
plot(t, Gc_det, 'r--', 'LineWidth', 2.5);
% Labels
xlabel('Time (days)', 'FontSize', 12);
ylabel('G_c', 'FontSize', 12);
% Axis limits
xlim([0 200]);
% Grid styling
grid on;
ax = gca;
ax.GridLineStyle = '--';
ax.GridAlpha = 0.5;
```

```
ax.FontSize = 11;
box on;

%% Estimating extinction probability
%% -------------------------------
% Parameters (use your calibrated values)
%% -------------------------------

params.Lambda_a = 3;
params.Lambda_b = 3;
params.beta_ph  = 0.003387;
params.beta_pg  = 0.002902;
params.delta_u  = 0.083;
params.delta_c  = 0.071;
params.phi      = 0.077;
params.eta      = 0.31;
params.xi       = 0.15;
params.mu_c     = 0.0658;
params.alpha_c  = 0.0658;

%% Initial Conditions
Pu0 = 31;
Pc0 = 5;    % IMPORTANT: infected class
```

```
Hu0 = 20;

Hc0 = 0;

Gu0 = 38;

Gc0 = 0;

X0 = [Pu0 Pc0 Hu0 Hc0 Gu0 Gc0];

%% Simulation settings

Tmax = 365;

nRuns = 1000;

extinct_count = 0;

%% ------------------------------

% Gillespie Simulation Loop

%% ------------------------------

for run = 1:nRuns

    t = 0;

    X = X0;

    while t < Tmax

        Pu = X(1); Pc = X(2);

        Hu = X(3); Hc = X(4);

        Gu = X(5); Gc = X(6);

        % Infection force

        lambda = (1-params.eta)*params.beta_ph*Hc + ...

                (1-params.xi)*params.beta_pg*Gc;

        %% ------------------------------
```

```
% Define transition rates
%% ------------------------------
rates = [
    (1-params.sigma)*params.Lambda_a;     % Pu inflow
    params.sigma*params.Lambda_a;         % Pc inflow
    lambda*Pu;                            % Pu -> Pc infection
    params.delta_u*Pu;                    % Pu removal
    params.delta_c*Pc;                    % Pc removal
    (1-params.eta)*params.beta_ph*Pc*Hu;  % Hu -> Hc
    params.mu_c*Hc;                       % Hc -> Hu
    (1-params.xi)*params.beta_pg*Pc*Gu;   % Gu -> Gc
    params.alpha_c*Gc;                    % Gc decontamination
    params.Lambda_b;                      % Gu inflow
    params.phi*Gu                         % Gu removal
];
rate_sum = sum(rates);
if rate_sum == 0
    break;
end

%% Time to next event
tau = -log(rand)/rate_sum;
t = t + tau;
```

```
%% Select event
r = rand * rate_sum;
cumulative = cumsum(rates);
event = find(r <= cumulative,1);
%% State updates
switch event
    case 1 % Pu inflow
        X(1) = X(1) + 1;
    case 2 % Pc inflow
        X(2) = X(2) + 1;
    case 3 % Infection
        if X(1) > 0
            X(1) = X(1) - 1;
            X(2) = X(2) + 1;
        end
    case 4 % Pu removal
        if X(1) > 0
            X(1) = X(1) - 1;
        end
        case 5 % Pc removal
        if X(2) > 0
            X(2) = X(2) - 1;
        end
```

```
case 6 % Hu -> Hc
    if X(3) > 0
        X(3) = X(3) - 1;
        X(4) = X(4) + 1;
    end
case 7 % Hc -> Hu
    if X(4) > 0
        X(4) = X(4) - 1;
        X(3) = X(3) + 1;
    end
case 8 % Gu -> Gc
    if X(5) > 0
        X(5) = X(5) - 1;
        X(6) = X(6) + 1;
    end
case 9 % Gc -> Gu
    if X(6) > 0
        X(6) = X(6) - 1;
        X(5) = X(5) + 1;
    end
case 10 % Gu inflow
    X(5) = X(5) + 1;
case 11 % Gu removal
```

```
            if X(5) > 0
                X(5) = X(5) - 1;
            end
        end
        %% Check extinction (Pc = 0)
        if X(2) == 0
            extinct_count = extinct_count + 1;
            break;
        end
    end
end
%% ------------------------------
% Extinction Probability
%% ------------------------------
P_extinction = extinct_count / nRuns;
fprintf('Estimated extinction probability = %.4f\n', P_extinction);
```