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MATHEMATICAL ANALYSIS OF A METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* MODEL IN HOSPITALS AND THE COMMUNITY

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Abstract. In this paper, we study a methicillin-resistant *Staphylococcus aureus* epidemic model taking into account both hospitals' and the general community dynamics. The model is designed to track the long-term dynamics of methicillin-resistant *Staphylococcus aureus* infections. Mathematical analysis of the developed model is carried out. The MRSA-free equilibrium $\mathscr{M}_a^o$ and the model reproduction number $\mathscr{R}_0$ are established. Numerical simulations are performed using previously published data from relevant scientific literature. It is shown that both the MRSA-free equilibrium and the MRSA-persistent equilibrium are locally asymptotically stable when $\mathscr{R}_0 < 1$ and $\mathscr{R}_0 > 1$, respectively. Numerical simulations are also conducted to ascertain the effects of variations in key parameter values on specific compartments: (i) hospitalized individuals exclusively, (ii) the general community exclusively, or (iii) both hospitalized individuals and the general community concurrently. It is shown that 1% increase in the values of β_h and β_c corresponds to approximately 27.1% and 8.3% increase in the value of $\mathscr{R}_0$, respectively. On the other hand, a 0.1% increase in the values of ε and ψ, and a 0.25% increase in the value of δ corresponds to approximately 0.53%, 0.498% and 0.267% decrease in the value of $\mathscr{R}_0$, respectively. The findings suggest the need for policymakers to implement robust measures aimed at minimizing infection transmission

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between both infected and susceptible individuals, encompassing both nosocomial environments and the wider community.

Keywords: *Staphylococcus aureus*; methicillin-resistant; community acquired infection; hospital acquired infection; reproduction number; numerical simulations.

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1. INTRODUCTION

Staphylococcus aureus (S. aureus) is a dangerous pathogen causing various disorders in humans such as soft tissue, skin, bone, joint, respiratory and cardiovascular disorders [1]. The recent emergence of methicillin-resistant *S. aureus* (MRSA) globally is of great concern since it imposes a high healthcare burden and significant morbidity and mortality [2]. Since the discovery of MRSA in 1961 until the late 1990s, MRSA was exclusively considered as a hospital-acquired (HA) infection [3, 4]. In the late 1990s, reports emerged regarding MRSA colonization and infection within the community with growing evidence of a steady increase of *S. aureus* infections in both hospitals and communities [5, 6, 7, 8]. However, it is believed that the extent of community-acquired methicillin-resistant *S. aureus* (CA-MRSA) infections is underestimated due to unclear epidemiological distinctions between the MRSA strains causing CA-MRSA and HA-MRSA infections [9, 10]. According to the Centers for Disease Control and Prevention (CDC) definition advocated in the 2000s, a CA-MRSA infection has been defined as an CA-MRSA infection if the patient lacks specific risk factors for healthcare exposure [11, 12, 9]. The common healthcare associated risk factors are hospitalization, residence in a long-term care facility, surgery, or receipt of hemodialysis during the previous year; presence of a percutaneous device or an indwelling catheter at the time culture samples were collected [11, 12]. However, linking CA-MRSA cases to healthcare risk factors can no longer optimize the extent of CA-MRSA infections as both HA-MRSA and CA-MRSA strains are gradually affecting both individuals who have had healthcare exposure and individuals who do not have such exposure [9, 13, 14].

MRSA infection have also been observed in developing countries, where MRSA prevalence rates are between 33% and 95% due to poorly resourced healthcare facilities [15]. High prevalence rates for MRSA infections necessitates the provision of better alternative drugs which

are usually expensive and out of reach for many people thereby compromising efforts to effectively control MRSA infections [5]. The worldwide emergence of CA-MRSA is evidence of the changing biology of MRSA strains and changing epidemiology of MRSA infections [3]. Some MRSA positive cases classified as healthcare-related were suspected to have emanated from long-time CA-MRSA asymptomatic cases which were silently carried into the hospital and then subsequently cause infections which may be classified as nosocomial [3]. Also, some reports have emerged of new high risk groups for MRSA infection which include children [6, 8], improverished individuals [16], inmates in prison [17, 18], and men who have sex with men [19]. Several countries have reported that CA-MRSA is spreading swiftly from the closed risk communities to the general population, and thus an issue of serious concern that needs to be checked [3]. The development of effective policies to control the further spread of *S. aureus* related infections has become an urgent priority [20].

Shortly after the introduction of methicillin in 1961, MRSA expressed resistance to methicillin by producing a novel penicillin-binding protein designated PBP2' (or PBP2a) that resulted in a low binding affinity to the $\beta-$lactam antibiotics [21, 22, 23]. Recently, *S. aureus* has become multi-resistant to the available important antibiotics such as ciprofloxacin, erythromycin and linezolid [24, 25], resulting in increased morbidity and mortality among patients [24]. The linezolid-resistant strain was observed to normally emerge during a 3 week course of treatment in deep-seated infections [25]. In a study conducted to investigate *S. aureus* resistance to the available antimicrobial agents in Ethiopia [5], it was observed that *S. aureus* had become notoriously resistant to almost all the available treatment regimens. The analysis showed that *S. aureus* had become highly resistant to methicillin, penicillin, ampicillin, tetracycline, cotrimoxaziole, doxycycline and erythromycin [5].

Some two interesting models for MRSA transmission that include both the hospital population and community population have been developed in [3] and [20]. In both models, the mathematical problem is formulated based on categorising individuals either as colonised/uncolonised hospitalized patients or colonised/uncolonised individuals in the community. In [20], MRSA transmission was assumed to take place in the hospital only with colonised cases transferred

from the hospital to the community. In this study, it was assumed that community transmission is unsustained thereby allowing discharged colonised individuals to recover without infecting uncolonised individuals in the community. The model was then improved in [3] to allow discharged colonised individuals to transmit the infection to uncolonised individuals in the community. The model also considered a scenario where the community contains MRSA strains which developed through community transmission independent of nosocomial infections. Some colonised individuals from the community were allowed to be admitted into the hospital and vice versa. However, both models did not take into account the vital dynamics which are essential especially if the models are to be employed for longer time periods. Also, the models were not examined mathematically for well posedness and other essential model properties. In this study, we extend the models developed in [3] and [20] to include vital dynamics. Also, we perform the mathematical analysis of the improved model to show that the proposed models in [3] and [20] have interesting dynamics of MRSA transmission in both the community and hospital. Results from this study will be highly desirable and will affirm that the models developed in [3] and [20] possess very appropriate features that warrant consideration in policy making. The mathematical analysis carried out in this study places the proposed models for CA-MRSA and HA-MRSA transmission on a firm footing that allows development of subsequent studies on this interesting aspect.

The structure of the paper is as follows: Section 2 presents the formulation of the model and the establishment of its basic properties. Stability analysis of the model is conducted in Section 3. Section 4 comprises numerical simulations, including parameter estimation and presentation of results. Finally, Section 5 provides the conclusion of the paper.

2. MODEL FORMULATION

We modify the models developed in [3] and [20]. The model developed in [20] considered the case where MRSA transmission is confined in a hospital only, with colonised cases in the community a result of hospital discharge of individuals colonised with MRSA. The model was modified in [3] to take into account MRSA transmission in the community. In this study, we modify the model in [3] to include vital dynamics not considered in [3] and [20]. This adds

realism to the system dynamics since the model will be employed to track CA-MRSA and HA-MRSA infections over a longer time span.

Model compartments. We formulate a seven-state system of nonlinear ordinary differential equations to track the evolution of CA-MRSA infections and HA-MRSA infections. In the model, persons can be hospitalized (N_1+z) where N_1 is the total number of non-isolated hospitalized patients and z is the number of isolated hospitalized patients where there is no transmission; recently discharged persons (N_2) and the general population in the community (N_3). We denote uncolonised/susceptible individuals by x and colonized/infected individuals by y. Thus, the model comprise of the following classes:

(1) x_1- uncolonised individuals in the hospital;

(2) y_1- colonised non-isolated individuals in the hospital;

(3) x_2- uncolonised individuals recently discharged from the hospital;

(4) y_2- colonised individuals recently discharged from the hospital;

(5) x_3- uncolonised individuals in the community;

(6) y_3- colonised individuals in the community;

(7) $z-$ colonised isolated individuals in the hospital;

Thus, the total human population at any given time t is given by

$$N(t) = N_1 + N_2 + N_3 + z = \sum_{n=1}^{3} x_n + \sum_{n=1}^{3} y_n + z.$$

Schematic diagram. The model is schematically depicted by the figure below.

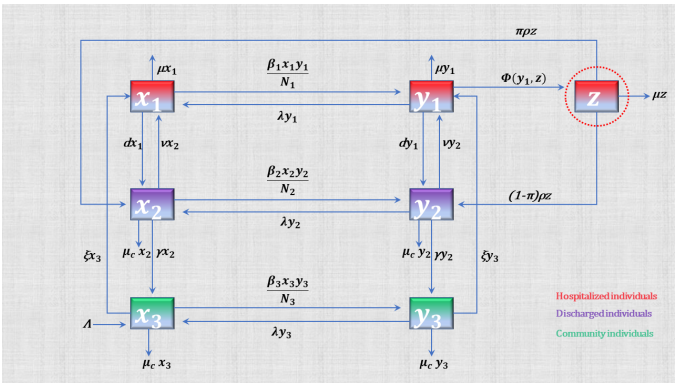


FIGURE 1. Model flow diagram for CA-MRSA and HA-MRSA transmission (adapted and modified from [3] and [20]).

Model equations. Combining the model details and assumptions given above together with the schematic diagram (Figure 1), we obtain the following system of ordinary differential equations:

$$
\left\{
\begin{aligned}
\frac{dx_1}{dt} &= \xi x_3 + \nu x_2 - \frac{\beta_1 x_1 y_1}{N_1} - p_1 x_1 + \lambda y_1, \\
\frac{dy_1}{dt} &= \frac{\beta_1 x_1 y_1}{N_1} + \nu y_2 + \xi y_3 - \Phi(y_1, z) - (p_1 + \lambda) y_1, \\
\frac{dz}{dt} &= \Phi(y_1, z) - (\mu + \rho) z, \\
\frac{dx_2}{dt} &= d x_1 + \pi \rho z - \frac{\beta_2 x_2 y_2}{N_2} - p_2 x_2 + \lambda y_2, \\
\frac{dy_2}{dt} &= \frac{\beta_2 x_2 y_2}{N_2} + d y_1 + (1-\pi)\rho z - (p_2 + \lambda) y_2, \\
\frac{dx_3}{dt} &= \Lambda + \gamma x_2 - \frac{\beta_3 x_3 y_3}{N_3} - p_3 x_3 + \lambda y_3, \\
\frac{dy_3}{dt} &= \frac{\beta_3 x_3 y_3}{N_3} + \gamma y_2 - (p_3 + \lambda) y_3,
\end{aligned}
\right. \tag{1}
$$

where $\Phi(y_1, z) = \begin{cases} \psi y_1, & \text{if} \quad z < N_{i\max}, \\ \min(\psi y_1, \rho N_{i\max}), & \text{if} \quad z = N_{i\max}, \end{cases}$ with $N_{i\max}$ denoting the number of beds in isolation unit. Here, $p_1 = \mu + d$, $p_2 = \mu_c + \nu + \gamma$ and $p_3 = \mu_c + \xi$. The initial conditions for system (1) are given as

$$x_1(0) \geq 0,\ x_2(0) \geq 0,\ x_3(0) > 0,\ y_1(0) \geq 0,\ y_2(0) \geq 0,\ y_3(0) \geq 0,\ z(0) \geq 0.$$

Parameters and assumptions of the model. Here, Λ represents the overall influx of individuals due to births or immigration, and μ_c denotes the natural mortality rate among community members. Since hospitalized individuals are immunocompromised, we consider death rate for these individuals that includes a disease-related death rate given by μ, where we assume $\mu > \mu_c$. The

other remaining parameter interpretations are as given in Table 1 ([3]) which is extracted and presented below for easy reference.

TABLE 1. Remaining parameter interpretations as given in [3]

Parameter	Description
β_1	Transmission rate for hospitalized individuals
β_2	Transmission rate for discharged individuals
β_3	Transmission rate for the general population
$N_{i\max}$	Number of available beds in the isolation unit
ψ	Isolation rate for hospitalized individuals
π	Proportion of individuals leaving isolation without MRSA
$1/\rho$	Mean length of stay in isolation
$1/\lambda$	Mean duration of carriage of MRSA
$1/d$	Mean length of stay in hospital
ν	Readmission rate for discharged individuals (high readmission)
ξ	Rate of admission for the general population (low readmission)
γ	Transition from high to low readmission

3. MODEL ANALYSIS

3.1. Analysis of model system (1)**.** We perform mathematical analysis of system (1) for the case when there are sufficient hospital beds in the isolation unit. This means $\Phi(y_1, z) = \psi y_1$.

3.1.1. *Positivity of solutions and invariant region.* Since model system (1) describes human population, it is important to demonstrate the existence and non-negativity of solutions for system (1) for all $t > 0$. Thus, we state the following theorem (Theorem 1) which illustrates that under any positive initial conditions, the solutions of system (1) will persist as non-negative for all $t > 0$.

Theorem 1. *Consider the following initial conditions for system* (1)*:* $x_1(0) > 0$, $y_1(0) > 0$, $z(0) > 0$, $x_2(0) > 0$, $y_2(0) > 0$, $x_3(0)$ *and* $y_3(0) > 0$. *There exists* $(x_1(t), y_1(t), z(t), x_2(t), y_2(t), x_3(t), y_3(t)) \in \mathbb{R}^7_+$ *which solve system* (1).

Proof. It is easy to show that solutions for system (1) will remain positive for all time $t > 0$. We use a simple proof by contradiction, similarly employed in previous studies, see for instance [26]. Suppose there exists t_1, t_2, t_3, t_4, t_5, t_6 and t_7 which are the respective initial times for compartments x_1, y_1, z, x_2, y_2, x_3 and y_3 satisfying

(2)

$$
\begin{aligned}
t_1: &\quad x_1(t_1) = 0,\ x_1'(t_1) < 0,\ x_1(t) > 0,\ y_1(t) > 0,\ z(t) > 0,\ x_2(t) > 0,\ y_2(t) > 0,\ x_3(t),\ y_3(t) > 0 \\
&\quad \text{for} \quad 0 < t \leq t_1 \quad \text{or there exists a} \\
t_2: &\quad y_1(t_2) = 0,\ y_1'(t_2) < 0,\ x_1(t) > 0,\ y_1(t) > 0,\ z(t) > 0,\ x_2(t) > 0,\ y_2(t) > 0,\ x_3(t),\ y_3(t) > 0 \\
&\quad \text{for} \quad 0 < t \leq t_2 \quad \text{or there exists a} \\
t_3: &\quad z(t_3) = 0,\ z'(t_3) < 0,\ x_1(t) > 0,\ y_1(t) > 0,\ z(t) > 0,\ x_2(t) > 0,\ y_2(t) > 0,\ x_3(t),\ y_3(t) > 0 \\
&\quad \text{for} \quad 0 < t \leq t_3 \quad \text{or there exists a} \\
t_4: &\quad x_2(t_4) = 0,\ x_2'(t_4) < 0,\ x_1(t) > 0,\ y_1(t) > 0,\ z(t) > 0,\ x_2(t) > 0,\ y_2(t) > 0,\ x_3(t),\ y_3(t) > 0 \\
&\quad \text{for} \quad 0 < t \leq t_4 \quad \text{or there exists a} \\
t_5: &\quad y_2(t_5) = 0,\ y_2'(t_5) < 0,\ x_1(t) > 0,\ y_1(t) > 0,\ z(t) > 0,\ x_2(t) > 0,\ y_2(t) > 0,\ x_3(t),\ y_3(t) > 0 \\
&\quad \text{for} \quad 0 < t \leq t_5 \quad \text{or there exists a} \\
t_6: &\quad x_3(t_6) = 0,\ x_3'(t_6) < 0,\ x_1(t) > 0,\ y_1(t) > 0,\ z(t) > 0,\ x_2(t) > 0,\ y_2(t) > 0,\ x_3(t),\ y_3(t) > 0 \\
&\quad \text{for} \quad 0 < t \leq t_6 \quad \text{or there exists a} \\
t_7: &\quad y_3(t_7) = 0,\ y_3'(t_7) < 0,\ x_1(t) > 0,\ y_1(t) > 0,\ z(t) > 0,\ x_2(t) > 0,\ y_2(t) > 0,\ x_3(t),\ y_3(t) > 0 \\
&\quad \text{for} \quad 0 < t \leq t_7.
\end{aligned}
$$

From system (1) we obtain

$$
\begin{aligned}
x_1'(t_1) &= \xi x_3(t_1) + \nu x_2(t_1) + \lambda y_1(t_1) > 0, \\
y_1'(t_2) &= \nu y_2(t_2) + \xi y_3(t_2) > 0, \\
z'(t_3) &= \psi y_1(t_3) > 0, \\
x_2'(t_4) &= d x_1(t_4) + \pi\rho z(t_4) + \lambda y_2(t_4) > 0, \\
y_2'(t_5) &= d y_1(t_5) + (1-\pi)\rho z(t_5) > 0, \\
x_3'(t_6) &= \Lambda + \gamma x_2(t_6) + \lambda y_3(t_6) > 0, \\
y_3'(t_7) &= \gamma y_2(t_7) > 0,
\end{aligned} \tag{3}
$$

which contradicts all the seven cases stated in (2). Therefore, $x_1(t) > 0$, $y_1(t) > 0$, $z(t) > 0$, $x_2(t) > 0$, $y_2(t) > 0$, $x_3(t) > 0$ and $y_3(t) > 0$ and this completes the proof. □

We study system (1) in the biologically feasible region given by:

$$\Omega = \left\{ (x_1, y_1, z, x_2, y_2, x_3, y_3) \in \mathbb{R}^7_+ \mid 0 \leq N \leq \frac{\Lambda}{\mu_c} \right\}. \tag{4}$$

We present the following proposition that guarantees the well-posedness of system (1), ensuring that all solutions with initial conditions that originate within Ω persist within this domain for all $t > 0$.

Proposition 1. The compact domain Ω as outlined in (4) is invariantly positive with respect to the system (1) and attracts all solutions in $\mathbb{R}^7_+$.

Proof. From system (1) we have that

$$\begin{aligned}
\frac{dN}{dt} &= \sum_{i=1}^{3} \left(\frac{dN_i}{dt} \right) + \frac{dz}{dt} = \Lambda - \mu(x_1 + y_1) - \mu z - \mu_c(x_2 + y_2) - \mu_c(x_3 + y_3) \\
&= \Lambda - \mu N_1 - \mu z - \mu_c N_2 - \mu_c N_3 < \Lambda - \mu_c N_1 - \mu_c z - \mu_c N_2 - \mu_c N_3 \text{ (since } \mu > \mu_c) \\
&= \Lambda - \mu_c N.
\end{aligned}$$

Thus, solving the differential inequality $\frac{dN}{dt} \leq \Lambda - \mu_c N$ gives $0 \leq N(t) \leq \frac{\Lambda}{\mu_c} + \left(N(0) - \frac{\Lambda}{\mu_c} \right) e^{-\mu_c t}$. Then, $\limsup_{t \to \infty} N \leq \frac{\Lambda}{\mu_c}$. Thus, the set Ω is attractive. Consequently, if system (1) vector field is confined to the boundary of set Ω, then it will not extend beyond the exterior of set Ω. This ensures that all solutions with initial conditions originating in Ω will persist inside Ω indefinitely for all time $t > 0$. □

3.1.2. *MRSA-free equilibrium and complexity of the reproduction number.* We now determine the MRSA-free equilibrium point and the reproduction number of model system (1). The MRSA-free equilibrium depicts a state in the community and hospital where all individuals are not colonized with MRSA-bacteria, that is, $y_i = z = 0,\ i = 1, 2, 3$. We represent the MRSA-free equilibrium point by

$$\begin{aligned}
\mathscr{M}^o &= \left(x_1^o, y_1^o, z, x_2^o, y_2^o, x_3^o, y_3^o \right) \\
&= \left(\frac{\Lambda\xi}{p_1 p_3 \left(1 - (\Theta_1 + \Theta_2)\right)}, 0, 0, \frac{d\Lambda\xi}{p_1 p_2 p_3 \left(1 - (\Theta_1 + \Theta_2)\right)}, 0, \frac{\Lambda(1 - \Theta_1)}{p_3 \left(1 - (\Theta_1 + \Theta_2)\right)}, 0 \right)
\end{aligned}$$

where $\Theta_1 = \dfrac{d\nu}{p_1 p_2}$, $\Theta_2 = \dfrac{d\gamma\xi}{p_1 p_2 p_3}$ and $\Theta_1 + \Theta_2 < 1$.

We now illustrate the complexity of computing the reproduction number for model system (1). The next generation matrix approach stated in [27] is applied on the computations of the non-negative F matrix and a non-singular M-matrix V to obtain

(5)
$$F = \begin{pmatrix} \beta_1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & \beta_2 & 0 \\ 0 & 0 & 0 & \beta_3 \end{pmatrix} \quad \text{and} \quad V = \begin{pmatrix} \lambda + p_1 + \psi & 0 & -\nu & -\xi \\ -\psi & \mu + \rho & 0 & 0 \\ -d & -((1-\Pi)\rho) & \lambda + p_2 & 0 \\ 0 & 0 & -\gamma & \lambda + p_3 \end{pmatrix}$$

which leads to a cumbersome expression for the reproduction number. We now perform some reasonable simplifications of system (1) below.

Simplification of the model. The model developed in [3] can be further simplified without loss of generality using the procedure explained below. This is to allow tractability of mathematical results. Since individuals discharged from the hospital will eventually belong to the general population, we can assume a constant re-admission rate for the general population. We thus make the following variable simplifications:

(6)
$$\begin{aligned} &x_1 = x_h, && x_2 + x_3 = x_c \\ &y_1 = y_h, && y_2 + y_3 = y_c, \\ &N = N_h + N_c + z, && N_h = x_h + y_h \quad \text{and} \quad N_c = x_c + y_c, \end{aligned}$$

where the subscripts h and c denote the hospital and community classes. This change of variables necessitates the following parameter adjustments:

(7)
$$\begin{aligned} &\beta_1 = \beta_h, && \beta_2 = \beta_3 = \beta_c \\ &d + \gamma = \delta, && \nu + \xi = \varepsilon, \end{aligned}$$

with similar interpretations for the subscripts h and c given above. The simplifications given in (6) and (7) will capture the possibility of individuals recently discharged acquiring MRSA from any colonised individuals in the community. This is an improvement of the model proposed in [3] since the model only considered recently discharged uncolonized individuals acquiring

MRSA from recently discharged colonized individuals. In summary, the model in [3] did not consider MRSA transmission from recently discharged individuals to the general population and vice versa. Thus, considering the suggested variable and parameter adjustments in (6) and (7), we have the following schematic diagram (Figure 2) for the adjusted model.

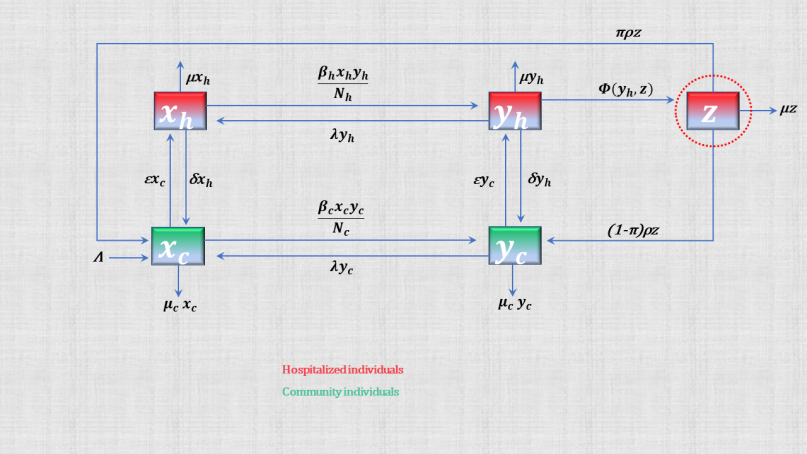


FIGURE 2. Adjusted model flow diagram for CA-MRSA and HA-MRSA transmission (adapted and modified from [3] and [20]).

Adjusted model equations. Combining the adjusted model details given above together with the schematic diagram (Figure 2), we obtain the following system of ordinary differential equations:

$$
\begin{cases}
\dfrac{dx_h}{dt} &= \varepsilon x_c - \dfrac{\beta_h x_h y_h}{N_h} - p_4 x_h + \lambda y_h, \\[2ex]
\dfrac{dy_h}{dt} &= \dfrac{\beta_h x_h y_h}{N_h} + \varepsilon y_c - \Phi(y_h, z) - (p_4 + \lambda) y_h, \\[2ex]
\dfrac{dz}{dt} &= \Phi(y_h, z) - p_6 z, \\[2ex]
\dfrac{dx_c}{dt} &= \Lambda + \delta x_h + \pi\rho z - \dfrac{\beta_c x_c y_c}{N_c} - p_7 x_c + \lambda y_c, \\[2ex]
\dfrac{dy_c}{dt} &= \dfrac{\beta_c x_c y_c}{N_c} + \delta y_h + (1-\pi)\rho z - (p_7 + \lambda) y_c,
\end{cases}
\tag{8}
$$

where $\Phi(y_h,z) = \begin{cases} \psi y_h, & \text{if} \quad z < N_{i\max}, \\ \min(\psi y_h, \rho N_{i\max}), & \text{if} \quad z = N_{i\max}, \end{cases}$ with $N_{i\max}$ defined as before. Here, $p_4 = \mu + \delta$, $p_6 = \mu + \rho$ and $p_7 = \mu_c + \varepsilon$. The initial conditions for the adjusted system (8) are given as

$$x_h(0) \geq 0,\ y_h(0) \geq 0,\ x_c(0) > 0,\ y_c(0) \geq 0,\ z(0) \geq 0.$$

3.2. Analysis of adjusted model system (8)**.** We perform mathematical analysis of system (8) for the case when there are sufficient hospital beds in the isolation unit. This means $\Phi(y_h,z) = \psi y_h$.

3.2.1. *Positivity of solutions and invariant region.* Since model system (8) describes human population, it is important to demonstrate the existence and non-negativity of solutions for system (8) for all $t > 0$. Thus, we state the following theorem (Theorem 2) which illustrates that under any positive initial conditions, the solutions of system (8) will persist as non-negative for all $t > 0$.

Theorem 2. *Consider the following initial conditions for system* (8)*:* $x_h(0) > 0$*,* $y_h(0) > 0$*,* $z(0) > 0$*,* $x_c(0) > 0$ *and* $y_c(0) > 0$*. There exists* $(x_h(t), y_h(t), z(t), x_c(t), y_c(t)) \in \mathbb{R}^5_+$ *which solve system* (8)*.*

Proof. It is easy to show that solutions for system (8) will remain positive for all time $t > 0$. We use a simple proof by contradiction, similarly employed in previous studies, see for instance [26]. Suppose there exists t_1, t_2, t_3, t_4 and t_5 which are the respective initial times for compartments x_h, y_h, z, x_c and y_c satisfying

$$\begin{aligned}
t_1: &\ \ x_h(t_1) = 0,\ x_h'(t_1) < 0,\ x_h(t) > 0,\ y_h(t) > 0,\ z(t) > 0,\ x_c(t) > 0,\ y_c(t) > 0 \\
&\ \ \text{for} \quad 0 < t \leq t_1 \quad \text{or there exists a} \\
t_2: &\ \ y_h(t_2) = 0,\ y_h'(t_2) < 0,\ x_h(t) > 0,\ y_h(t) > 0,\ z(t) > 0,\ x_c(t) > 0,\ y_c(t) > 0 \\
&\ \ \text{for} \quad 0 < t \leq t_2 \quad \text{or there exists a} \\
t_3: &\ \ z(t_3) = 0,\ z'(t_3) < 0,\ x_h(t) > 0,\ y_h(t) > 0,\ z(t) > 0,\ x_c(t) > 0,\ y_c(t) > 0 \\
&\ \ \text{for} \quad 0 < t \leq t_3 \quad \text{or there exists a}
\end{aligned} \tag{9}$$

$$
\begin{aligned}
t_4: \quad & x_c(t_4)=0,\ x_c'(t_4)<0,\ x_h(t)>0,\ y_h(t)>0,\ z(t)>0,\ x_c(t)>0,\ y_c(t)>0 \\
& \text{for} \quad 0<t\leq t_4 \quad \text{or there exists a} \\
t_5: \quad & y_c(t_5)=0,\ y_c'(t_5)<0,\ x_h(t)>0,\ y_h(t)>0,\ z(t)>0,\ x_c(t)>0,\ y_c(t)>0 \\
& \text{for} \quad 0<t\leq t_5.
\end{aligned}
$$

From system (8) we obtain

$$
\begin{aligned}
x_h'(t_1) &= \varepsilon x_c(t_1)+\lambda y_h(t_1)>0, \\
y_h'(t_2) &= \varepsilon y_c(t_2)>0, \\
z'(t_3) &= \psi y_h(t_3)>0, \\
x_c'(t_4) &= \Lambda+\delta x_h(t_4)+\pi\rho z(t_4)+\lambda y_c(t_4)>0, \\
y_c'(t_5) &= \delta y_h(t_5)+(1-\pi)\rho z(t_5)>0,
\end{aligned} \tag{10}
$$

which contradicts all the five cases stated in (9). Therefore, $x_h(t)>0$, $y_h(t)>0$, $z(t)>0$, $x_c(t)>0$ and $y_c(t)>0$ and this completes the proof. □

We study system (8) in the biologically feasible region given by:

$$
\Omega_a=\left\{(x_h,y_h,z,x_c,y_c)\in\mathbb{R}^5_+ \mid 0\leq N\leq\frac{\Lambda}{\mu_c}\right\}. \tag{11}
$$

We present the following proposition that guarantees the well-posedness of system (8), ensuring that all solutions with initial conditions that originate within Ω_a persist within this domain for all $t>0$.

Proposition 2. The compact domain Ω_a as outlined in (11) is invariantly positive with respect to the system (8) and attracts all solutions in $\mathbb{R}^5_+$.

Proof. From system (8) we have that

$$
\begin{aligned}
\frac{dN}{dt} &= \frac{dN_h}{dt}+\frac{dN_c}{dt}+\frac{dz}{dt}=\Lambda-\mu(x_h+y_h)-\mu z-\mu_c(x_c+y_c) \\
&= \Lambda-\mu N_h-\mu z-\mu_c N_c<\Lambda-\mu_c N_h-\mu_c z-\mu_c N_c \ (\text{since } \mu>\mu_c) \\
&= \Lambda-\mu_c N.
\end{aligned}
$$

Thus, solving the differential inequality $\frac{dN}{dt}\leq\Lambda-\mu_c N$ gives $0\leq N(t)\leq\frac{\Lambda}{\mu_c}+\left(N(0)-\frac{\Lambda}{\mu_c}\right)e^{-\mu_c t}$. Then, $\limsup_{t\to\infty} N\leq\frac{\Lambda}{\mu_c}$. Thus, the set Ω_a is attractive. Consequently, if system (8) vector field is confined to the boundary of set Ω_a, then it will not extend beyond the

exterior of set Ω_a. This ensures that all solutions with initial conditions originating in Ω_a will persist inside Ω_a indefinitely for all time $t > 0$. □

3.2.2. *MRSA-free equilibrium and the reproduction number.* We now determine the MRSA-free equilibrium point and the reproduction number of model system (8). The MRSA-free equilibrium depicts a state in the community and hospital where all individuals are not colonized with MRSA-bacteria, that is, $y_h = y_c = z = 0$. We represent the MRSA-free equilibrium point by

$$\mathscr{M}_a^o = (x_h^o, y_h^o, z, x_c^o, y_c^o) = \left(\frac{\varepsilon\Lambda}{p_4 p_7 (1-\Psi)}, 0, 0, \frac{\Lambda}{p_7(1-\Psi)}, 0\right)$$

where $\Psi = \dfrac{\delta\varepsilon}{p_4 p_7} < 1$.

The next generation matrix approach stated in [27] is applied on the computations of the non-negative F matrix and a non-singular M-matrix V to obtain

$$F = \begin{pmatrix} \beta_h & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & \beta_c \end{pmatrix} \quad \text{and} \quad V = \begin{pmatrix} p_4 + p_5 & 0 & -\varepsilon \\ -\psi & p_6 & 0 \\ -\delta & -((1-\Pi)\rho) & \lambda + p_7 \end{pmatrix} \tag{12}$$

where $p_5 = \psi + \lambda$ and p_4, p_6 and p_7 are defined as before. Consequently, the reproduction number of the model system (8) is obtained as

$$\mathscr{R}_0 = \frac{p_6(\beta_c(p_4+p_5)+\beta_h(\lambda+p_7)) + \sqrt{p_6^2(\beta_c(p_4+p_5)+\beta_h(\lambda+p_7))^2 + 4p_6\varepsilon\beta_c\beta_h(\rho\psi(1-\Pi)+p_6\delta)}}{2p_6(p_4+p_5)(\lambda+p_7)[1-(\Psi_1+\Psi_2)]} \tag{13}$$

where $\Psi_1 = \dfrac{\varepsilon\rho\psi(1-\Pi)}{p_6(p_4+p_5)(\lambda+p_7)}$ and $\Psi_2 = \dfrac{\varepsilon\delta}{(p_4+p_5)(\lambda+p_7)}$ with $\Psi_1 + \Psi_2 < 1$.

The following theorem (Theorem 3) is derived from the work of van den Driessche and Watmough [27].

Theorem 3. *The MRSA-free equilibrium $\mathscr{M}_a^o$ for the adjusted model* (8) *is locally asymptotically stable if $\mathscr{R}_0 < 1$ and is unstable if $\mathscr{R}_0 > 1$.*

3.2.3. *MRSA-persistent equilibrium.* We now establish the MRSA-persistent equilibrium of the adjusted model system (8) denoted by $\mathscr{M}_a^* = \left(x_h^*, y_h^*, z^*, x_c^*, y_c^*\right)$. This is obtained by solving system (14) below:

$$
\left\{
\begin{array}{rl}
0 &= \varepsilon x_c^* - \lambda_h^* x_h^* - p_4 x_h^* + \lambda y_h^*, \\
0 &= \lambda_h^* x_h^* + \varepsilon y_c^* - \psi y_h^* - (p_4 + \lambda) y_h^*, \\
0 &= \psi y_h^* - p_6 z^*, \\
0 &= \Lambda + \delta x_h^* + \pi\rho z^* - \lambda_c^* x_c^* - p_7 x_c^* + \lambda y_c^*, \\
0 &= \lambda_c^* x_c^* + \delta y_h^* + (1-\pi)\rho z^* - (p_7 + \lambda) y_c^*,
\end{array}
\right. \tag{14}
$$

where $\lambda_h^* = \dfrac{\beta_h y_h^*}{N_h^*}$ and $\lambda_c^* = \dfrac{\beta_c y_c^*}{N_c^*}$. Due to the model complexity, the MRSA-persistent equilibrium is expressed in terms of λ_h^* and λ_c^*. From the second equation of (14), we express x_h^* in terms of y_h^* and y_c^* to obtain

$$
x_h^* = \frac{y_h^*(\lambda + p_4 + \psi) - \varepsilon y_c^*}{\lambda_h^*}. \tag{15}
$$

From the third equation of (14) we express z^* in terms y_h^* to obtain

$$
z^* = \frac{\psi y_h^*}{p_6}. \tag{16}
$$

From the fifth equation we express x_c^* in terms of y_h^* and y_c^* to obtain

$$
x_c^* = \frac{p_6\left(y_c^*(\lambda + p_7) - \delta y_h^*\right) - (1-\pi)\rho\,\psi y_h^*}{p_6 \lambda_c^*}. \tag{17}
$$

Substituting (15) and (17) into the first equation of (14), we obtain

$$
-\left(y_h^*(p_4 + \psi)\right) + \frac{\varepsilon\left(p_6\left(y_c^*(\lambda_c^* + \lambda + p_7) - \delta y_h^*\right) - (1-\pi)\rho\,\psi y_h^*\right)}{p_6 \lambda_c^*} + \frac{p_4\left(\varepsilon y_c^* - y_h^*(\lambda + p_4 + \psi)\right)}{\lambda_h^*} = 0. \tag{18}
$$

Substituting (15) and (17) into the fourth equation of (14), we obtain

$$\frac{\Lambda\lambda_c^*}{\lambda_c^*}+\frac{\rho\psi y_h^*(\lambda_c^*+p_7(1-\pi))}{p_6\lambda_c^*}$$

(19)
$$+\frac{\delta y_h^*\left(\lambda_c^*\left(\lambda_h^*+\lambda+p_4+\psi\right)+p_7\lambda_h^*\right)+y_c^*\left(-\delta\varepsilon\lambda_c^*-p_7\lambda_h^*\left(\lambda_c^*+\lambda+p_7\right)\right)}{\lambda_h^*\lambda_c^*}=0.$$

Solving the equations (18) and (19) for y_h^* and y_c^* simultaneously gives

$$y_h^*=\frac{A_h^*}{B_h^*}\quad\text{and}\quad y_c^*=\frac{A_c^*}{B_c^*} \tag{20}$$

where A_h^*, B_h^*, A_c^* and B_c^* are given in Appendix 1. Substituting the expressions given in (20) into the expressions (15), (16) and (17), we obtain the MRSA-persistent equilibrium $\mathscr{M}_a^*=\left(x_h^*,y_h^*,z^*,x_c^*,y_c^*\right)$ of the adjusted model system (8) in terms of λ_h^* and λ_c^*.

The following theorem (Theorem 4) on the local stability of the MRSA-persistent equilibrium is established numerically in the next section 4.

Theorem 4. *The MRSA-persistent equilibrium* $\mathscr{M}_a^*=\left(x_h^*,y_h^*,z^*,x_c^*,y_c^*\right)$ *of the adjusted model system* (8) *is locally asymptotically stable if and only if* $\mathscr{R}_0>1$.

4. Numerical Simulations

We now numerically simulate the model system (8) using MATLAB programming language and present some important numerical results.

4.1. Parameter Estimation. The model considered in this study is a follow-up model on the model developed in [3]. We make use of the model parameters presented in [3]. These parameter values are given in Table 2 below. The following initial conditions were used: $x_h(0)=6$, $y_h(0)=2$, $z(0)=1$, $x_c(0)=165500$, $y_c(0)=35$.

TABLE 2. Values of parameters employed for performing numerical simulations

Parameter	Parameter Description	Value	Reference
Λ	Recruitment rate	0.0077	[28]
β_h	Transmission rate for hospitalized individuals	0.1115	[3]
β_c	Transmission rate for the general population	0.001	[3]
$N_{i\max}$	Number of available beds in the isolation unit	30	[3]
ψ	Isolation rate for hospitalized individuals	0.02	[3]
π	Proportion of individuals leaving isolation without MRSA	0.25	[3]
$1/\rho$	Mean length of stay in isolation, days	20	[3]
$1/\lambda$	Mean duration of carriage of MRSA, days	370	[3]
$1/\delta$	Mean length of stay in hospital, days	8	[3]
ε	Readmission rate for discharged individuals	0.00633	[3]
μ	Death rate for hospitalized individuals	0.04353	[29]
μ_c	Death rate for the general population	0.0077	[28]

4.2. Numerical results.

4.2.1. *Local stability of the MRSA-free equilibrium point $\mathscr{M}_a^o$.* We present some results obtained after numerically simulating the adjusted model system (8). We present numerical results to support the analytical results obtained in section 3.2.2 and theorem 3.

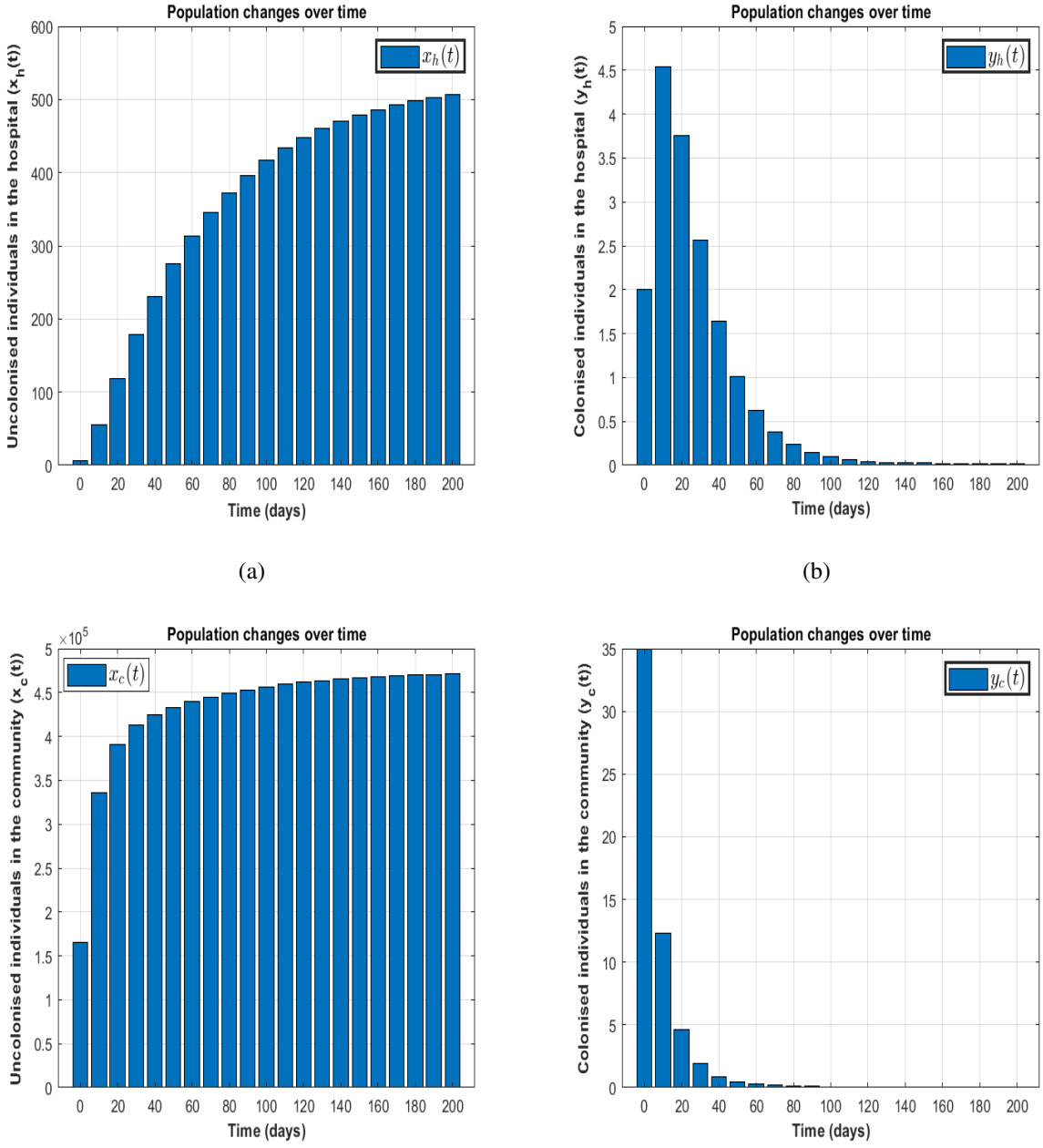


FIGURE 3. Changes in the populations of (a) uncolonised individuals in the hospital $(x_h(t))$, (b) colonised individuals in the hospital $(y_h(t))$, (c) uncolonised individuals in the community $(x_c(t))$, (d) colonised individuals in the community $(y_c(t))$, for the case $\mathscr{R}_0 = 0.2996 < 1$.

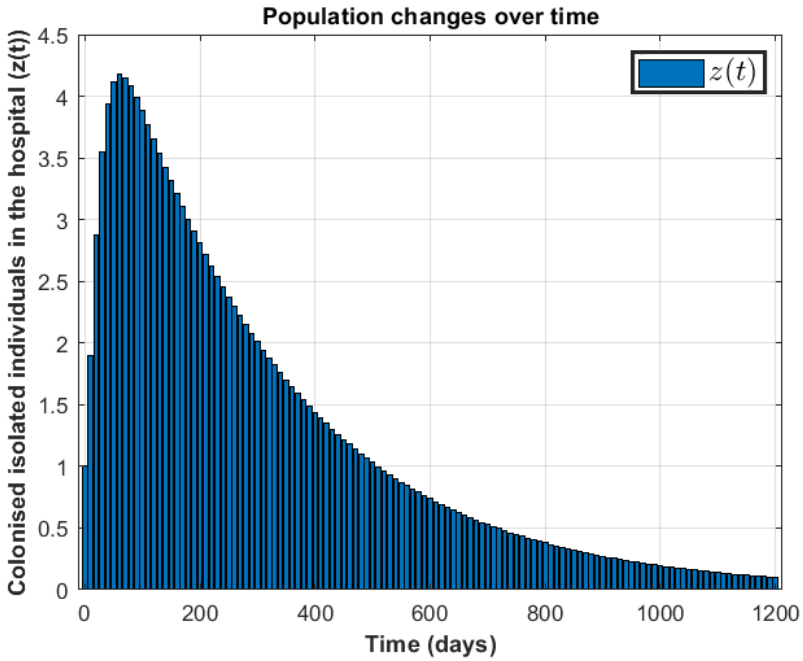


FIGURE 4. Changes in the populations of colonised isolated individuals in the hospital $(z(t))$, for the case $\mathscr{R}_0 = 0.2996 < 1$.

Figure 3 and figure 4 presents the trajectories of the populations of hospitalized and non-hospitalized individuals for the case when $\mathscr{R}_0 = 0.2996 < 1$.

4.2.2. *Local stability of the MRSA-persistent equilibrium point* $\mathscr{M}_a^*$. We present some results obtained after numerically simulating the adjusted model system (8). We present numerical results to support the analytical results obtained in section 3.2.3 and theorem 4.

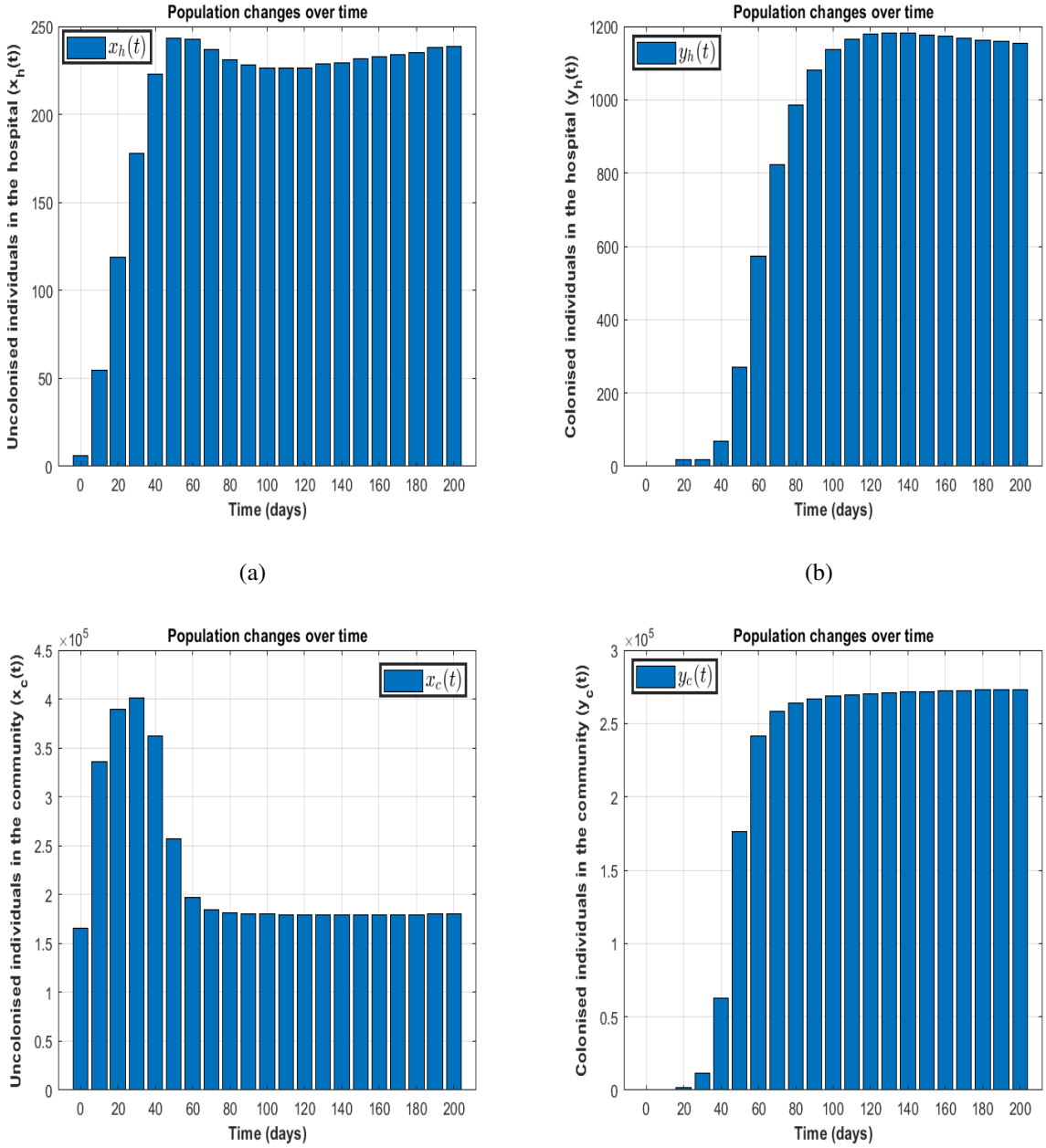


FIGURE 5. Changes in the populations of (a) uncolonised individuals in the hospital $(x_h(t))$, (b) colonised individuals in the hospital $(y_h(t))$, (c) uncolonised individuals in the community $(x_c(t))$, (d) colonised individuals in the community $(y_c(t))$, for the case $\mathscr{R}_0 = 2.9964 > 1$.

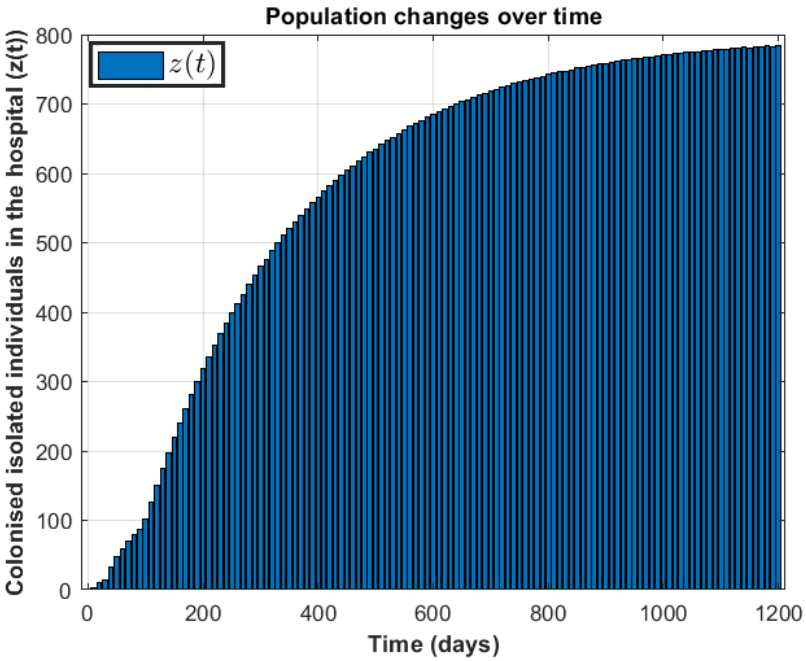


FIGURE 6. Changes in the populations of colonised isolated individuals in the hospital $(z(t))$, for the case $\mathscr{R}_0 = 2.9964 > 1$.

Figure 5 and figure 6 presents the trajectories of the populations of hospitalized and non-hospitalized individuals for the case when $\mathscr{R}_0 = 2.9964 > 1$.

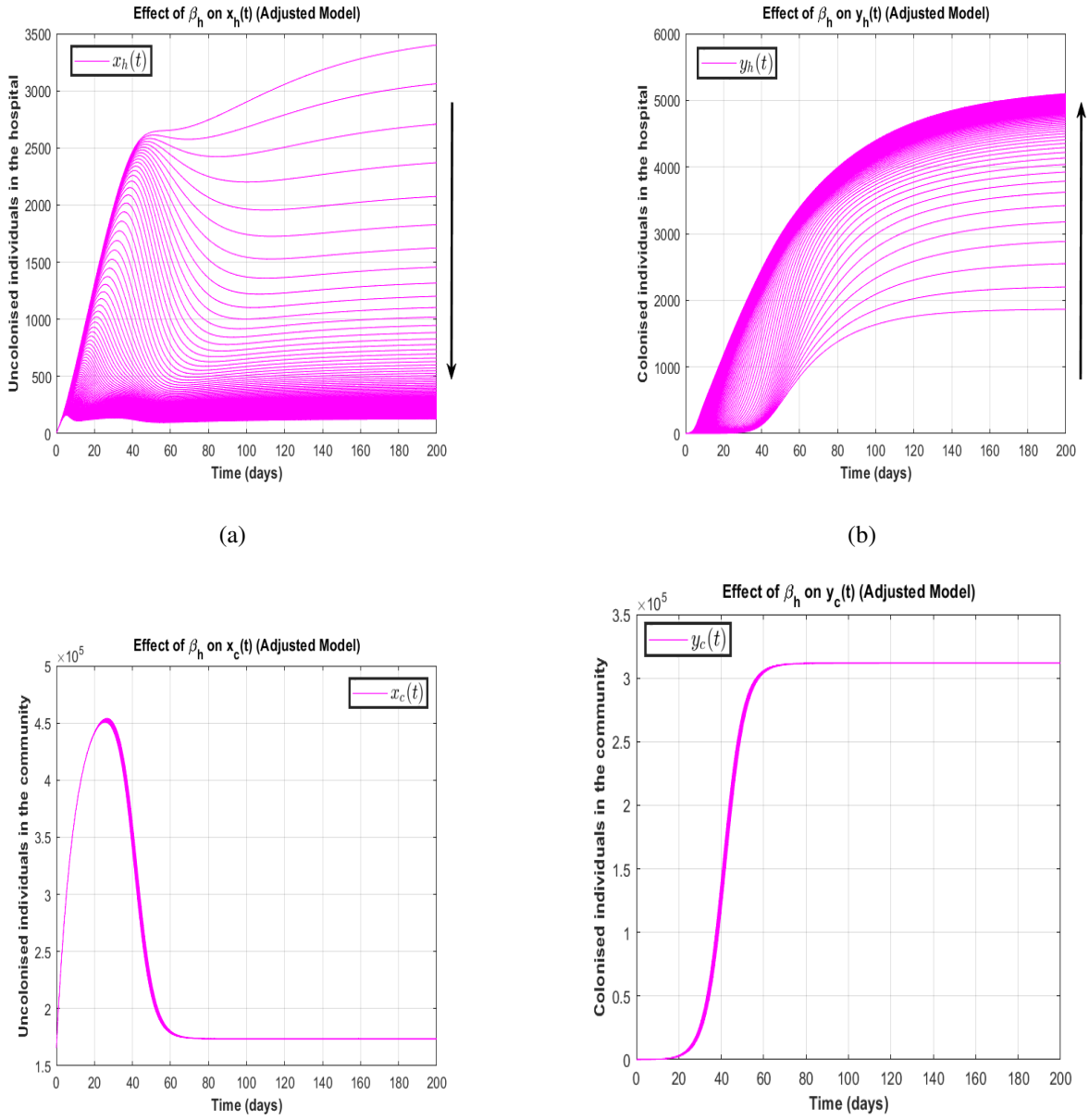


FIGURE 7. (a) Effects of varying the parameter β_h, on the population changes of (a) uncolonised individuals in the hospital $(x_h(t))$, (b) colonised individuals in the hospital $(y_h(t))$, (c) uncolonised individuals in the community $(x_c(t))$, (d) colonised individuals in the community $(y_c(t))$. An upward-pointing arrow signifies that with an increase in the parameter value, the population also increases, whereas a downward-pointing arrow denotes that with an increase in the parameter value, the population decreases. No arrow indicates no parameter significance.

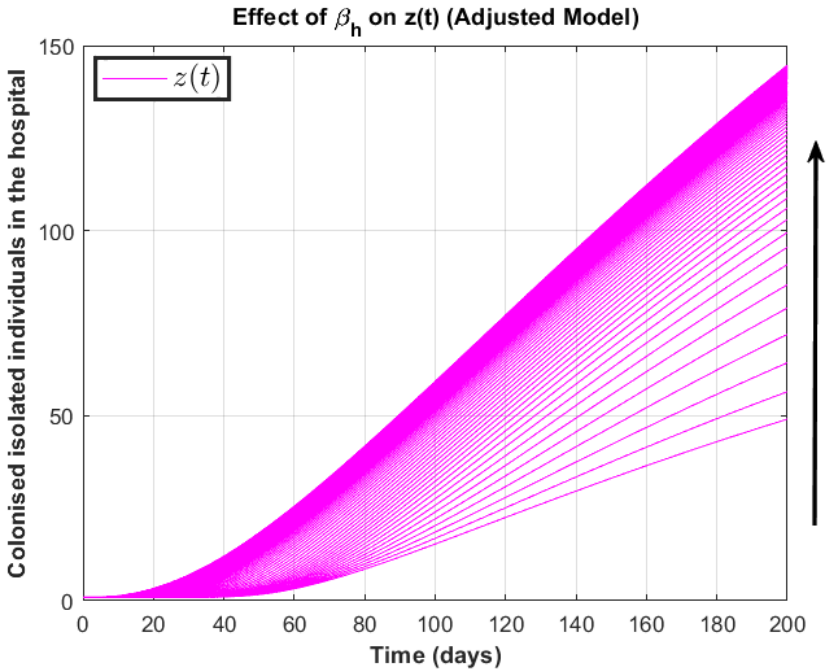
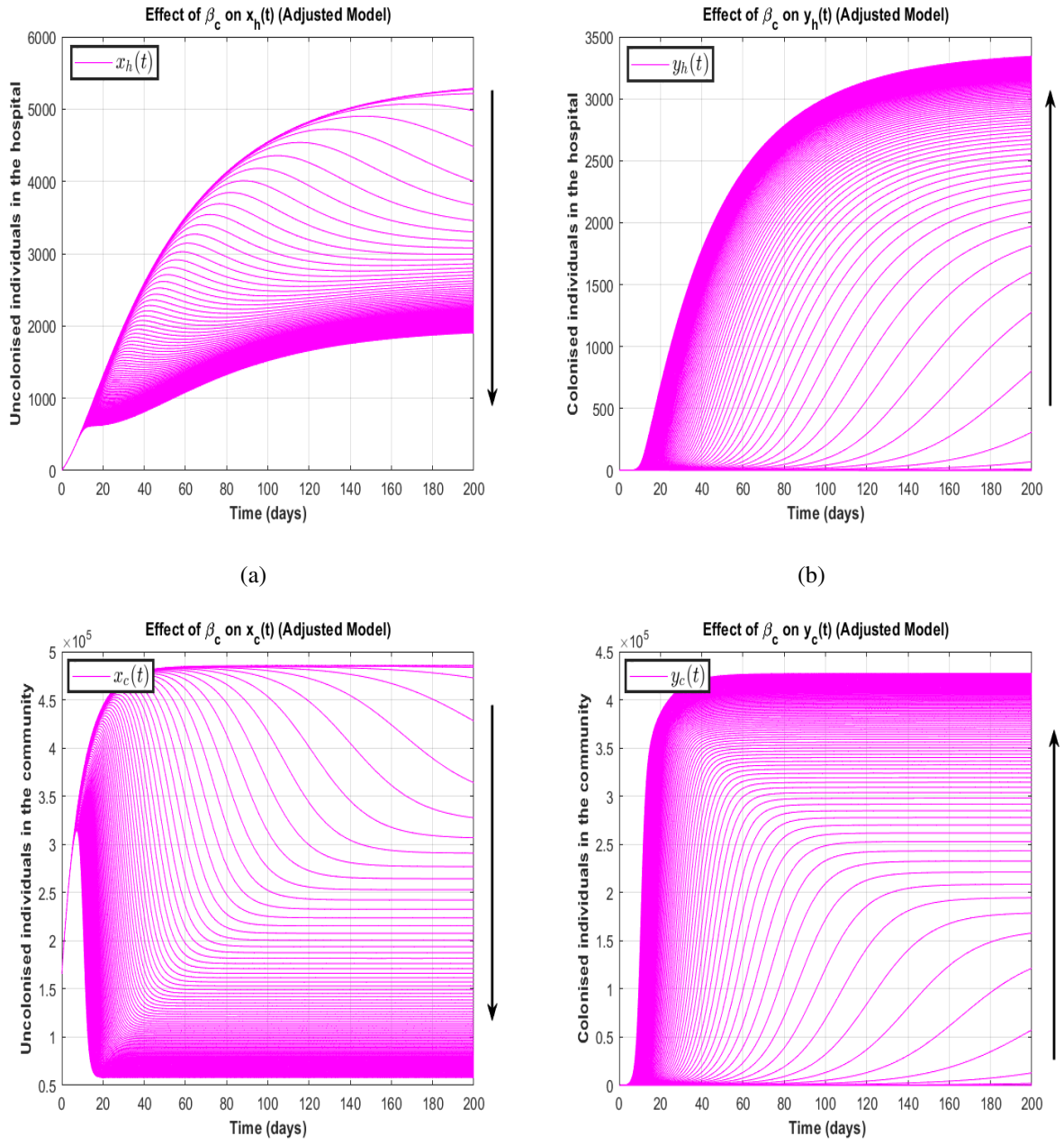


FIGURE 8. Effects of varying the parameter β_h, on the population changes of colonised isolated individuals in the hospital $(z(t))$. An upward-pointing arrow signifies that with an increase in the parameter value, the population increases.

4.2.3. *Impact of β_h on population trajectories.* Figures 7(a)-(d) and figure 8 illustrate the impact of varying the parameter β_h on the population trajectories of model system (8). The parameter β_h is varied from a value of 0.0 up to 1.0 with a step size of 0.01. The results show that an increase in the value of β_h has a significant impact on the hospitalized compartments only and an insignificant impact on the general community. Increasing the value of β_h will result in an increase in MRSA infections in the hospital. An increase of the value of β_h with 0.01 corresponds to an increase of the value of $\mathscr{R}_0$ with 0.271036. The simulated results gives a maximum β_h value of $\beta_h = 1$ corresponding to a maximum $\mathscr{R}_0$ value of $\mathscr{R}_0 = 29.8945$. The results obtained in this section are reflective of the need to put in place some measures that reduce nosocomial MRSA infections.



(a) (b)

(c) (d)

FIGURE 9. (a) Effects of varying the parameter β_c, on the population changes of (a) uncolonised individuals in the hospital $(x_h(t))$, (b) colonised individuals in the hospital $(y_h(t))$, (c) uncolonised individuals in the community $(x_c(t))$, (d) colonised individuals in the community $(y_c(t))$. An upward-pointing arrow signifies that with an increase in the parameter value, the population also increases, whereas a downward-pointing arrow denotes that with an increase in the parameter value, the population decreases.

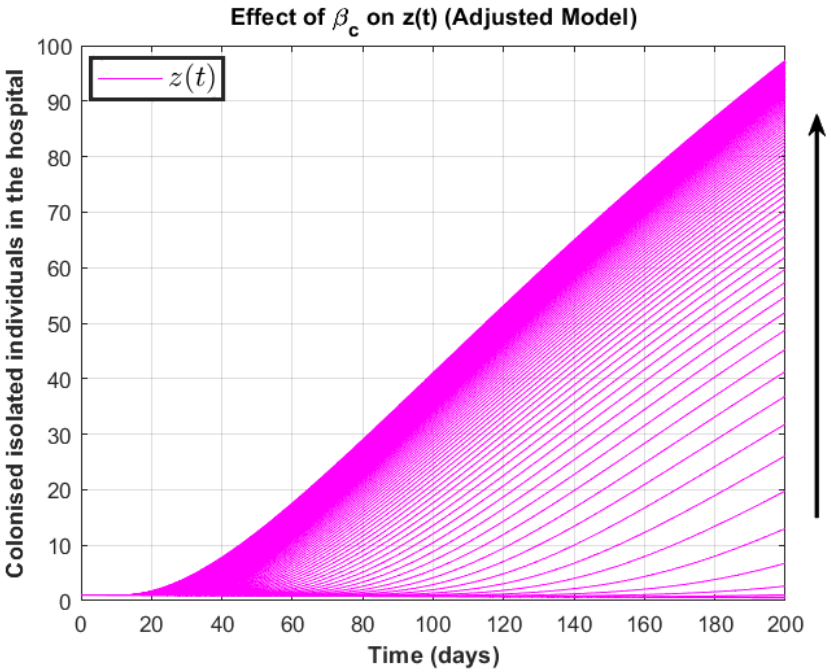


FIGURE 10. Effects of varying the parameter β_c, on the population changes of colonised isolated individuals in the hospital $(z(t))$. An upward-pointing arrow signifies that with an increase in the parameter value, the population increases.

4.2.4. *Impact of β_c on population trajectories.* Figures 9(a)-(d) and figure 10 illustrate the impact of varying the parameter β_c on the population trajectories of model system (8). The parameter β_c is varied from a value of 0.0 up to 1.0 with a step size of 0.01. The results show that an increase in the value of β_c has a significant impact on both the hospitalized compartments and the general community. Increasing the value of β_c will result in an increase in MRSA infections in both the hospital and the general community. An increase of the value of β_c with 0.01 corresponds to an increase of the value of $\mathscr{R}_0$ with 0.083451. The simulated results gives a maximum β_c value of $\beta_c = 1$ corresponding to a maximum $\mathscr{R}_0$ value of $\mathscr{R}_0 = 9.0202$. The results obtained in this section are reflective of the effect that the admission of the already MRSA-infected individuals in the community have on hospital infections. Thus, it is encouraged to put in place MRSA detection measures upon initial hospital admission in order to reduce MRSA infections in both the hospital and the general community.

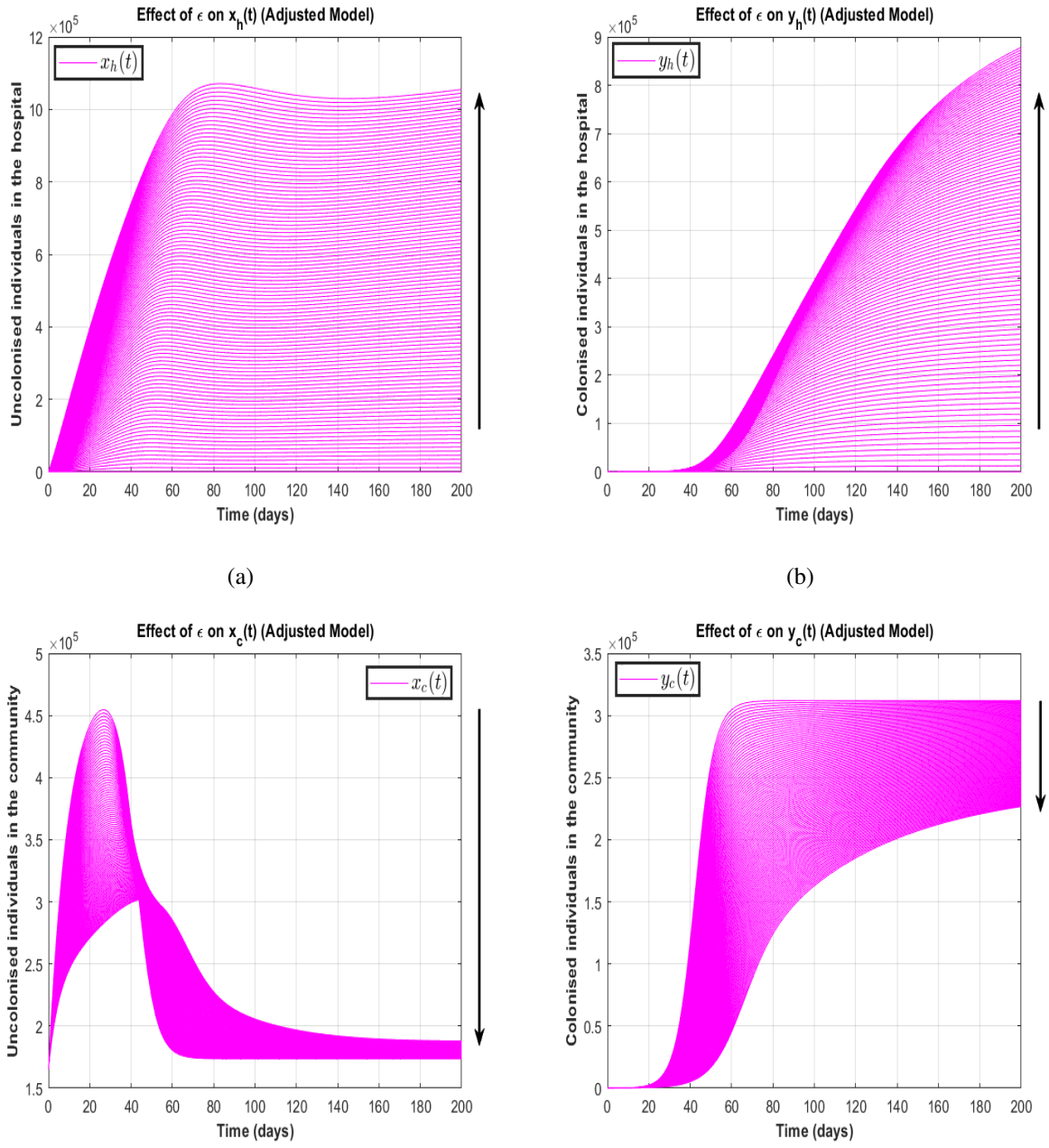


FIGURE 11. (a) Effects of varying the parameter ϵ, on the population changes of (a) uncolonised individuals in the hospital $(x_h(t))$, (b) colonised individuals in the hospital $(y_h(t))$, (c) uncolonised individuals in the community $(x_c(t))$, (d) colonised individuals in the community $(y_c(t))$. An upward-pointing arrow signifies that with an increase in the parameter value, the population also increases, whereas a downward-pointing arrow denotes that with an increase in the parameter value, the population decreases.

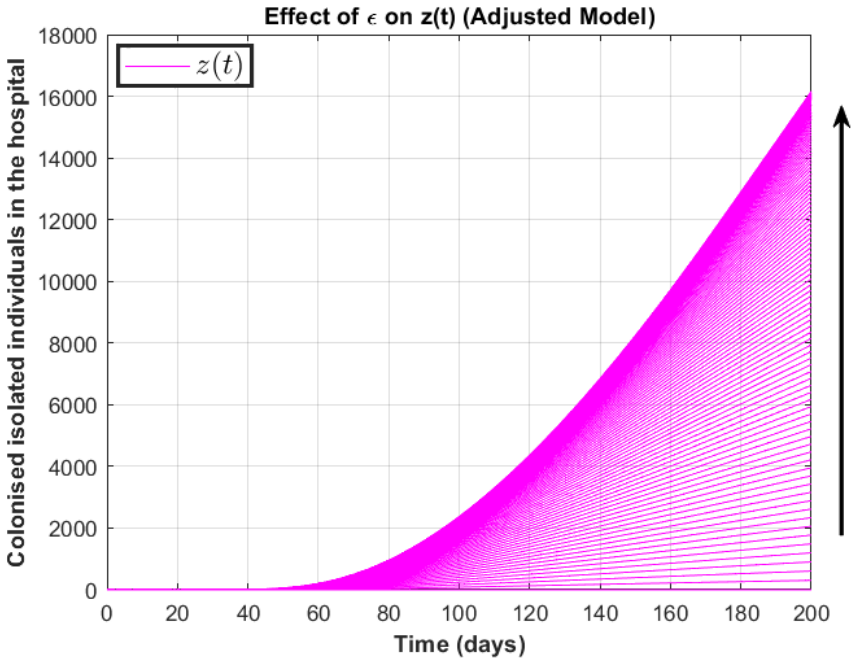


FIGURE 12. Effects of varying the parameter ε, on the population changes of colonised isolated individuals in the hospital $(z(t))$. An upward-pointing arrow signifies that with an increase in the parameter value, the population increases.

4.2.5. *Impact of* ε *on population trajectories.* Figures 11(a)-(d) and figure 12 illustrate the impact of varying the parameter ε on the population trajectories of model system (8). The parameter ε is varied from a value of 0.0 up to 0.1 with a step size of 0.001. The results show that an increase in the value of ε has a significant impact on both the hospitalized compartments and the general community. Increasing the value of ε will result in a decrease in MRSA infections in the general community and an increase in MRSA infections in the hospital. The increase in MRSA infections in the hospital might be a result of inadequate screening of individuals upon admission that result in admission of already MRSA infected individuals from the community. Overall, an increase of the value of ε with 0.001 corresponds to a decrease of the value of $\mathscr{R}_0$ with 0.005248.

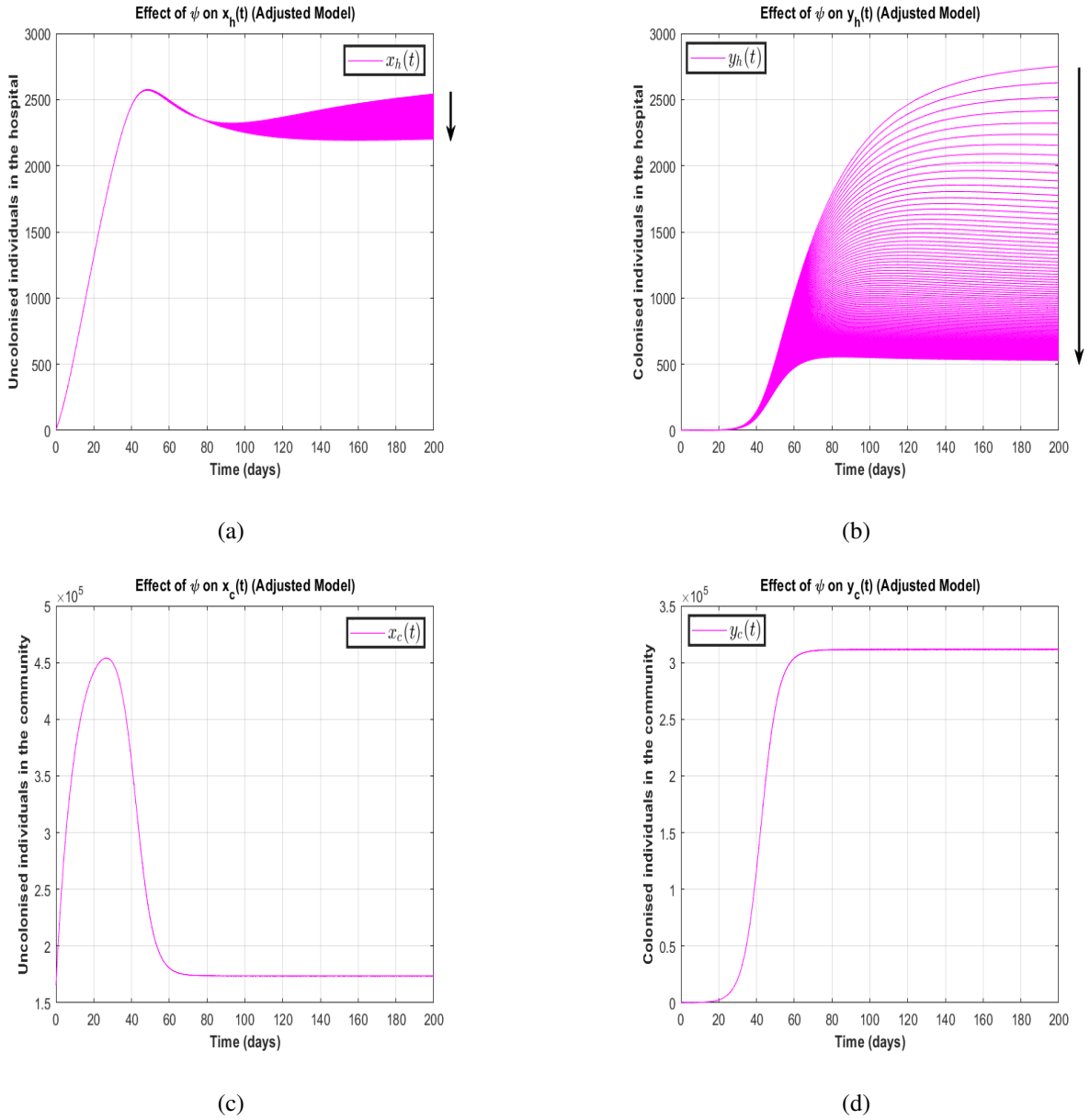


FIGURE 13. (a) Effects of varying the parameter ψ, on the population changes of (a) uncolonised individuals in the hospital $(x_h(t))$, (b) colonised individuals in the hospital $(y_h(t))$, (c) uncolonised individuals in the community $(x_c(t))$, (d) colonised individuals in the community $(y_c(t))$. An upward-pointing arrow signifies that with an increase in the parameter value, the population also increases, whereas a downward-pointing arrow denotes that with an increase in the parameter value, the population decreases. No arrow indicates no parameter significance.

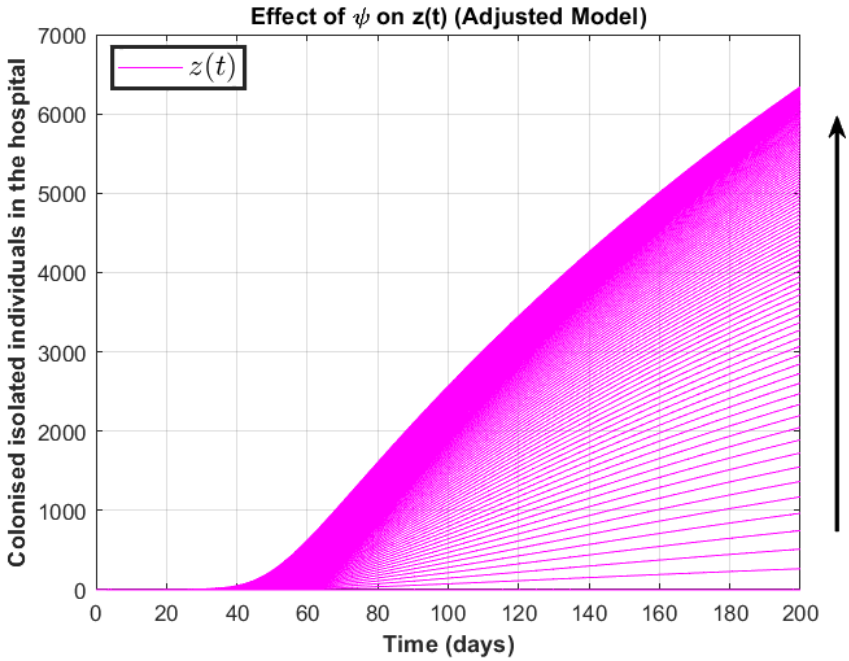


FIGURE 14. Effects of varying the parameter ψ, on the population changes of colonised isolated individuals in the hospital $(z(t))$. An upward-pointing arrow signifies that with an increase in the parameter value, the population increases.

4.2.6. *Impact of* ψ *on population trajectories.* Figures 13(a)-(d) and figure 14 illustrate the impact of varying the parameter ψ on the population trajectories of model system (8). The parameter ψ is varied from a value of 0.0 up to 0.1 with a step size of 0.001. The results show that an increase in the value of ψ has a significant impact on the hospitalized compartments only, especially the colonised hospitalized individuals. An increase in the value of ψ will lead to a substantial decrease in the population of colonised hospitalized individuals. On the other hand, an increase in the value of ψ has an insignificant impact on the general community. Overall, an increase of the value of ψ with 0.001 corresponds to a decrease of the value of $\mathscr{R}_0$ with 0.00498.

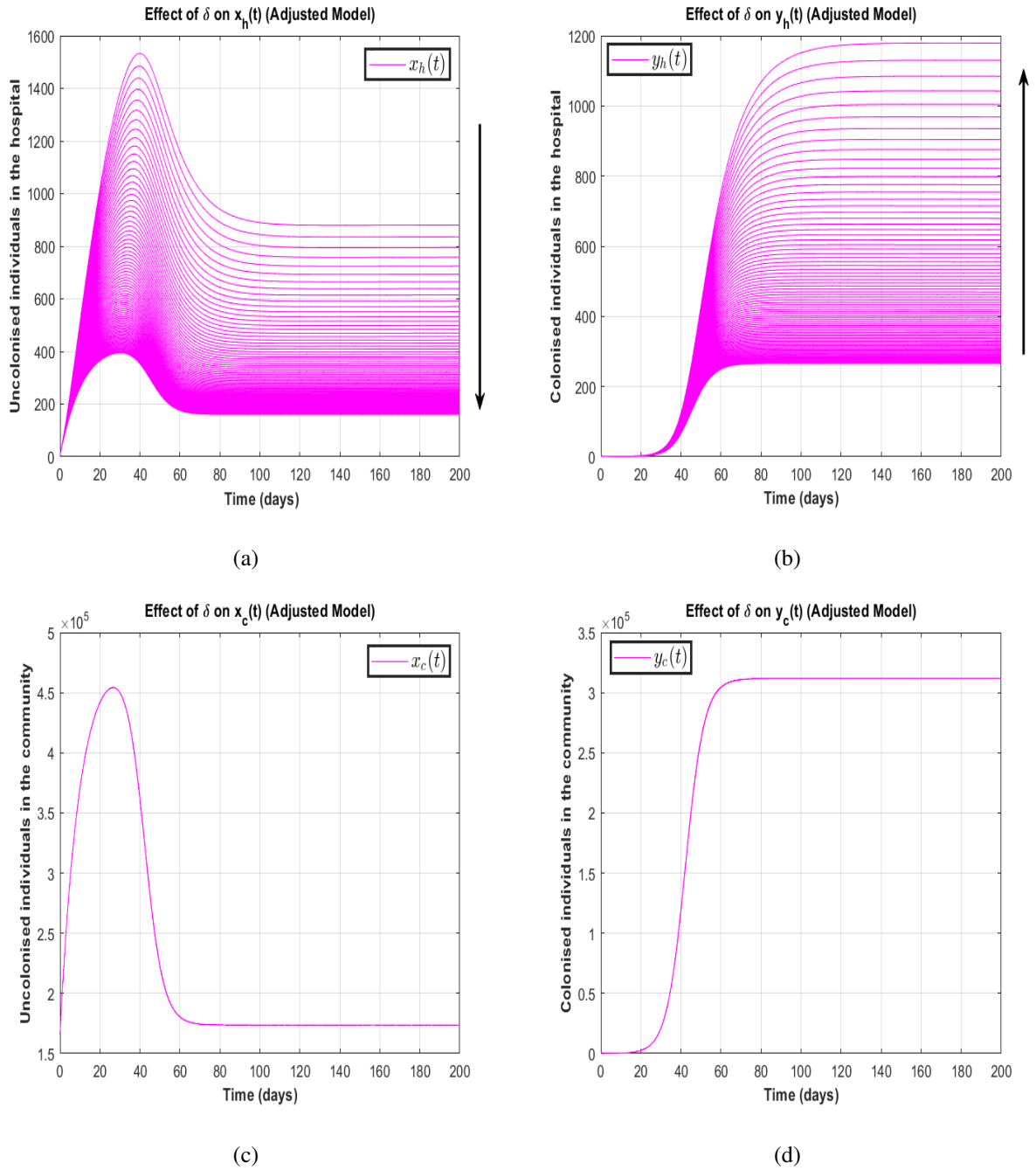


FIGURE 15. (a) Effects of varying the parameter δ, on the population changes of (a) uncolonised individuals in the hospital $(x_h(t))$, (b) colonised individuals in the hospital $(y_h(t))$, (c) uncolonised individuals in the community $(x_c(t))$, (d) colonised individuals in the community $(y_c(t))$. An upward-pointing arrow signifies that with an increase in the parameter value, the population also increases, whereas a downward-pointing arrow denotes that with an increase in the parameter value, the population decreases. No arrow indicates no parameter significance.

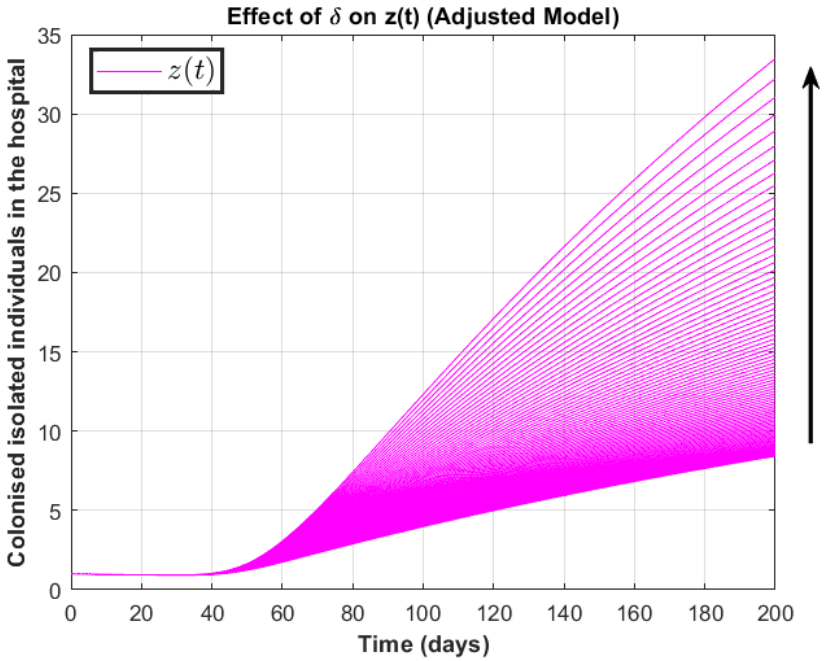


FIGURE 16. Effects of varying the parameter δ, on the population changes of colonised isolated individuals in the hospital $(z(t))$. An upward-pointing arrow signifies that with an increase in the parameter value, the population increases.

4.2.7. *Impact of δ on population trajectories.* Figures 15(a)-(d) and figure 16 illustrate the impact of varying the parameter δ on the population trajectories of model system (8). The parameter δ is varied from a value of 0.05 up to 0.25 with a step size of 0.0025. The results show that an increase in the value of δ has a significant impact on the hospitalized compartments only and an insignificant impact on the general community. Increasing the value of δ will result in an increase in MRSA infections in the hospital. This is due to the fact that prolonged hospital stays tend to elevate the risk of nosocomial infections. Overall, an increase of the value of δ with 0.0025 corresponds to a decrease of the value of $\mathscr{R}_0$ with 0.002673. This might be as a result of more MRSA infected individuals confined to the hospital thereby making them unable to transmit the infection to the general community.

5. CONCLUSION

We developed an MRSA dynamic transmission model in both nosocomial settings and the general population. The model is initially designed using a seven state system of ordinary differential equations that is later simplified and adjusted to a five state system of ordinary differential equations for easy of theoretical analysis. The initial seven state system of ordinary differential equations was observed to be theoretically complex to derive simple epidemic thresholds such as the model's reproduction number. Thus, the model was carefully simplified to allow derivation of important epidemic thresholds.

Model analysis was carried out via the adjusted MRSA infection model (8). The MRSA-free equilibrium point $\mathscr{M}_a^o$ was established and the model reproduction number was derived using the next generation matrix approach. Some numerical results were obtained to support the local stability of $\mathscr{M}_a^o$ whenever the reproduction number is less than unit. Due to the complexity of the model, the MRSA-persistent equilibrium $\mathscr{M}_a^*$ was presented in terms of the force of infection. Similarly, as done on the MRSA-free equilibrium, the MRSA-persistent equilibrium point was shown to be locally asymptotically stable whenever the model reproduction number $\mathscr{R}_0$ is greater than unit.

Numerical simulations were carried out using data provided in relevant scientific studies. Of interest was the question on how parameter variations would impact the model outcomes considering (i) the hospitalized individuals only, (ii) the general community only, or (iii) both the hospitalized individuals and the general community. Only key parameters were selected for consideration. These are β_h, β_c, ε, ψ and δ. It was observed that the parameters β_h, ψ and δ had a significant impact on the hospitalized population only and an insignificant impact on the general population. This is a reflection that these are the key parameters that policy makers must take note of to effectively control nosocomial infections. On the other hand, the remaining parameters β_c and ε were observed to have a significant impact on both the hospitalized population and the general community. This is a reflection that for a broader control of MRSA infections, policy makers must focus on these parameters inorder to curb further spread of MRSA infections in both the hospital and the general community.

The results obtained in this study are critical in informing public health control of MRSA infections in both the hospitals and the general community. However, the model considered in this study has several limitations. The model has simplified the complex dynamics within hospital settings, by not taking into account the different interaction patterns amongst health-care workers and patients, and varying levels of infection control measures. This might lead to a reduced accuracy in model results. The model can thus be improved by encompassing a more detailed representation of interactions in both the hospital and the general community. Incorporating individual-level variability and spatial structure can also provide a more realistic representation of MRSA infection spread.

Appendix 1. Terms constituting y_h^* and y_c^* given in (20).

(21)

$$A_h^* = \Lambda p_6 \varepsilon \left(\lambda_h^* (\lambda_c^* + \lambda + p_7) + p_4 \lambda_c^*\right),$$

$$\begin{aligned} B_h^* = {} & p_6(p_4(-\delta\varepsilon(\lambda_c^* + \lambda) + p_7(\lambda_c^*(\lambda_h^* + \lambda + \psi) - 2\delta\varepsilon + \lambda\lambda_h^* + \lambda(\lambda + \psi)) + p_7^2(\lambda_h^* + \lambda + \psi)) \\ & -\lambda_h^*(\lambda_c^* + \lambda + p_7)(\delta\varepsilon - p_7\psi) + \delta\varepsilon(-\lambda\lambda_c^* + \delta\varepsilon - \lambda(\lambda + \psi) - p_7(\lambda + \psi)) + p_7 p_4^2(\lambda_c^* + \lambda + p_7)) \\ & -\rho\psi\varepsilon(\lambda_h^*(\lambda_c^* + \lambda + p_7) + p_4(\lambda_c^* + p_7(1 - \pi)) - \delta(1 - \pi)\varepsilon), \end{aligned}$$

$$A_c^* = \Lambda\lambda_h^* (p_6 (\lambda_c^* (p_4 + \psi) + \delta\varepsilon) + (1 - \pi)\rho\psi\varepsilon) + \Lambda p_4 p_6 \lambda_c^* (\lambda + p_4 + \psi),$$

$$\begin{aligned} B_c^* = {} & \rho\psi\varepsilon(-\lambda_h^*(\lambda_c^* + \lambda + p_7) + p_4(p_7(\pi - 1) - \lambda_c^*) + \delta(1 - \pi)\varepsilon) + p_6(p_4(-\delta\varepsilon(\lambda_c^* + \lambda) \\ & + p_7(\lambda_c^*(\lambda_h^* + \lambda + \psi) - 2\delta\varepsilon + \lambda\lambda_h^* + \lambda(\lambda + \psi)) + p_7^2(\lambda_h^* + \lambda + \psi)) - \lambda_h^*(\lambda_c^* + \lambda + p_7)(\delta\varepsilon - p_7\psi) \\ & + \delta\varepsilon(-\lambda\lambda_c^* + \delta\varepsilon - \lambda(\lambda + \psi) - p_7(\lambda + \psi)) + p_7 p_4^2(\lambda_c^* + \lambda + p_7)). \end{aligned}$$

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

REFERENCES

[1] F.D. Lowy, Staphylococcus aureus Infections, N. Engl. J. Med. 339 (1998), 520–532. https://doi.org/10.1056/nejm199808203390806.

[2] S.Y. Park, D.R. Chung, Y.R. Kang, et al. Comparison of subsequent infection in methicillin-resistant Staphylococcus aureus nasal carriers between ST72 community-genotype and hospital genotypes: a retrospective cohort study, Antimicrob. Resist. Infect. Control. 6 (2017), 60. https://doi.org/10.1186/s13756-017-0220-1.

[3] R.L. Skov, K.S. Jensen, Community-associated meticillin-resistant Staphylococcus aureus as a cause of hospital-acquired infections, J. Hosp. Infect. 73 (2009), 364–370. https://doi.org/10.1016/j.jhin.2009.07.004.

[4] M.P. Jevons, "Celbenin" - resistant Staphylococci, Br. Med. J. 1 (1961), 124–125. https://doi.org/10.1136/bmj.1.5219.124-a.

[5] S. Deyno, S. Fekadu, A. Astatkie, Resistance of Staphylococcus aureus to antimicrobial agents in Ethiopia: a meta-analysis, Antimicrob. Resist. Infect. Control. 6 (2017), 85. https://doi.org/10.1186/s13756-017-0243-7.

[6] B.C. Herold, Community-acquired methicillin-resistant staphylococcus aureus in children with no identified predisposing risk, JAMA. 279 (1998), 593–598. https://doi.org/10.1001/jama.279.8.593.

[7] T.S. Naimi, Comparison of community- and health care–associated methicillin-resistant staphylococcus aureus infection, JAMA. 290 (2003), 2976–2984. https://doi.org/10.1001/jama.290.22.2976.

[8] S.L. Kaplan, K.G. Hulten, B.E. Gonzalez, et al. Three-year surveillance of community-acquired staphylococcus aureus infections in children, Clinic. Infect. Dis. 40 (2005), 1785–1791. https://doi.org/10.1086/430312.

[9] M.Z. David, D. Glikman, S.E. Crawford, et al. What is community-associated methicillin-resistant staphylococcus aureus?, J. Infect. Dis. 197 (2008), 1235–1243. https://doi.org/10.1086/533502.

[10] R. Skov, O. Gudlaugsson, H. Hardardottir, et al. Proposal for common Nordic epidemiological terms and definitions for methicillin-resistant Staphylococcus aureus (MRSA), Scandinavian J. Infect. Dis. 40 (2008), 495–502. https://doi.org/10.1080/00365540701864658.

[11] CDC, Community-associated mrsa information for clinicians, Centers for Disease Control and Prevention, Atlanta, (2005).

[12] M.A. Morrison, J.C. Hageman, R.M. Klevens, Case definition for community-associated methicillin-resistant Staphylococcus aureus, J. Hosp. Infect. 62 (2006), 241. https://doi.org/10.1016/j.jhin.2005.07.011.

[13] C.L. Maree, R.S. Daum, S. Boyle-Vavra, et al. Community-associated Methicillin-resistant staphy lococcus aureus isolates and healthcare-associated infections, Emerg. Infect. Dis. 13 (2007), 236–242. https://doi.org/10.3201/eid1302.060781.

[14] R. Klevens, M. Morrison, S. Fridkin, et al. Community-associated Methicillin-resistant Staphylococcus aureus and Healthcare Risk Factors, Emerg. Infect. Dis. 12 (2006), 1991–1993. https://doi.org/10.3201/eid1212.060505.

[15] WHO, Antimicrobial resistance: global report on surveillance, World Health Organization, (2014).

[16] E.D. Charlebois, D.R. Bangsberg, N.J. Moss, et al. Population-based community prevalence of Methicillin-resistant staphylococcus aureus in the urban poor of San Francisco, Clinic. Infect. Dis. 34 (2002), 425–433. https://www.jstor.org/stable/4461890.

[17] R. Culpepper, S. Chapman, A. Kennedy, M. Currier, Methicillin-resistant staphylococcus aureus skin or soft tissue infections in a state prison-Mississippi, 2000, JAMA. 287 (2002), 181–182. https://doi.org/10.1001/jama.287.2.181.

[18] E.S. Pan, B.A. Diep, H.A. Carleton, et al. Increasing prevalence of Methicillin-resistant staphylococcus aureus infection in California jails, Clinic. Infect. Dis. 37 (2003), 1384–1388. https://doi.org/10.1086/379019.

[19] CDC, Outbreaks of community-associated methicillin-resistant Staphylococcus aureus skin infections–Los Angeles County, California, 2002-2003. MMWR Morb Mortal Wkly Rep. 52 (2003), 88.

[20] B.S. Cooper, G.F. Medley, S.P. Stone, et al. Methicillin-resistantStaphylococcus aureusin hospitals and the community: Stealth dynamics and control catastrophes, Proc. Natl. Acad. Sci. U.S.A. 101 (2004), 10223–10228. https://doi.org/10.1073/pnas.0401324101.

[21] B.J. Hartman, A. Tomasz, Low-affinity penicillin-binding protein associated with beta-lactam resistance in Staphylococcus aureus, J. Bacteriol. 158 (1984), 513–516. https://doi.org/10.1128/jb.158.2.513-516.1984.

[22] P.E. Reynolds, D.F.J. Brown, Penicillin-binding proteins of β-lactam-resistant strains of staphylococcus aureus: effect of growth conditions, FEBS lett. 192 (1985), 28–32. https://doi.org/10.1016/0014-5793(85)80036-3.

[23] Y. Utsui, T. Yokota, Role of an altered penicillin-binding protein in methicillin- and cephem-resistant Staphylococcus aureus, Antimicrob. Agents Chemother. 28 (1985), 397–403. https://doi.org/10.1128/aac.28.3.397.

[24] S. Tsiodras, H.S. Gold, G. Sakoulas, et al. Linezolid resistance in a clinical isolate of Staphylococcus aureus, The Lancet 358 (2001), 207–208. https://doi.org/10.1016/s0140-6736(01)05410-1.

[25] P. Wilson, Linezolid resistance in clinical isolates of Staphylococcus aureus, J. Antimicrob. Chemother. 51 (2002), 186–188. https://doi.org/10.1093/jac/dkg104.

[26] C.P. Bhunu, W. Garira, Z. Mukandavire, et al. Tuberculosis transmission model with chemoprophylaxis and treatment, Bull. Math. Biol. 70 (2008), 1163–1191. https://doi.org/10.1007/s11538-008-9295-4.

[27] P. van den Driessche, J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, Math. Biosci. 180 (2002), 29–48. https://doi.org/10.1016/s0025-5564(02)00108-6.

[28] D.R. MacFadden, D.N. Fisman, W.P. Hanage, et al. The relative impact of community and hospital antibiotic use on the selection of extended-spectrum beta-lactamase–producing escherichia coli, Clinic. Infect. Dis. 69 (2018), 182–188. https://doi.org/10.1093/cid/ciy978.

[29] J. Lowden, R. Miller Neilan, M. Yahdi, Optimal control of vancomycin-resistant enterococci using preventive care and treatment of infections, Math. Biosci. 249 (2014), 8–17. https://doi.org/10.1016/j.mbs.2014.01.004.