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A stochastic dynamical model for nosocomial infections with co-circulation of sensitive and resistant bacterial strains

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Abstract
Nosocomial infections (hospital-acquired) has been an important public health problem, which may make those patients with infections or involved visitors and hospital personnel at higher risk of worse clinical outcomes or infection, and then consume more healthcare resources. Taking into account the stochasticity of the death and discharge rate of patients staying in hospitals, in this paper, we propose a stochastic dynamical model describing the transmission of nosocomial pathogens among patients admitted for hospital stays. The stochastic terms of the model are incorporated to capture the randomness arising from death and discharge processes of patients. Firstly, a sufficient condition is established for the stochastic extinction of disease. It shows that introducing randomness in the model will result in lower potential of nosocomial outbreaks. Further, we establish a threshold criterion on the existence of stationary distribution and ergodicity for any positive solution of the model. Particularly, the spectral radius form of stochastic threshold value is calculated in the special case. Moreover, the numerical simulations are conducted to both validate the theoretical results and investigate the effect of prevention and control strategies on the prevalence of nosocomial infection. We show that enhancing hygiene, targeting colonized and infected patients, improving antibiotic treatment accuracy, shortening treatment periods are all crucial factors to contain nosocomial infections.

Keywords Stochastic dynamical model · Nosocomial infection · Extinction · Stationary distribution.

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1 Introduction

Nosocomial infection refers to infections acquired during stays in health-care facilities. Patients admitted for hospital stays are under severe health conditions with weakened immune systems, thus are extremely vulnerable to pathogens circulating among patient population. According to the report of World Health Organization (World Health Organization 2006), about 1.4 million people are ill because of infections acquired in hospitals at any given moment across the world. Approximately one-fourth patient may be affected and the death toll reaches 5–10% of patients in some developing countries. Further, the high frequency of antibiotic prescriptions could create an environmental pressure for the transmission of drug-resistant pathogens (Stenehjem et al. 2016), such as methicillin-susceptible *Staphylococcus aureus* (MRSA), Vancomycin-resistant *Enterococci* (VRE), and Multidrug-resistant *Pseudomonas aeruginosa*. A new report in 2022 (World Health Organization 2022) revealed that high levels (above 50%) of resistance were reported in bacteria frequently causing bloodstream infections in hospitals, such as *Klebsiella pneumoniae* and *Acinetobacter spp*. These life-threatening infections require treatment with last-resort antibiotics, such as *carbapenems*. Therefore, hospitals are believed as the epicenter of the spread of many drug-resistant pathogens. How to reduce health care-associated infection and the spread of antimicrobial resistance in hospitals has always become a focus of concern.

As is well known, deterministic differential equation models have been developed to simulate the transmission dynamics of antimicrobial pathogens in hospital populations, where interventions such as hand hygiene, staff cohorting, antibiotic stewardship, treatment accuracy, de-colonization, and isolation have been shown as effective strategies to prevent and control the outbreak of nosocomial infections (Austin et al. 1999; Bonhoeffer et al. 1997; Cen et al. 2017; Cooper et al. 2004; D'Agata et al. 2005; Feng et al. 2019; Smith et al. 2004). Indeed the foundations of epidemic modelling are largely based upon deterministic equations for the dynamics of populations. However, deterministic models are only suitable when the numbers of the susceptible and the infective are large (Bailey 1964). Usually disease outbreaks start from only a few cases, and therefore incorporating stochasticity into the deterministic compartmental models is necessary. Moreover, stochastic models can pick up intrinsic perturbations and give a more accurate prediction, especially if the population size is small (Sun and Hsieh 2010). There are various types of stochastic fluctuations which can be incorporated into the deterministic dynamics according to different situations. Among these consist of making the constant parameters under the influence of direct random fluctuation using Gaussian white noise (see e.g. Wang et al. 2018, 2021). This is a routine method to include the effect of environmental variation in the disease transmission coefficient. In reality, the death and discharge rate of patients staying in hospitals is subject to change stochastically: patients without nosocomial infections may experience low death rate and high discharge rate, whereas infected patients may experience the opposite. Given the small number of hospital patient population, any unexpected change

of population in each compartment would significantly alter the distribution of different patient types hence impact the transmission dynamics. For example, a random death or discharge of the only infectious patient could make the pathogen extinct right away. Thus models considering randomness could generate rich simulated scenarios that coincide with realistic observations. Browne et al. (2017) introduced randomness in the infected patient population and obtained almost surely exponential stability in probability of solution for a reduced two-dimensional stochastic differential equation (SDE) model.

In this paper, we investigate a six-dimensional SDE model with features including (1) uncolonized, colonized, and infected patients; (2) co-circulation of sensitive and resistant bacterial strains; and (3) randomness of death and discharge for all patients. For this model, we will mainly carry out the investigation of dynamical behaviors including the stochastic extinction of nosocomial infections and existence of ergodic stationary distribution, as well as the numerical simulations and analysis. The main contributions and innovations in this paper are the following aspects:

(1) A sufficient criterion on stochastic extinction of nosocomial pathogens is established by applying the spectral radius analysis method which is extended from deterministic models or stochastic models with only one infection route to our stochastic model with sensitive and resistant strains infection routes.
(2) We find a threshold depending on the variance of the random events, under which the model admits a stationary distribution with solutions being ergodic by constructing a suitable Lyapunov function, and further derive the spectral radius form of stochastic threshold value in the special case.
(3) In the numerical simulations, we first calibrate the transmission rates to known range of the healthcare associated infection acquisition, and then conduct global sensitivity analysis to investigate the influence of the key parameters on the basic reproductive number for nosocomial outbreak and the healthcare associated infection acquisition. Afterwards we explore the effect of prevention and control strategies on the prevalence of nosocomial infection.
(4) The numerical examples are provided to verify the stochastic extinction of nosocomial pathogens and to compare the behaviors of stochastic model and the corresponding deterministic model.

The rest of this paper is organized as follows. Model description is given in next section. Stochastic extinction and the existence of a ergodic stationary distribution of solutions are investigated in Sect. 3. Numerical simulations are provided in Sect. 4. A brief conclusion and discussion is presented in Sect. 5.

2 Model description

Nosocomial infection is also called hospital-acquired infection, including those infections occurred during hospitalization or acquired in hospital but occurred after discharge from hospital. The main infection targets are patients, hospital staff, emergency cases, visitors and patients' families. It is usually divided into two kinds: exogenous infections (or cross infections) and endogenous infections (or autogenous infections).

Pathogens causing exogenous infections come from outside the patient's body, for instance, other patients, carriers of pathogens (hospital staff and visitors), contaminated medical equipment, blood products, the ward environment. While the pathogens responsible for endogenous infection are normal flora within or on the surface of the patient's body. Usually, due to the long-term use of antibiotics, immunosuppressants, or hormones by patients, the patient's microbiota is dysregulated, and lead to abnormal proliferation of drug-sensitive bacteria and development of drug-resistant bacteria.

We consider the co-circulation of antibiotic-sensitive and antibiotic-resistant bacterial strains among patients admitted in a hospital. Denote S as the uncolonized patients, E and E_R respectively as patients colonized by sensitive and resistant strain, I and I_R as patients infected by sensitive and resistant strain, and R as patients whose infections are under control after sufficient periods of antibiotic treatments.

We assume a constant patient admission rate Λ and assume that all newly admitted patients are uncolonized. Patients staying in the hospital are assumed to experience an average rate resulted from death and discharge, μ, and are subject to extra randomness based on their infection status. That is, patients in each compartment may experience an extra death and discharge rate modeled by a Wiener process, $B_i(t)$ $(1 \leq i \leq 6)$, where $dB_i(t)$ follows a normal distribution with mean zero and variance dt. In other words, the extra rate of per-unit random death and discharge for each patient class will follow a normal distribution with mean zero and variance σ_i $(1 \leq i \leq 6)$.

Infected patients are assumed to experience excess constant death rates, d_1 and d_2, with respect to infection of sensitive and resistant strains. We ignore the roles of transmission by healthcare workers in our model, and assume β_1 and β_2 as the transmission rates of sensitive and resistant strains. Occasionally, patients may develop acute infections upon immediate contraction with bacteria. So we assume patients contracting the sensitive strain would either enter the colonized class with a probability of p (slow progression) or enter the infected class with a probability of $1-p$ (fast progression). Patients contracting the resistant strain would follow similar dynamics with a colonization probability of q and infection probability of $1-q$. Patients colonized with sensitive and resistant strains can develop infections at rate δ and ν, respectively. Infected patients with sensitive and resistant strains may have their infections under control by appropriate antibiotics at rate k and α, respectively, and then enter the class R where they stop spreading the bacteria to others. Patients infected with susceptible strain would develop mutations against the empiric antibiotics at rate η and become infected by the resistant strain. Particularly, we assume well-treated patients may terminate the treatment at rate γ and may either return to the infected class with probability θ or stay colonized by the sensitive strain with probability $1-\theta$. The model equations are then listed below:

$$\begin{cases} dS = (\Lambda - \mu S - (\beta_1 I + \beta_2 I_R)S)dt + \sigma_1 S dB_1(t), \\ dE = (p\beta_1 SI - (\mu+\delta)E + (1-\theta)\gamma R)dt + \sigma_2 E dB_2(t), \\ dI = ((1-p)\beta_1 SI + \delta E - (\eta+\mu+d_1+k)I + \theta\gamma R)dt + \sigma_3 I dB_3(t), \\ dE_R = (q\beta_2 SI_R - (\mu+\nu)E_R)dt + \sigma_4 E_R dB_4(t), \\ dI_R = ((1-q)\beta_2 SI_R + \eta I - (\alpha+\mu+d_2)I_R + \nu E_R)dt + \sigma_5 I_R dB_5(t), \\ dR = (kI - (\mu+\gamma)R + \alpha I_R)dt + \sigma_6 R dB_6(t), \end{cases} \tag{2.1}$$

with initial values $S(0) > 0$ and $E(0), I(0), E_R(0), I_R(0), R(0) \geq 0$. $B_i(t)$ $(1 \leq i \leq 6)$ are mutually independent standard Brownian motions with $B_i(0) = 0$, and $\sigma_i^2 > 0$ denotes the intensity of $B_i(t)$, respectively. All parameters in model (2.1) are positive constants.

3 Main results

Let $(\Omega, \mathcal{F}, \{\mathcal{F}_t\}_{t\geq 0}, \mathbb{P})$ be a complete probability space with a filtration $\{\mathcal{F}_t\}_{t\geq 0}$ satisfying the usual conditions. We assume that model (2.1) is defined on probability space $(\Omega, \mathcal{F}, \{\mathcal{F}_t\}_{t\geq 0}, \mathbb{P})$. Denote $\mathbb{R}^n_+ = \{x = (x_1, x_2, \ldots, x_n) \in \mathbb{R}^n : x_i > 0, 1 \leq i \leq n\}$. For convenience, we denote $x(t) = (S(t), E(t), I(t), E_R(t), I_R(t), R(t))$.

Lemma 3.1 *For any initial value $x(0) \in \mathbb{R}^6_+$, solution $x(t)$ of model (2.1) exists uniquely and remains in $\mathbb{R}^6_+$ for all $t \geq 0$ with probability one.*

The proof of Lemma 3.1 is similar to Theorem 3.1 given in Mao (2008) by using the following assistant function

$$V(x) = \left(S - a - a\ln\frac{S}{a}\right) + (E - 1 - \ln E) + (I - 1 - \ln I) + (E_R - 1 - \ln E_R) + (I_R - 1 - \ln I_R) + (R - 1 - \ln R)$$

with $a = \min\{\frac{\mu+d_1}{\beta_1}, \frac{\mu+d_2}{\beta_2}\}$.

Next, we introduce the following results on the stationary distribution and ergodic properties of solutions for stochastic differential equations.

Let $\mathbf{y}(t) = (y_1(t), y_2(t), \ldots, y_n(t))$ be a regular time-homogeneous Markov process in $\mathbb{R}^n_+$ described by the following stochastic differential equation

$$d\mathbf{y}(t) = b(\mathbf{y}(t))dt + \sum_{r=1}^{k} \sigma_r(\mathbf{y}(t))dB_r(t), \tag{3.1}$$

where $b(\mathbf{y}) = (b_1(\mathbf{y}), b_2(\mathbf{y}), \ldots, b_n(\mathbf{y}))$, $\sigma_r(\mathbf{y}) = (\sigma_r^1(\mathbf{y}), \sigma_r^2(\mathbf{y}) \ldots, \sigma_r^n(\mathbf{y}))$, and $B_r(t)$ $(r = 1, 2, \ldots, k)$ are independent standard Brownian motions defined on $(\Omega, \mathcal{F}, \{\mathcal{F}_t\}_{t\geq 0}, \mathbb{P})$. The diffusion matrix $\mathbf{A}$ of model (3.1) is defined as follow

$$\mathbf{A}(\mathbf{y}) = (a_{ij}(\mathbf{y})), \quad a_{ij}(\mathbf{y}) = \sum_{r=1}^{k} \sigma_r^i(\mathbf{y})\sigma_r^j(\mathbf{y}).$$

Lemma 3.2 (Khasminskii 2011; Zhu and Yin 2007) The Markov process $\mathbf{y}(t)$ has a unique ergodic stationary distribution $\pi(\cdot)$ if there exists a bounded open domain $U \subset \mathbb{R}^n_+$ with regular boundary and closure $\bar{U} \subset \mathbb{R}^n_+$, such that the following two conditions are satisfied.

(i) *In the domain U and some neighborhood thereof, the smallest eigenvalue of the diffusion matrix $\mathbf{A}(\mathbf{y})$ is bounded away from zero.*

(ii) *There exists a nonnegative $\mathcal{C}^2$-function $V(\cdot) : \mathbb{R}^n_+ \to \mathbb{R}_+$ such that for some constant $\alpha > 0$*

$$\mathscr{L}V(\mathbf{y}) = \sum_{i=1}^{n} b_i(\mathbf{y})\frac{\partial V(\mathbf{y})}{\partial y_i} + \frac{1}{2}\sum_{i,j=1}^{n} a_{ij}(\mathbf{y})\frac{\partial^2 V(\mathbf{y})}{\partial y_i y_j} \leq -\alpha, \ \forall\, \mathbf{y} \in \mathbb{R}^n_+ \setminus U.$$

Furthermore, if $f(\mathbf{y})$ is a Borel measurable function with respect to measure π defined on $\mathbb{R}^n_+$, then we also have

$$\mathbb{P}\left(\lim_{T\to\infty}\frac{1}{T}\int_0^T f(\mathbf{y}(t))dt = \int_{\mathbb{R}^n_+} f(\mathbf{y})\pi(d\mathbf{y})\right) = 1.$$

3.1 Stochastic extinction

In this subsection, we first focus on the possibility for nosocomial pathogens to become extinct. By applying spectral radius analysis method, we will establish the sufficient criterion on stochastic extinction of nosocomial pathogens. For this purpose, we need to introduce the corresponding deterministic version of model (2.1). When $\sigma_i \equiv 0$ $(i = 1, \ldots, 6)$, model (2.1) degenerates into the following deterministic one

$$\begin{cases} \frac{dS}{dt} = \Lambda - \mu S - (\beta_1 I + \beta_2 I_R)S, \\ \frac{dE}{dt} = p\beta_1 SI - (\mu+\delta)E + (1-\theta)\gamma R, \\ \frac{dI}{dt} = (1-p)\beta_1 SI + \delta E - (\eta+\mu+d_1+k)I + \theta\gamma R, \\ \frac{dE_R}{dt} = q\beta_2 SI_R - (\mu+\nu)E_R, \\ \frac{dI_R}{dt} = (1-q)\beta_2 SI_R + \eta I - (\alpha+\mu+d_2)I_R + \nu E_R, \\ \frac{dR}{dt} = kI + \alpha I_R - (\mu+\gamma)R. \end{cases} \tag{3.2}$$

Obviously, model (3.2) has a unique disease-free equilibrium $P_0 = (S_0, 0, 0, 0, 0, 0)$, where $S_0 = \frac{\Lambda}{\mu}$. Using next generation matrix approach (Driessche and Watmough 2002), the rates of appearance of new infection and transition of patients are

$$\mathcal{F} = \begin{pmatrix} p\beta_1 SI + (1-\theta)\gamma R \\ (1-p)\beta_1 SI + \delta E + \theta\gamma R \\ q\beta_2 SI_R \\ (1-q)\beta_2 SI_R + \eta I + \nu E_R \\ kI + \alpha I_R \end{pmatrix}, \ \mathcal{V} = \begin{pmatrix} (\mu+\delta)E \\ (\eta+\mu+d_1+k)I \\ (\mu+\nu)E_R \\ (\alpha+\mu+d_2)I_R \\ (\mu+\gamma)R \end{pmatrix},$$

respectively. Calculating the Jacobi matrices of $\mathcal{F}$ and $\mathcal{V}$ at P_0, we obtain

$$\mathbf{F} = \begin{pmatrix} 0 & p\beta_1 S_0 & 0 & 0 & (1-\theta)\gamma \\ \delta & (1-p)\beta_1 S_0 & 0 & 0 & \theta\gamma \\ 0 & 0 & 0 & q\beta_2 S_0 & 0 \\ 0 & \eta & \nu & (1-q)\beta_2 S_0 & 0 \\ 0 & k & 0 & \alpha & 0 \end{pmatrix},$$

$$\mathbf{V} = \begin{pmatrix} \mu+\delta & 0 & 0 & 0 & 0 \\ 0 & \mu+\eta+k+d_1 & 0 & 0 & 0 \\ 0 & 0 & \mu+\nu & 0 & 0 \\ 0 & 0 & 0 & \mu+\alpha+d_2 & 0 \\ 0 & 0 & 0 & 0 & \mu+\gamma \end{pmatrix}.$$

Further calculating $\mathbf{V}^{-1}\mathbf{F}$, we can obtain

$$\mathbf{V}^{-1}\mathbf{F} = \begin{pmatrix} 0 & \frac{p\beta_1 S_0}{\mu+\delta} & 0 & 0 & \frac{(1-\theta)\gamma}{\mu+\delta} \\ \frac{\delta}{\eta+\mu+d_1+k} & \frac{(1-p)\beta_1 S_0}{\eta+\mu+d_1+k} & 0 & 0 & \frac{\theta\gamma}{\eta+\mu+d_1+k} \\ 0 & 0 & 0 & \frac{q\beta_2 S_0}{\mu+\nu} & 0 \\ 0 & \frac{\eta}{\alpha+\mu+d_2} & \frac{\nu}{\alpha+\mu+d_2} & \frac{(1-q)\beta_2 S_0}{\alpha+\mu+d_2} & 0 \\ 0 & \frac{k}{\mu+\gamma} & 0 & \frac{\alpha}{\mu+\gamma} & 0 \end{pmatrix}.$$

Thus, the basic reproduction number of model (3.2) can be defined by $\mathcal{R}_0 = \rho(\mathbf{V}^{-1}\mathbf{F})$, where ρ denotes the spectral radius of $\mathbf{V}^{-1}\mathbf{F}$. Using the Perron-Trobenius theorem (Berman and Plemmons 1979), the nonnegative matrix $\mathbf{V}^{-1}\mathbf{F}$ has a positive left eigenvector $(\xi_1, \xi_2, \xi_3, \xi_4, \xi_5)$ corresponding to eigenvalue $\mathcal{R}_0$ satisfying

$$(\xi_1, \xi_2, \xi_3, \xi_4, \xi_5)\mathcal{R}_0 = (\xi_1, \xi_2, \xi_3, \xi_4, \xi_5)\mathbf{V}^{-1}\mathbf{F}. \tag{3.3}$$

Theorem 3.1 *If $\sigma_1^2 < 2\mu$, then solution $x(t)$ of model (2.1) with initial value $x(0) \in \mathbb{R}_+^6$ satisfies*

$$\limsup_{t\to\infty} \frac{1}{t} \ln\Big(\rho_1 E(t) + \rho_2 I(t) + \rho_3 E_R(t) + \rho_4 I_R(t) + \rho_5 R(t)\Big) \le m,$$

where

$$\begin{aligned} m = {} & \Big[\frac{\beta_1(\rho_1 p + \rho_2(1-p))}{\rho_2} + \frac{\beta_2(\rho_3 q + \rho_4(1-q))}{\rho_4}\Big]\frac{S_0\sigma_1}{(2\mu-\sigma_1^2)^{\frac{1}{2}}} - \Big(2\sum_{i=2}^{6}\sigma_i^{-2}\Big)^{-1} \\ & + \min\{\mu+\delta, \eta+\mu+d_1+k, \mu+\nu, \alpha+\mu+d_2, \mu+\gamma\}(\mathcal{R}_0-1)\mathbf{I}_{\{\mathcal{R}_0\le 1\}} \\ & + \max\{\mu+\delta, \eta+\mu+d_1+k, \mu+\nu, \alpha+\mu+d_2, \mu+\gamma\}(\mathcal{R}_0-1)\mathbf{I}_{\{\mathcal{R}_0>1\}}, \end{aligned}$$

with $\rho_1 = \frac{\xi_1}{\mu+\delta}$, $\rho_2 = \frac{\xi_2}{\eta+\mu+d_1+k}$, $\rho_3 = \frac{\xi_3}{\mu+\nu}$, $\rho_4 = \frac{\xi_4}{\alpha+\mu+d_2}$ and $\rho_5 = \frac{\xi_5}{\mu+\gamma}$, and $\mathbf{I}$ is an indicator function.

Particularly, if $m < 0$, *then* $\lim_{t\to\infty} E(t) = 0$, $\lim_{t\to\infty} I(t) = 0$, $\lim_{t\to\infty} E_R(t) = 0$, $\lim_{t\to\infty} I_R(t) = 0$, $\lim_{t\to\infty} R(t) = 0$ *a.s., and* $\lim_{t\to\infty} \frac{1}{t}\int_0^t S(s)ds = \int_0^\infty x\pi(x)dx$ *a.s., where* $\pi(x)$ *is given in* (3.5) *below.*

Proof From the first equation of model (2.1) and Lemma 3.1, we can obtain

$$dS \le (\Lambda - \mu S)dt + \sigma_1 S dB_1(t).$$

Consider the following auxiliary system

$$dX = (\Lambda - \mu X)dt + \sigma_1 X dB_1(t). \tag{3.4}$$

It is easy to obtain by Theorem 1.16 in Kutoyants (2004) that system (3.4) has the ergodic property with invariant density

$$\pi(x) = H\sigma_1^{-2} x^{-2-\frac{2\mu}{\sigma_1^2}} e^{-\frac{2\Lambda}{\sigma_1^2 x}} \tag{3.5}$$

for all $x \in (0, \infty)$, here $H = \sigma_1^2 (\frac{2\Lambda}{\sigma_1^2})^{1+\frac{2\mu}{\sigma_1^2}} \Gamma^{-1}(1 + \frac{2\mu}{\sigma_1^2})$ is a constant such that $\int_0^\infty \pi(x)dx = 1$, and any solution $X(t)$ of system (3.4) satisfies

$$\lim_{t\to\infty} \frac{1}{t}\int_0^t X(s)ds = \int_0^\infty x\pi(x)dx \quad a.s.. \tag{3.6}$$

Let $X(t)$ be the solution of system (3.4) with initial value $X(0) = S(0)$. By the comparison theorem of stochastic differential equation (Ikeda and Watanabe 1977), we obtain

$$S(t) \le X(t) \quad \text{for all} \quad t \ge 0 \quad a.s..$$

Now, we define a C^2-function $W : \mathbb{R}^5_+ \to (0, +\infty)$ by

$$W(E, I, E_R, I_R, R) = \rho_1 E + \rho_2 I + \rho_3 E_R + \rho_4 I_R + \rho_5 R.$$

Denote $U = \ln W$. Using Itô formula, we obtain

$$\begin{aligned} dU = {} & \mathscr{L}U dt + \frac{1}{W}\big(\rho_1\sigma_2 E dB_2(t) + \rho_2\sigma_3 I dB_3(t) + \rho_3\sigma_4 E_R dB_4(t) \\ & + \rho_4\sigma_5 I_R dB_5(t) + \rho_5\sigma_6 R dB_6(t)\big), \end{aligned} \tag{3.7}$$

where

$$\begin{aligned}\mathscr{L}U &= \frac{\rho_1}{W}\big(p\beta_1 SI - (\mu+\delta)E + (1-\theta)\gamma R\big) + \frac{\rho_2}{W}\big((1-p)\beta_1 SI + \delta E - (\eta+\mu \\ &\quad + d_1 + k)I + \theta\gamma R\big) + \frac{\rho_3}{W}\big(q\beta_2 SI_R - (\mu+\nu)E_R\big) + \frac{\rho_4}{W}\big((1-q)\beta_2 SI_R \\ &\quad + \eta I - (\alpha+\mu+d_2)I_R + \nu E_R\big) + \frac{\rho_5}{W}\big(kI - (\mu+\gamma)R + \alpha I_R\big) \\ &\quad - \frac{(\rho_1\sigma_2 E)^2}{2W^2} - \frac{(\rho_2\sigma_3 I)^2}{2W^2} - \frac{(\rho_3\sigma_4 E_R)^2}{2W^2} - \frac{(\rho_4\sigma_5 I_R)^2}{2W^2} - \frac{(\rho_5\sigma_6 R)^2}{2W^2} \\ &= \frac{1}{W}\Big\{\rho_1\big(p\beta_1 S_0 I - (\mu+\delta)E + (1-\theta)\gamma R\big) + \rho_1 p\beta_1(S-S_0)I \\ &\quad + \rho_2\big((1-p)\beta_1 S_0 I + \delta E - (\eta+\mu+d_1+k)I + \theta\gamma R\big) \\ &\quad + \rho_2(1-p)\beta_1(S-S_0)I + \rho_3\big(q\beta_2 S_0 I_R - (\mu+\nu)E_R\big) \\ &\quad + \rho_3 q\beta_2 q(S-S_0)I_R + \rho_4\big((1-q)\beta_2 S_0 I_R + \eta I - (\alpha+\mu+d_2)I_R + \nu E_R\big) \\ &\quad + \rho_4\beta_2(1-q)(S-S_0)I_R + \rho_5\big(kI - (\mu+\gamma)R + \alpha I_R\big)\Big\} \\ &\quad - \frac{(\rho_1\sigma_2 E)^2}{2W^2} - \frac{(\rho_2\sigma_3 I)^2}{2W^2} - \frac{(\rho_3\sigma_4 E_R)^2}{2W^2} - \frac{(\rho_4\sigma_5 I_R)^2}{2W^2} - \frac{(\rho_5\sigma_6 R)^2}{2W^2}.\end{aligned}$$

Since

$$\begin{aligned}W^2 &= \left(\rho_1\sigma_2 E\cdot\frac{1}{\sigma_2} + \rho_2\sigma_3 I\cdot\frac{1}{\sigma_3} + \rho_3\sigma_4 E_R\cdot\frac{1}{\sigma_4} + \rho_4\sigma_5 I_R\cdot\frac{1}{\sigma_5} + \rho_5\sigma_6 R\cdot\frac{1}{\sigma_6}\right)^2 \\ &\le \Big[(\rho_1\sigma_2 E)^2 + (\rho_2\sigma_3 I)^2 + (\rho_3\sigma_4 E_R)^2 + (\rho_4\sigma_5 I_R)^2 + (\rho_5\sigma_6 R)^2\Big]\sum_{i=2}^{6}\frac{1}{\sigma_i^2},\end{aligned}$$

and by (3.3), we further obtain

$$\begin{aligned}\mathscr{L}U &\le \frac{\beta_1(S-S_0)I}{W}\Big[\rho_1 p + \rho_2(1-p)\Big] + \frac{\beta_2(S-S_0)I_R}{W}\Big[\rho_3 q + \rho_4(1-q)\Big] - \left(2\sum_{i=2}^{6}\sigma_i^{-2}\right)^{-1} \\ &\quad + \frac{1}{W}(\xi_1,\xi_2,\xi_3,\xi_4,\xi_5)\left(\mathbf{V}^{-1}\mathbf{F}(E,I,E_R,I_R,R)^T - (E,I,E_R,I_R,R)^T\right) \\ &\le \Big[\frac{\beta_1(\rho_1 p + \rho_2(1-p))}{\rho_2} + \frac{\beta_2(\rho_3 q + \rho_4(1-q))}{\rho_4}\Big]|X-S_0| - \left(2\sum_{i=2}^{6}\sigma_i^{-2}\right)^{-1} \\ &\quad + \frac{1}{W}(\mathcal{R}_0-1)(\xi_1 E + \xi_2 I + \xi_3 E_R + \xi_4 I_R + \xi_5 R) \\ &\le \Big[\frac{\beta_1(\rho_1 p + \rho_2(1-p))}{\rho_2} + \frac{\beta_2(\rho_3 q + \rho_4(1-q))}{\rho_4}\Big]|X-S_0| - \Big(2\sum_{i=2}^{6}\sigma_i^{-2}\Big)^{-1} \\ &\quad + \min\{\mu+\delta, \eta+\mu+d_1+k, \mu+\nu, \alpha+\mu+d_2, \mu+\gamma\}(\mathcal{R}_0-1)\mathbf{I}_{\{\mathcal{R}_0\le 1\}} \\ &\quad + \max\{\mu+\delta, \eta+\mu+d_1+k, \mu+\nu, \alpha+\mu+d_2, \mu+\gamma\}(\mathcal{R}_0-1)\mathbf{I}_{\{\mathcal{R}_0>1\}},\end{aligned}$$

where

$$\mathbf{I}_{\{\mathcal{R}_0\le 1\}}=\begin{cases}1, & \text{if } \mathcal{R}_0\le 1,\\ 0, & \text{if } \mathcal{R}_0>1,\end{cases} \text{ and } \mathbf{I}_{\{\mathcal{R}_0>1\}}=\begin{cases}1, & \text{if } \mathcal{R}_0>1,\\ 0, & \text{if } \mathcal{R}_0\le 1.\end{cases}$$

By (3.7) and the above inequality, we have

$$\begin{aligned}dU\le&\Big[\frac{\beta_1(\rho_1 p+\rho_2(1-p))}{\rho_2}+\frac{\beta_2(\rho_3 q+\rho_4(1-q))}{\rho_4}\Big]|X-S_0|-\left(2\sum_{i=2}^{6}\sigma_i^{-2}\right)^{-1}\\&+\min\{\mu+\delta,\eta+\mu+d_1+k,\mu+\nu,\alpha+\mu+d_2,\mu+\gamma\}(\mathcal{R}_0-1)\mathbf{I}_{\{\mathcal{R}_0\le 1\}}\\&+\max\{\mu+\delta,\eta+\mu+d_1+k,\mu+\nu,\alpha+\mu+d_2,\mu+\gamma\}(\mathcal{R}_0-1)\mathbf{I}_{\{\mathcal{R}_0>1\}}\\&+\frac{1}{W}\Big(\rho_1\sigma_2 E dB_2(t)+\rho_2\sigma_3 I dB_3(t)+\rho_3\sigma_4 E_R dB_4(t)+\rho_4\sigma_5 I_R dB_5(t)+\rho_5\sigma_6 R dB_6(t)\Big).\end{aligned}$$

Integrating the above inequality from 0 to t and then dividing t on both sides leads to

$$\begin{aligned}\frac{U(t)}{t}\le&\frac{U(0)}{t}+\left[\frac{\beta_1(\rho_1 p+\rho_2(1-p))}{\rho_2}+\frac{\beta_2(\rho_3 q+\rho_4(1-q))}{\rho_4}\right]\frac{1}{t}\int_0^t|X(s)-S_0|ds\\&+\min\{\mu+\delta,\eta+\mu+d_1+k,\mu+\nu,\alpha+\mu+d_2,\mu+\gamma\}(\mathcal{R}_0-1)\mathbf{I}_{\{\mathcal{R}_0\le 1\}}\\&+\max\{\mu+\delta,\eta+\mu+d_1+k,\mu+\nu,\alpha+\mu+d_2,\mu+\gamma\}(\mathcal{R}_0-1)\mathbf{I}_{\{\mathcal{R}_0>1\}}\\&-\left(2\sum_{i=2}^{6}\sigma_i^{-2}\right)^{-1}+\frac{1}{t}[M_1(t)+M_2(t)+M_3(t)+M_4(t)+M_5(t)],\end{aligned}\tag{3.8}$$

where $M_1(t)=\int_0^t\frac{\rho_1\sigma_2 E(s)}{W(s)}dB_2(s)$, $M_2(t)=\int_0^t\frac{\rho_2\sigma_3 I(s)}{W(s)}dB_3(s)$, $M_3(t)=\int_0^t\frac{\rho_3\sigma_4 E_R(s)}{W(s)}dB_4(s)$, $M_4(t)=\int_0^t\frac{\rho_4\sigma_5 I_R(s)}{W(s)}dB_5(s)$ and $M_5(t)=\int_0^t\frac{\rho_5\sigma_6 R(s)}{W(s)}dB_6(s)$ are five local martingales. Because the quadratic variation of $M_1(t)$ is

$$\langle M_1,M_1\rangle_t=(\rho_1\sigma_2)^2\int_0^t\left(\frac{E(s)}{W(s)}\right)^2ds\le\sigma_2^2 t,$$

by using the strong law of large numbers for martingale, it yields (Mao 2008) $\lim_{t\to\infty}\frac{M_1(t)}{t}=0$. Similarly, we can obtain $\lim_{t\to\infty}\frac{M_i(t)}{t}=0$ $(i=2,\dots,5)$. In addition, since $X(t)$ is ergodic and $\int_0^\infty x\pi(x)dx<\infty$, we have

$$\lim_{t\to\infty}\frac{1}{t}\int_0^\infty|X(s)-S_0|ds=\int_0^\infty|x-S_0|\pi(x)dx\le\left(\int_0^\infty(x-S_0)^2\pi(x)dx\right)^{\frac{1}{2}}.\tag{3.9}$$

Furthermore, we calculate $\int_0^\infty (x-S_0)^2\pi(x)dx$. We first have $\int_0^\infty (x-S_0)^2\pi(x)dx = a_0 - 2a_1S_0 + S_0^2$, where $a_0 = \int_0^\infty x^2\pi(x)dx$ and $a_1 = \int_0^\infty x\pi(x)dx$. Because

$$\begin{aligned} a_0 &= \int_0^\infty x^2\pi(x)dx = H\sigma_1^{-2}\int_0^\infty x^{-\frac{2\mu}{\sigma_1^2}} e^{-\frac{2\mu}{\sigma_1^2 x}}dx \\ &= H\sigma_1^{-2}\left(\frac{2\Lambda}{\sigma_1^2}\right)^{1-\frac{2\mu}{\sigma_1^2}}\int_0^\infty t^{\frac{2\mu}{\sigma_1^2}-2}e^{-t}dt \\ &= H\sigma_1^{-2}\left(\frac{2\Lambda}{\sigma_1^2}\right)^{1-\frac{2\mu}{\sigma_1^2}}\Gamma\left(\frac{2\mu}{\sigma_1^2}\right) \\ &= \left(\frac{2\Lambda}{\sigma_1^2}\right)^2\frac{\Gamma\left(\frac{2\mu}{\sigma_1^2}-1\right)}{\Gamma\left(\frac{2\mu}{\sigma_1^2}+1\right)} = \frac{2\Lambda^2}{\mu(2\mu-\sigma_1^2)} = \frac{2\Lambda S_0}{2\mu-\sigma_1^2} \end{aligned}$$

and

$$\begin{aligned} a_1 &= \int_0^\infty x\pi(x)dx = H\sigma_1^{-2}\int_0^\infty x^{-(1+\frac{2\mu}{\sigma_1^2})} e^{-\frac{2\Lambda}{\sigma_1^2 x}}dx \\ &= H\sigma_1^{-2}\left(\frac{2\Lambda}{\sigma_1^2}\right)^{-\frac{2\mu}{\sigma_1^2}}\int_0^\infty t^{\frac{2\mu}{\sigma_1^2}-1}e^{-t}dt \\ &= H\sigma_1^{-2}\left(\frac{2\Lambda}{\sigma_1^2}\right)^{-\frac{2\mu}{\sigma_1^2}}\Gamma\left(\frac{2\mu}{\sigma_1^2}\right) \\ &= \frac{2\Lambda}{\sigma_1^2}\frac{\Gamma\left(\frac{2\mu}{\sigma_1^2}\right)}{\Gamma\left(\frac{2\mu}{\sigma_1^2}+1\right)} = \frac{\Lambda}{\mu} = S_0. \end{aligned}$$

So, we obtain

$$\int_0^\infty (x-S_0)^2\pi(x)dx = \frac{S_0^2\sigma_1^2}{2\mu-\sigma_1^2}. \tag{3.10}$$

Taking the superior limit on both sides in (3.8) and combining with (3.9), (3.10) and $\lim_{t\to\infty}\frac{M_i(t)}{t} = 0$ for $i = 1,\ldots,5$, we obtain

$$\begin{aligned} &\limsup_{t\to\infty}\frac{U(t)}{t} \\ &\le \Big[\frac{\beta_1(\rho_1 p+\rho_2(1-p))}{\rho_2} + \frac{\beta_2(\rho_3 q+\rho_4(1-q))}{\rho_4}\Big]\frac{S_0\sigma_1}{(2\mu-\sigma_1^2)^{\frac{1}{2}}} - \Big(2\sum_{i=2}^{6}\sigma_i^{-2}\Big)^{-1} \\ &\quad + \min\{\mu+\delta,\eta+\mu+d_1+k,\mu+\nu,\alpha+\mu+d_2,\mu+\gamma\}(\mathcal{R}_0-1)\mathbf{I}_{\{\mathcal{R}_0\le 1\}} \\ &\quad + \max\{\mu+\delta,\eta+\mu+d_1+k,\mu+\nu,\alpha+\mu+d_2,\mu+\gamma\}(\mathcal{R}_0-1)\mathbf{I}_{\{\mathcal{R}_0>1\}} = m, \end{aligned}$$

which is the required statement. If $m < 0$, then it is concluded that

$$\limsup_{t\to\infty} \frac{\ln E(t)}{t} < 0, \ \limsup_{t\to\infty} \frac{\ln I(t)}{t} < 0, \ \limsup_{t\to\infty} \frac{\ln E_R(t)}{t} < 0,$$
$$\limsup_{t\to\infty} \frac{\ln I_R(t)}{t} < 0, \ \limsup_{t\to\infty} \frac{\ln R(t)}{t} < 0, \ a.s..$$

It means $\limsup_{t\to\infty} E(t) = 0$ $a.s.$, then by the positivity of the solution we further obtain $\lim_{t\to\infty} E(t) = 0$ $a.s.$. Similarly, we can obtain $\lim_{t\to\infty} I(t) = \lim_{t\to\infty} E_R(t) = \lim_{t\to\infty} I_R(t) = \lim_{t\to\infty} R(t) = 0$ $a.s.$.

When $\lim_{t\to\infty} E(t) = 0$, $\lim_{t\to\infty} I(t) = 0$, $\lim_{t\to\infty} E_R(t) = 0$, $\lim_{t\to\infty} I_R(t) = 0$, $\lim_{t\to\infty} R(t) = 0$ $a.s.$, then from the first equation of model (2.1) we further obtain

$$dS = (\Lambda - \mu S)dt + \sigma_1 S dB_1(t),$$

which is equivalent to the Eq. (3.4). Thus, from (3.6) we immediately obtain $\lim_{t\to\infty} \frac{1}{t}\int_0^t S(s)ds = \int_0^\infty x\pi(x)dx$ $a.s.$ This finishes the proof. □

Remark 3.1 Theorem 3.1 indicates that when $\sigma_1^2 < 2\mu$ and $m < 0$ hold, nosocomial infection go to extinction with probability one. Meanwhile, the distribution of uncolonized patients $S(t)$ weakly converge to the ergodic invariant distribution with the density $\pi(x)$. This result provides a distinction between our model (2.1) and its deterministic version (3.2), which indicates that large randomness in death and discharge can lead to pathogen extinction in the stochastic system while the pathogens are prevalent in the deterministic system under the same parameter values since in this case there exists a possibility that the basic reproduction number $\mathcal{R}_0$ for the deterministic model (3.2) is greater than 1. A numerical example provided in Sect. 4.5 shows that the solution for the deterministic model is uniformly persistent as $\mathcal{R}_0 = 1.048$ while the solution for the stochastic model becomes extinct (see Fig. 14). Therefore, randomness may play a critical role in the transmission dynamics of nosocomial pathogens and should be considered in modeling when significant uncertainty exists in the outflow of patient population.

Remark 3.2 In the proof of Theorem 3.1, the spectral radius analysis method is used, which is applied to deterministic models or stochastic models with only one infection route. However, model (2.1) is six-dimensional SDE one and there are sensitive and resistant strains infection routes, so the construction of Lyapunov function in Theorem 3.1 is challenging and innovative by using the spectral radius analysis method. This is a highlight in this paper. On the other hand, although the explicit expression of the basic reproduction number $\mathcal{R}_0$ for the deterministic model (3.2) can not be obtained owing to the complexity of $\mathbf{V}^{-1}\mathbf{F}$, an equivalent representation will be given in a special situation in the next subsection.

3.2 Stationary distribution

We define the basic reproductive number for nosocomial outbreak

$$\widetilde{\Re}_0^S = \max\{\widetilde{\Re}_{01}^S, \widetilde{\Re}_{02}^S\},$$

where

$$\widetilde{\Re}_{01}^S = \frac{p\beta_1\Lambda\delta}{(\mu+\frac{\sigma_1^2}{2})(\mu+\delta+\frac{\sigma_2^2}{2})(\eta+\mu+k+d_1+\frac{\sigma_3^2}{2})} + \frac{(1-p)\beta_1\Lambda}{(\mu+\frac{\sigma_1^2}{2})(\eta+\mu+k+d_1+\frac{\sigma_3^2}{2})} + \frac{\theta\gamma k}{(\eta+\mu+k+d_1+\frac{\sigma_3^2}{2})(\mu+\gamma+\frac{\sigma_6^2}{2})}$$

and

$$\widetilde{\Re}_{02}^S = \frac{q\beta_2\Lambda\nu}{(\mu+\frac{\sigma_1^2}{2})(\mu+\nu+\frac{\sigma_4^2}{2})(\alpha+\mu+d_2+\frac{\sigma_5^2}{2})} + \frac{(1-q)\beta_2\Lambda}{(\mu+\frac{\sigma_1^2}{2})(\alpha+\mu+d_2+\frac{\sigma_5^2}{2})} + \frac{\theta\gamma\alpha\eta}{(\eta+\mu+k+d_1+\frac{\sigma_3^2}{2})(\alpha+\mu+d_2+\frac{\sigma_5^2}{2})(\mu+\gamma+\frac{\sigma_6^2}{2})}.$$

Theorem 3.2 *If $\widetilde{\Re}_0^S > 1$, then solution $x(t)$ of model (2.1) with initial value $x(0) \in \mathbb{R}_+^6$ is ergodic and admits a stationary distribution $\pi(\cdot)$.*

Proof From $\widetilde{\Re}_0^S > 1$, we can choose a positive constant ϕ such that $\lambda > 0$, where

$$\lambda \triangleq (\eta+\mu+d_1+k+\frac{\sigma_3^2}{2})(\widetilde{\Re}_{01}^S-1) + \phi(\alpha+\mu+d_2+\frac{\sigma_5^2}{2})(\widetilde{\Re}_{02}^S-1).$$

In fact, if $\widetilde{\Re}_{01}^S > 1$ and $\widetilde{\Re}_{02}^S > 1$ we can choose $\phi = 1$, if $\widetilde{\Re}_{01}^S \le 1$ and $\widetilde{\Re}_{02}^S > 1$ we can choose $\phi > 1$ large enough, and if $\widetilde{\Re}_{01}^S > 1$ and $\widetilde{\Re}_{02}^S \le 1$ we can choose $\phi > 0$ small enough.

The diffusion matrix of model (2.1) is given by

$$\mathbf{A} = \mathrm{diag}(\sigma_1^2S^2, \sigma_2^2E^2, \sigma_3^2I^2, \sigma_4^2E_R^2, \sigma_5^2I_R^2, \sigma_6^2R^2).$$

Let Z be any bounded domain in $\mathbb{R}_+^6$ with the closure $\bar{Z} \subset \mathbb{R}_+^6$, then we obviously have

$$\Delta = \min_{x\in\bar{Z}}\{\sigma_1^2S^2, \sigma_2^2E^2, \sigma_3^2I^2, \sigma_4^2E_R^2, \sigma_5^2I_R^2, \sigma_6^2R^2\} > 0,$$

where $x = (S, E, I, E_R, I_R, R)$. For any $x \in \bar{Z}$ and $\zeta = (\zeta_1, \zeta_2, \ldots, \zeta_6)^T \in \mathbb{R}_+^6$, we further obtain

$$\zeta^T\mathbf{A}\zeta = \sigma_1^2S^2\zeta_1^2 + \sigma_2^2E^2\zeta_2^2 + \sigma_3^2I^2\zeta_3^2 + \sigma_4^2E_R^2\zeta_4^2 + \sigma_5^2I_R^2\zeta_5^2 + \sigma_6^2R^2\zeta_6^2 \ge \Delta|\zeta|^2,$$

which indicates that the smallest eigenvalue of the diffusion matrix $\mathbf{A}(x)$ is bounded away from zero in the domain Z and some neighborhood thereof, i.e., condition (i) in Lemma 3.2 is satisfied.

Now, we show the feasibility of condition (ii) of Lemma 3.2. For this purpose, two steps are organized to formulate a suitable Lyapunov function $V(x)$ and a compact subset U_ε such that $\mathscr{L}V(x) \leq -1$ for all $x \in \mathbb{R}^6_+ \backslash U_\varepsilon$, where $\mathscr{L}V(x)$ is defined in condition (ii) of Lemma 3.2, which is the factor of dt in Itô formula (see Mao 2008) for $V(x)$, where $x = (S, E, I, E_R, I_R, R)$.

Step 1 Construct a non-negative Lyapunov function $V(x)$.

Choose a sufficiently small positive constant θ satisfying $\rho \triangleq \mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2 \vee \sigma_5^2 \vee \sigma_6^2) > 0$. Then, we define a C^2-function $H : \mathbb{R}^6_+ \to (0, +\infty)$ by

$$H(x) = MV_1 + V_2 + V_3,$$

where

$$\begin{aligned}
V_1 &= -\ln I - c_{11}\ln E - \phi(\ln I_R + c_{21}\ln E_R) - (c_{12} + c_{13} + \phi(c_{22} + c_{23}))\ln S \\
&\quad - c_{14}\ln R - \phi(c_{24}\ln I + c_{25}\ln R) + \frac{\beta_1(c_{12} + c_{13} + \phi(c_{22} + c_{23}))}{\eta} I_R, \\
V_2 &= -\ln S - \ln E - \ln I - \ln E_R - \ln R - \frac{\beta_1}{\eta} I_R, \\
V_3 &= \frac{1}{\theta + 1}(S + E + I + E_R + I_R + R)^{\theta+1},
\end{aligned}$$

with

$$\begin{aligned}
c_{11} &= \frac{p\beta_1\Lambda\delta}{\left(\mu + \frac{\sigma_1^2}{2}\right)\left(\mu + \delta + \frac{\sigma_2^2}{2}\right)^2}, \quad c_{12} = \frac{p\beta_1\Lambda\delta}{\left(\mu + \frac{\sigma_1^2}{2}\right)^2\left(\mu + \delta + \frac{\sigma_2^2}{2}\right)}, \\
c_{13} &= \frac{(1-p)\beta_1\Lambda}{\left(\mu + \frac{\sigma_1^2}{2}\right)^2}, \\
c_{14} &= \frac{\theta\gamma k}{\left(\mu + \gamma + \frac{\sigma_6^2}{2}\right)^2}, \quad c_{21} = \frac{q\beta_2\Lambda\nu}{\left(\mu + \frac{\sigma_1^2}{2}\right)\left(\mu + \nu + \frac{\sigma_4^2}{2}\right)^2}, \\
c_{22} &= \frac{q\beta_2\Lambda\nu}{\left(\mu + \frac{\sigma_1^2}{2}\right)^2\left(\mu + \nu + \frac{\sigma_4^2}{2}\right)}, \\
c_{23} &= \frac{(1-q)\beta_2\Lambda}{\left(\mu + \frac{\sigma_1^2}{2}\right)^2}, \quad c_{24} = \frac{\theta\gamma\alpha\eta}{\left(\eta + \mu + d_1 + k + \frac{\sigma_3^2}{2}\right)^2\left(\mu + \gamma + \frac{\sigma_6^2}{2}\right)},
\end{aligned}$$

$$c_{25} = \frac{\theta\gamma\alpha\eta}{\left(\eta+\mu+d_1+k+\frac{\sigma_3^2}{2}\right)\left(\mu+\gamma+\frac{\sigma_6^2}{2}\right)^2}$$

and M is a positive constant satisfying the condition

$$-M\lambda + J < -2,$$

where

$$J = \sup_{I_R\in\mathbb{R}_+}\left\{-\frac{\rho}{2}{I_R}^{\theta+1} + (\beta_2+\frac{\beta_1}{\eta}(\alpha+\mu+d_2))I_R + 5\mu+\delta+\eta+k \right.$$
$$\left. +\nu+\gamma+d_1+\frac{\sigma_1^2}{2}+\frac{\sigma_2^2}{2}+\frac{\sigma_3^2}{2}+\frac{\sigma_4^2}{2}+\frac{\sigma_6^2}{2}+D\right\} < \infty$$

and

$$D = \sup_{x\in\mathbb{R}_+^6}\left\{\Lambda(S+E+I+E_R+I_R+R)^\theta - \frac{\rho}{2}(S+E+I+E_R+I_R+R)^{\theta+1}\right\} < \infty.$$

Since $H(x)$ is continuous and $\liminf_{k\to+\infty}\min_{x\in\mathbb{R}_+^6\setminus U_k} H(x) = +\infty$, where $U_k = (\frac{1}{k},k)\times(\frac{1}{k},k)\times(\frac{1}{k},k)\times(\frac{1}{k},k)\times(\frac{1}{k},k)\times(\frac{1}{k},k)$, then $H(x)$ has a minimum point $x^* = (S^*, E^*, I^*, E_R^*, I_R^*, R^*) \in \mathbb{R}_+^6$.

Now, we structure a Lyapunov function as follows

$$V(x) = MV_1 + V_2 + V_3 - H(x^*).$$

Obviously, $V(x)$ is a nonnegative C^2-function. By applying Itô formula, we get

$$\begin{aligned}
\mathscr{L}V_1 = &-(1-p)\beta_1 S - \frac{c_{13}\Lambda}{S} + c_{13}\left(\mu+\frac{\sigma_1^2}{2}\right) - \frac{\delta E}{I} - \frac{c_{11}p\beta_1 SI}{E} - \frac{c_{12}\Lambda}{S}\\
&+c_{11}\left(\mu+\delta+\frac{\sigma_2^2}{2}\right) + c_{12}\left(\mu+\frac{\sigma_1^2}{2}\right) - \frac{\theta\gamma R}{I} - \frac{c_{14}kI}{R} - \frac{c_{11}(1-\theta)\gamma R}{E} - \frac{c_{14}\alpha I_R}{R}\\
&+(c_{12}+c_{13})(\beta_1 I+\beta_2 I_R) + \eta+\mu+d_1+k+\frac{\sigma_3^2}{2} + c_{14}\left(\mu+\gamma+\frac{\sigma_6^2}{2}\right)\\
&+\phi\big(-(1-q)\beta_2 S - \frac{c_{23}\Lambda}{S} + c_{23}\left(\mu+\frac{\sigma_1^2}{2}\right) - \frac{c_{21}q\beta_2 SI_R}{E_R} - \frac{c_{22}\Lambda}{S} - \frac{\nu E_R}{I_R}\\
&+c_{21}\left(\mu+\nu+\frac{\sigma_4^2}{2}\right) + c_{22}\left(\mu+\frac{\sigma_1^2}{2}\right) - \frac{\eta I}{I_R} - \frac{c_{24}\theta\gamma R}{I} - \frac{c_{25}\alpha I_R}{R}\\
&+c_{24}\left(\eta+\mu+d_1+k+\frac{\sigma_3^2}{2}\right) + c_{25}\left(\mu+\gamma++\frac{\sigma_6^2}{2}\right) - c_{24}(1-p)\beta_1 S\\
&-\frac{c_{24}\delta E}{I} - \frac{c_{25}kI}{R} + (c_{22}+c_{23})(\beta_1 I+\beta_2 I_R) + \alpha+\mu+d_2+\frac{\sigma_5^2}{2}\big)\\
&-\frac{\beta_1\nu}{\eta}\big(c_{12}+c_{13}+\phi(c_{22}+c_{23})\big)E_R + \frac{\beta_1}{\eta}(\alpha+\mu+d_2)\big(c_{12}+c_{13}+\phi(c_{22}+c_{23})\big)I_R
\end{aligned}$$

$$
\begin{aligned}
&-\beta_1(c_{12}+c_{13}+\phi(c_{22}+c_{23}))I-\frac{\beta_1}{\eta}\big(c_{12}+c_{13}+\phi(c_{22}+c_{23})\big)(1-q)\beta_2 SI_R\\
\le\ &-2\sqrt{c_{13}(1-p)\beta_1\Lambda}+c_{13}\left(\mu+\frac{\sigma_1^2}{2}\right)-3\sqrt[3]{c_{11}c_{12}p\beta_1\Lambda\delta}+c_{11}\left(\mu+\delta+\frac{\sigma_2^2}{2}\right)\\
&+c_{12}\left(\mu+\frac{\sigma_1^2}{2}\right)-2\sqrt{c_{14}\theta\gamma k}+c_{14}\left(\mu+\gamma+\frac{\sigma_6^2}{2}\right)+\eta+\mu+d_1+k+\frac{\sigma_3^2}{2}\\
&+\phi\big(-2\sqrt{c_{23}(1-q)\beta_2\Lambda}+c_{23}\left(\mu+\frac{\sigma_1^2}{2}\right)-3\sqrt[3]{c_{24}c_{25}\theta\gamma\alpha\eta}+c_{24}\,(\eta+\mu+d_1+k\\
&+\frac{\sigma_3^2}{2}\right)+c_{25}\left(\mu+\gamma+\frac{\sigma_6^2}{2}\right)-3\sqrt[3]{c_{21}c_{22}q\beta_2\Lambda\nu}+c_{21}\left(\mu+\nu+\frac{\sigma_4^2}{2}\right)+c_{22}\left(\mu+\frac{\sigma_1^2}{2}\right)\\
&+\alpha+\mu+d_2+\frac{\sigma_5^2}{2}\big)+\big(c_{12}+c_{13}+\phi(c_{22}+c_{23})\big)\big(\beta_2+\frac{\beta_1}{\eta}(\alpha+\mu+d_2)\big)I_R\\
=\ &-\frac{(1-p)\beta_1\Lambda}{\mu+\frac{\sigma_1^2}{2}}-\frac{p\beta_1\Lambda\delta}{\left(\mu+\frac{\sigma_1^2}{2}\right)\left(\mu+\delta+\frac{\sigma_2^2}{2}\right)}-\frac{\theta\gamma k}{\mu+\gamma+\frac{\sigma_6^2}{2}}+\eta+\mu+d_1+k+\frac{\sigma_3^2}{2}
\end{aligned}
$$

$$
\begin{aligned}
&+\phi\big(-\frac{(1-q)\beta_2\Lambda}{\mu+\frac{\sigma_1^2}{2}}-\frac{q\beta_2\Lambda\nu}{\left(\mu+\frac{\sigma_1^2}{2}\right)\left(\mu+\nu+\frac{\sigma_4^2}{2}\right)}-\frac{\theta\gamma\alpha\eta}{\left(\eta+\mu+d_1+k+\frac{\sigma_3^2}{2}\right)\left(\mu+\gamma+\frac{\sigma_6^2}{2}\right)}\\
&+\alpha+\mu+d_2+\frac{\sigma_5^2}{2}\big)+\big(c_{12}+c_{13}+\phi(c_{22}+c_{23})\big)\big(\beta_2+\frac{\beta_1}{\eta}(\alpha+\mu+d_2)\big)I_R\\
=\ &-\left(\eta+\mu+d_1+k+\frac{\sigma_3^2}{2}\right)(\widetilde{\mathfrak{R}}_{01}^S-1)-\phi\left(\alpha+\mu+d_2+\frac{\sigma_5^2}{2}\right)(\widetilde{\mathfrak{R}}_{02}^S-1)\\
&+\big(c_{12}+c_{13}+\phi(c_{22}+c_{23})\big)\big(\beta_2+\frac{\beta_1}{\eta}(\alpha+\mu+d_2)\big)I_R\\
=\ &-\lambda+\big(c_{12}+c_{13}+\phi(c_{22}+c_{23})\big)\big(\beta_2+\frac{\beta_1}{\eta}(\alpha+\mu+d_2)\big)I_R,
\end{aligned}
$$

$$
\begin{aligned}
\mathscr{L}V_2=\ &-\frac{\Lambda}{S}+\beta_1 I+\beta_2 I_R-\frac{p\beta_1 SI}{E}-\frac{(1-\theta)\gamma R}{E}-(1-p)\beta_1 S-\frac{\delta E}{I}-\frac{\theta\gamma R}{I}\\
&-\frac{q\beta_2 SI_R}{E_R}-\frac{kI}{R}-\frac{\alpha I_R}{R}-\frac{\beta_1\beta_2(1-q)SI_R}{\eta}-\frac{\beta_1\nu E_R}{\eta}+\frac{\beta_1(\alpha+\mu+d_2)I_R}{\eta}\\
&-\beta_1 I+5\mu+\delta+\eta+k+\nu+\gamma+d_1+\frac{\sigma_1^2}{2}+\frac{\sigma_2^2}{2}+\frac{\sigma_3^2}{2}+\frac{\sigma_4^2}{2}+\frac{\sigma_6^2}{2}\\
\le\ &-\frac{\Lambda}{S}-\frac{(1-\theta)\gamma R}{E}-\frac{\theta\gamma R}{I}-\frac{q\beta_2 SI_R}{E_R}-\frac{\alpha I_R}{R}+(\beta_2+\frac{\beta_1}{\eta}(\alpha+\mu+d_2))I_R\\
&+5\mu+\delta+\eta+k+\nu+\gamma+d_1+\frac{\sigma_1^2}{2}+\frac{\sigma_2^2}{2}+\frac{\sigma_3^2}{2}+\frac{\sigma_4^2}{2}+\frac{\sigma_6^2}{2}
\end{aligned}
$$

and

$$
\begin{aligned}
\mathscr{L}V_3=\ &(S+E+I+E_R+I_R+R)^\theta(\Lambda-\mu(S+E)-(\mu+d_1)I-\mu E_R\\
&-(\mu+d_2)I_R-\mu R)+\frac{\theta}{2}(S+E+I+E_R+I_R+R)^{\theta-1}\\
&\times(\sigma_1{}^2S^2\vee\sigma_2{}^2E^2\vee\sigma_3{}^2I^2\vee\sigma_4{}^2E_R{}^2\vee\sigma_5{}^2I_R{}^2\vee\sigma_6{}^2R^2)\\
\le\ &(S+E+I+E_R+I_R+R)^\theta(\Lambda-\mu(S+E+I+E_R+I_R+R))\\
&+\frac{\theta}{2}(S+E+I+E_R+I_R+R)^{\theta+1}(\sigma_1{}^2\vee\sigma_2{}^2\vee\sigma_3{}^2\vee\sigma_4{}^2\vee\sigma_5{}^2\vee\sigma_6{}^2)
\end{aligned}
$$

$$
\begin{aligned}
&= \Lambda(S+E+I+E_R+I_R+R)^{\theta} - \rho(S+E+I+E_R+I_R+R)^{\theta+1} \\
&\le D - \frac{\rho}{2}(S^{\theta+1}+E^{\theta+1}+I^{\theta+1}+{E_R}^{\theta+1}+{I_R}^{\theta+1}+R^{\theta+1}).
\end{aligned}
$$

Therefore, one can obtain

$$
\begin{aligned}
\mathscr{L}V \le & -M\lambda + M(c_{12}+c_{13}+\phi(c_{22}+c_{23}))(\beta_2+\frac{\beta_1}{\eta}(\alpha+\mu+d_2))I_R - \frac{\Lambda}{S} \\
& - \frac{(1-\theta)\gamma R}{E} - \frac{\theta\gamma R}{I} - \frac{q\beta_2 S I_R}{E_R} - \frac{\alpha I_R}{R} + (\beta_2+\frac{\beta_1}{\eta}(\alpha+\mu+d_2))I_R \\
& - \frac{\rho}{2}(S^{\theta+1}+E^{\theta+1}+I^{\theta+1}+{E_R}^{\theta+1}+{I_R}^{\theta+1}+R^{\theta+1}) + D + 5\mu \\
& + \delta+\eta+k+\nu+\gamma+d_1+\frac{\sigma_1^2}{2}+\frac{\sigma_2^2}{2}+\frac{\sigma_3^2}{2}+\frac{\sigma_4^2}{2}+\frac{\sigma_6^2}{2}.
\end{aligned} \tag{3.11}
$$

Step 2. Prove $\mathscr{L}V \le -1$ for all $x \in \mathbb{R}^6_+ \backslash U_\varepsilon$, where U_ε is defined as

$$
\begin{aligned}
U_\varepsilon = \{x \in \mathbb{R}^6_+, & \varepsilon < S < \frac{1}{\varepsilon}, \varepsilon < I_R < \frac{1}{\varepsilon}, \varepsilon^3 < E_R < \frac{1}{\varepsilon^3}, \varepsilon^2 < R < \frac{1}{\varepsilon^2}, \\
& \varepsilon^3 < I < \frac{1}{\varepsilon^3}, \varepsilon^3 < E < \frac{1}{\varepsilon^3}\},
\end{aligned}
$$

and $0 < \varepsilon < 1$ is a small enough constant such that the following conditions hold

$$
M\big(c_{12}+c_{13}+\phi(c_{22}+c_{23})\big)\left(\beta_2+\frac{\beta_1}{\eta}(\alpha+\mu+d_2)\right)\varepsilon \le 1, \tag{3.12a}
$$

$$
(1+F)\max\left\{\frac{1}{\Lambda}, \frac{1}{q\beta_2}, \frac{1}{\alpha}, \frac{1}{\theta\gamma}, \frac{1}{(1-\theta)\gamma}\right\} \le \frac{1}{\varepsilon}, \tag{3.12b}
$$

$$
-\frac{\rho}{4\varepsilon^{1+\theta}} + F \le -1, \tag{3.12c}
$$

where

$$
\begin{aligned}
F = \sup_{I_R \in \mathbb{R}_+} \Bigg\{ & \Bigg[M\big(c_{12}+c_{13}+\phi(c_{22}+c_{23})\big)\left(\beta_2+\frac{\beta_1}{\eta}(\alpha+\mu+d_2)\right) + \beta_2 \\
& + \frac{\beta_1}{\eta}(\alpha+\mu+d_2)\Bigg] I_R - \frac{\rho}{4} I_R^{1+\theta} + 5\mu + \delta+\eta+k+\nu+\gamma+d_1 \\
& + \frac{\sigma_1^2}{2}+\frac{\sigma_2^2}{2}+\frac{\sigma_3^2}{2}+\frac{\sigma_4^2}{2}+\frac{\sigma_6^2}{2} + D \Bigg\} < \infty.
\end{aligned}
$$

For the sake of convenience, we divide $U_\varepsilon^c \triangleq \mathbb{R}_+^6 \setminus U_\varepsilon$ into the following twelve domains

$$
\begin{aligned}
&D_1 = \{x \in \mathbb{R}_+^6, 0 < S < \varepsilon\}, \quad D_2 = \{x \in \mathbb{R}_+^6, 0 < I_R < \varepsilon\},\\
&D_3 = \{x \in \mathbb{R}_+^6, 0 < E_R < \varepsilon^3, S \geq \varepsilon, I_R \geq \varepsilon\}, \quad D_4 = \{x \in \mathbb{R}_+^6, 0 < R < \varepsilon^2, I_R \geq \varepsilon\},\\
&D_5 = \{x \in \mathbb{R}_+^6, 0 < I < \varepsilon^3, R \geq \varepsilon^2\}, \quad D_6 = \{x \in \mathbb{R}_+^6, 0 < E < \varepsilon^3, R \geq \varepsilon^2\},\\
&D_7 = \{x \in \mathbb{R}_+^6, S > \frac{1}{\varepsilon}\}, \quad D_8 = \{x \in \mathbb{R}_+^6, I_R > \frac{1}{\varepsilon}\},\\
&D_9 = \{x \in \mathbb{R}_+^6, E_R > \frac{1}{\varepsilon^3}\}, D_{10} = \{x \in \mathbb{R}_+^6, R > \frac{1}{\varepsilon^2}\},\\
&D_{11} = \{x \in \mathbb{R}_+^6, I > \frac{1}{\varepsilon^3}\}, \quad D_{12} = \{x \in \mathbb{R}_+^6, E > \frac{1}{\varepsilon^3}\}.
\end{aligned}
$$

Clearly, $U_\varepsilon^c = D_1 \cup D_2 \cup \cdots \cup D_{12}$. In the following, we will prove $\mathscr{L}V(x) \leq -1$ for all $x \in U_\varepsilon^c$, that is, this conclusion holds on the above twelve domains.

Case 1. When $x \in D_2$, it yields from (3.11)

$$
\begin{aligned}
\mathscr{L}V \leq & -M\lambda + M\big(c_{12} + c_{13} + \phi(c_{22} + c_{23})\big)\left(\beta_2 + \frac{\beta_1}{\eta}(\alpha + \mu + d_2)\right) I_R - \frac{\rho}{2} {I_R}^{1+\theta}\\
& + (\beta_2 + \frac{\beta_1}{\eta}(\alpha + \mu + d_2)) I_R + 5\mu + \delta + \eta + k + \nu + \gamma + d_1 + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2}\\
& + \frac{\sigma_3^2}{2} + \frac{\sigma_4^2}{2} + \frac{\sigma_6^2}{2} + D\\
\leq & -M\lambda + M\big(c_{12} + c_{13} + \phi(c_{22} + c_{23})\big)\big(\beta_2 + \frac{\beta_1}{\eta}(\alpha + \mu + d_2)\big) I_R + J\\
\leq & -2 + M\big(c_{12} + c_{13} + \phi(c_{22} + c_{23})\big)\big(\beta_2 + \frac{\beta_1}{\eta}(\alpha + \mu + d_2)\big)\varepsilon.
\end{aligned}
$$

By condition (3.12a), we can get $\mathscr{L}V \leq -1$ on D_2.

Case 2. When $x \in D^* \triangleq D_1 \cup D_3 \cup D_4 \cup D_5 \cup D_6$, one can see that

$$
\begin{aligned}
&\mathscr{L}V \leq -\frac{\Lambda}{S} + F \leq -\frac{\Lambda}{\varepsilon} + F, \ x \in D_1,\\
&\mathscr{L}V \leq -\frac{q\beta_2 S I_R}{E_R} + F \leq -\frac{q\beta_2}{\varepsilon} + F, \ x \in D_3,\\
&\mathscr{L}V \leq -\frac{\alpha I_R}{R} + F \leq -\frac{\alpha}{\varepsilon} + F, \ x \in D_4,\\
&\mathscr{L}V \leq -\frac{\theta\gamma R}{I} + F \leq -\frac{\theta\gamma}{\varepsilon} + F, \ x \in D_5,\\
&\mathscr{L}V \leq -\frac{(1-\theta)\gamma R}{E} + F \leq -\frac{(1-\theta)\gamma}{\varepsilon} + F, \ x \in D_6.
\end{aligned}
$$

It follows from the above inequalities and condition (3.12b) that $\mathscr{L}V \leq -1$ on D^*.

Case 3. When $x \in D_7$, we have from (3.11)

$$\mathscr{L}V \leq -\frac{\rho}{2}S^{\theta+1} + F \leq -\frac{\rho}{4\varepsilon^{\theta+1}} + F.$$

Similarly, when $x \in \bigcup_{i=8}^{12} D_i$ we can also derive $\mathscr{L}V \leq -\frac{\rho}{4\varepsilon^{\theta+1}} + F$. From these inequalities and condition (3.12c), we finally have $\mathscr{L}V \leq -1$ on $D^{**} \triangleq \bigcup_{i=7}^{12} D_i$.

In summary of the above discussions, we finally obtain $\mathscr{L}V \leq -1$ for all $x \in U_\varepsilon^c$. Therefore, the condition (ii) of Lemma 3.2 is satisfied. Thus, based on Lemma 3.2, it can be obtained that the solution $x(t)$ of model (2.1) with initial value $x(0) \in \mathbb{R}_+^6$ is ergodic and has a stationary distribution $\pi(\cdot)$. This completes the proof. □

Remark 3.3 When threshold value $\widetilde{\mathfrak{R}}_0^S < 1$, it does not necessarily mean that the solution of model (2.1) is stochastic extinction. In Sect. 4, we would provide two numerical examples to illustrate that under condition $\widetilde{\mathfrak{R}}_0^S < 1$, it is possible that the solution $x(t)$ of model (2.1) with initial value $x(0) \in \mathbb{R}_+^6$ also could admit a ergodic stationary distribution (see Fig. 7 in Sect. 4.2), or $x(t)$ would go to extinction (see Fig. 15 in Sect. 4.5).

Now, we consider a special case for model (2.1), that is, $\theta = 1$ and $\alpha = 0$, then model (2.1) becomes to

$$\begin{cases} dS = (\Lambda - \mu S - (\beta_1 I + \beta_2 I_R)S)dt + \sigma_1 S dB_1(t), \\ dE = (p\beta_1 SI - (\mu+\delta)E)dt + \sigma_2 E dB_2(t), \\ dI = ((1-p)\beta_1 SI + \delta E - (\eta+\mu+d_1+k)I + \gamma R)dt + \sigma_3 I dB_3(t), \\ dE_R = (q\beta_2 SI_R - (\mu+\nu)E_R)dt + \sigma_4 E_R dB_4(t), \\ dI_R = ((1-q)\beta_2 SI_R + \eta I - (\mu+d_2)I_R + \nu E_R)dt + \sigma_5 I_R dB_5(t), \\ dR = (kI - (\mu+\gamma)R)dt + \sigma_6 R dB_6(t). \end{cases} \tag{3.13}$$

The corresponding deterministic version of model (3.13) is

$$\begin{cases} \frac{dS}{dt} = \Lambda - \mu S - (\beta_1 I + \beta_2 I_R)S, \\ \frac{dE}{dt} = p\beta_1 SI - (\mu+\delta)E, \\ \frac{dI}{dt} = (1-p)\beta_1 SI + \delta E - (\eta+\mu+d_1+k)I + \gamma R, \\ \frac{dE_R}{dt} = q\beta_2 SI_R - (\mu+\nu)E_R, \\ \frac{dI_R}{dt} = (1-q)\beta_2 SI_R + \eta I - (\mu+d_2)I_R + \nu E_R, \\ \frac{dR}{dt} = kI - (\mu+\gamma)R. \end{cases} \tag{3.14}$$

In addition, when $\theta = 1$ and $\alpha = 0$, the values $\widetilde{\mathfrak{R}}_{01}^S$ and $\widetilde{\mathfrak{R}}_{02}^S$ separately become to

$$\mathfrak{R}_{01}^S = \frac{p\beta_1\Lambda\delta}{(\mu+\frac{\sigma_1^2}{2})(\mu+\delta+\frac{\sigma_2^2}{2})(\eta+\mu+k+d_1+\frac{\sigma_3^2}{2})} + \frac{(1-p)\beta_1\Lambda}{(\mu+\frac{\sigma_1^2}{2})(\eta+\mu+k+d_1+\frac{\sigma_3^2}{2})} + \frac{\gamma k}{(\eta+\mu+k+d_1+\frac{\sigma_3^2}{2})(\mu+\gamma+\frac{\sigma_6^2}{2})}$$

and

$$\mathfrak{R}_{02}^S = \frac{q\beta_2\Lambda\nu}{(\mu+\frac{\sigma_1^2}{2})(\mu+\nu+\frac{\sigma_4^2}{2})(\mu+d_2+\frac{\sigma_5^2}{2})} + \frac{(1-q)\beta_2\Lambda}{(\mu+\frac{\sigma_1^2}{2})(\mu+d_2+\frac{\sigma_5^2}{2})}.$$

Further, the threshold value $\widetilde{\mathfrak{R}}_0^S = \max\{\widetilde{\mathfrak{R}}_{01}^S, \widetilde{\mathfrak{R}}_{02}^S\}$ becomes to $\mathfrak{R}_0^S = \max\{\mathfrak{R}_{01}^S, \mathfrak{R}_{02}^S\}$. Hence, by Theorem 3.2, we have the following corollary on the existence of ergodic stationary distribution for the solution of model (3.13).

Corollary 3.1 *If $\mathfrak{R}_0^S = \max\{\mathfrak{R}_{01}^S, \mathfrak{R}_{02}^S\} > 1$, then solution $x(t)$ of model (3.13) with initial value $x(0) \in \mathbb{R}_+^6$ is ergodic and admits a stationary distribution.*

In the following, it would indicate that the threshold value $\mathfrak{R}_0^S = \max\{\mathfrak{R}_{01}^S, \mathfrak{R}_{02}^S\}$ is just right the extension of the basic reproduction number of corresponding deterministic model (3.14) in the stochastic case. In fact, when $\sigma_i \equiv 0$ $(i = 1, \ldots, 6)$, we see that model (3.13) becomes to the deterministic model (3.14), the threshold values $\mathfrak{R}_{0i}^S$ become to $\mathcal{R}_{0i}$ for $i = 1, 2$, where

$$\begin{aligned} \mathcal{R}_{01} &= \frac{p\beta_1\Lambda\delta(\mu+\gamma) + (1-p)\beta_1\Lambda(\mu+\delta)(\mu+\gamma) + \gamma k\mu(\mu+\delta)}{\mu(\mu+\delta)(\eta+\mu+k+d_1)(\mu+\gamma)}, \\ \mathcal{R}_{02} &= \frac{q\beta_2\Lambda\nu + (1-q)\beta_2\Lambda(\mu+\nu)}{\mu(\mu+\nu)(\mu+d_2)} \end{aligned} \tag{3.15}$$

and $\mathfrak{R}_0^S = \max\{\mathfrak{R}_{01}^S, \mathfrak{R}_{02}^S\}$ becomes to $\mathcal{R}_0 = \max\{\mathcal{R}_{01}, \mathcal{R}_{02}\}$.

Now, we will prove that the constant $\mathcal{R}_0 = \max\{\mathcal{R}_{01}, \mathcal{R}_{02}\}$ is exactly the basic reproductive number of model (3.14).

In fact, we can directly use the next generation matrix approach to calculate the basic reproduction number of model (3.14). Let

$$\widetilde{\mathcal{F}} = \begin{pmatrix} p\beta_1 SI \\ (1-p)\beta_1 SI \\ q\beta_2 SI_R \\ (1-q)\beta_2 SI_R \\ 0 \end{pmatrix},$$

$$\widetilde{\mathcal{V}} = \begin{pmatrix} (\mu+\delta)E \\ (\eta+\mu+d_1+k)I - \delta E - \gamma R \\ (\mu+\nu)E_R \\ (\mu+d_2)I_R - \eta I - \nu E_R \\ -kI + (\mu+\gamma)R \end{pmatrix}.$$

Hence, by calculating the Jacobi matrices of $\widetilde{\mathcal{F}}$ and $\widetilde{\mathcal{V}}$ at P_0, we obtain

$$\widetilde{\mathbf{F}} = \begin{pmatrix} 0 & p\beta_1 S_0 & 0 & 0 & 0 \\ 0 & (1-p)\beta_1 S_0 & 0 & 0 & 0 \\ 0 & 0 & 0 & q\beta_2 S_0 & 0 \\ 0 & 0 & 0 & (1-q)\beta_2 S_0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$\widetilde{\mathbf{V}} = \begin{pmatrix} \mu+\delta & 0 & 0 & 0 & 0 \\ -\delta & \eta+\mu+d_1+k & 0 & 0 & -\gamma \\ 0 & 0 & \mu+\nu & 0 & 0 \\ 0 & -\eta & -\nu & \mu+d_2 & 0 \\ 0 & -k & 0 & 0 & \mu+\gamma \end{pmatrix}.$$

It can be obtained by calculation

$$\widetilde{\mathbf{F}}\widetilde{\mathbf{V}}^{-1} = \begin{pmatrix} \frac{p\beta_1 S_0 \delta h_3 h_4 h_5}{|\widetilde{\mathbf{V}}|} & \frac{p\beta_1 S_0 h_1 h_3 h_4 h_5}{|\widetilde{\mathbf{V}}|} & 0 & 0 & \frac{p\beta_1 S_0 \gamma h_1 h_3 h_4}{|\widetilde{\mathbf{V}}|} \\ \frac{(1-p)\beta_1 S_0 \delta h_3 h_4 h_5}{|\widetilde{\mathbf{V}}|} & \frac{(1-p)\beta_1 S_0 h_1 h_3 h_4 h_5}{|\widetilde{\mathbf{V}}|} & 0 & 0 & \frac{(1-p)\beta_1 S_0 \gamma h_1 h_3 h_4}{|\widetilde{\mathbf{V}}|} \\ \frac{q\beta_2 S_0 \delta \eta h_3 h_5}{|\widetilde{\mathbf{V}}|} & \frac{q\beta_2 S_0 \eta h_1 h_3 h_5}{|\widetilde{\mathbf{V}}|} & \frac{q\beta_2 S_0 h_1 \nu (h_2 h_5 - k\gamma)}{|\widetilde{\mathbf{V}}|} & \frac{q\beta_2 S_0 h_1 h_3 (h_2 h_5 - k\gamma)}{|\widetilde{\mathbf{V}}|} & \frac{q\beta_2 S_0 h_1^2 h_3 \gamma \eta)}{|\widetilde{\mathbf{V}}|} \\ \frac{(1-q)\beta_2 S_0 \delta \eta h_3 h_5}{|\widetilde{\mathbf{V}}|} & \frac{(1-q)\beta_2 S_0 \delta \eta h_3 h_5}{|\widetilde{\mathbf{V}}|} & \frac{(1-q)\beta_2 S_0 h_1 \nu (h_2 h_5 - k\gamma)}{|\widetilde{\mathbf{V}}|} & \frac{(1-q)\beta_2 S_0 h_1 h_3 (h_2 h_5 - k\gamma)}{|\widetilde{\mathbf{V}}|} & \frac{(1-q)\beta_2 S_0 h_1 h_3 \gamma \eta}{|\widetilde{\mathbf{V}}|} \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

where $h_1 = \mu+\delta$, $h_2 = \eta+\mu+d_1+k$, $h_3 = \mu+\nu$, $h_4 = \alpha+\mu+d_2$, $h_5 = \mu+\gamma$, and $|\widetilde{\mathbf{V}}|$ denotes the determinant of matrix $\widetilde{\mathbf{V}}$. We know that the basic reproduction number R_0 of model (3.14) can be defined by $R_0 = \rho(\widetilde{\mathbf{F}}\widetilde{\mathbf{V}}^{-1})$.

By carefully calculating, we can obtain the characteristic equation of the matrix $\widetilde{\mathbf{F}}\widetilde{\mathbf{V}}^{-1}$ taking the following form

$$\begin{aligned} &\lambda^3 \left(\lambda - \frac{p\beta_1 S_0 \Lambda(\mu+\gamma) + (1-p)\beta_1 \Lambda(\mu+\delta)(\mu+\gamma)}{\mu(\mu+\delta)(\eta+\mu+d_1+k)(\mu+\gamma) - \mu(\mu+\delta)k\gamma} \right) \\ &\times \left(\lambda - \frac{q\beta_2 \Lambda\nu + (1-q)\beta_2 \Lambda(\mu+\nu)}{\mu(\mu+\nu)(\mu+d_2)} \right) = 0. \end{aligned} \tag{3.16}$$

Obviously, Eq. (3.16) have a triple root $\lambda = 0$ and two single roots

$$\lambda_1 = \frac{p\beta_1 S_0 \Lambda(\mu+\gamma) + (1-p)\beta_1 \Lambda(\mu+\delta)(\mu+\gamma)}{\mu(\mu+\delta)(\eta+\mu+d_1+k)(\mu+\gamma) - \mu(\mu+\delta)k\gamma},$$
$$\lambda_2 = \frac{q\beta_2 \Lambda v + (1-q)\beta_2 \Lambda(\mu+\nu)}{\mu(\mu+\nu)(\mu+d_2)}.$$

Therefore, we further obtain $R_0 = \rho(\widetilde{\mathbf{F}}\widetilde{\mathbf{V}}^{-1}) = \max\{\lambda_1, \lambda_2\}$.

On the other hand, from (3.15) we can obtain $\text{sign}(\mathcal{R}_{01} - 1) = \text{sign}(\lambda_1 - 1)$. Since $\mathcal{R}_{02} = \lambda_2$, we further easily prove $\text{sign}\big(\max\{\lambda_1, \lambda_2\} - 1\big) = \text{sign}\big(\max\{\mathcal{R}_{01}, \mathcal{R}_{02}\} - 1\big)$. This implies that the basic reproduction number R_0 can also be defined by $R_0 = \max\{\mathcal{R}_{01}, \mathcal{R}_{02}\}$, that is, we finally have $R_0 = \mathcal{R}_0$.

Therefore, the above discussions show that the threshold value $\mathfrak{R}_0^S$ of stochastic model (3.13) is a direct extension of the basic reproduction number R_0 of corresponding deterministic model (3.14). From this, we further have $\mathfrak{R}_0^S = \rho(\widetilde{\mathbf{F}}^S(\widetilde{\mathbf{V}}^S)^{-1})$, where

$$\widetilde{\mathbf{F}}^S = \begin{pmatrix} 0 & \frac{p\beta_1\Lambda}{\mu+\frac{1}{2}\sigma_1^2} & 0 & 0 & 0 \\ 0 & \frac{(1-p)\beta_1\Lambda}{\mu+\frac{1}{2}\sigma_1^2} & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{q\beta_2\Lambda}{\mu+\frac{1}{2}\sigma_1^2} & 0 \\ 0 & 0 & 0 & \frac{(1-q)\beta_2\Lambda}{\mu+\frac{1}{2}\sigma_1^2} & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$\widetilde{\mathbf{V}}^S = \begin{pmatrix} \mu+\delta+\frac{1}{2}\sigma_2^2 & 0 & 0 & 0 & 0 \\ -\delta & \eta+\mu+d_1+k+\frac{1}{2}\sigma_3^2 & 0 & 0 & -\gamma \\ 0 & 0 & \mu+\nu+\frac{1}{2}\sigma_4^2 & 0 & 0 \\ 0 & -\eta & -\nu & \mu+d_2+\frac{1}{2}\sigma_5^2 & 0 \\ 0 & -k & 0 & 0 & \mu+\gamma+\frac{1}{2}\sigma_6^2 \end{pmatrix}.$$

This further shows that the stochastic threshold value $\mathfrak{R}_0^S$ also can be defined by using the next generation matrix method. Therefore, Corollary 3.1 can also be stated in the following form:

If $\mathfrak{R}_0^S = \rho(\widetilde{\mathbf{F}}^S(\widetilde{\mathbf{V}}^S)^{-1}) > 1$, then solution $x(t)$ of model (3.13) with initial value $x(0) \in \mathbb{R}_+^6$ is ergodic and admits a stationary distribution.

Remark 3.4 In the general case $\alpha > 0$ and $0 \le \theta < 1$ of model (2.1), for the corresponding deterministic model (3.2) we take

$$\mathcal{F} = \begin{pmatrix} p\beta_1 SI \\ (1-p)\beta_1 SI \\ q\beta_2 SI_R \\ (1-q)\beta_2 SI_R \\ 0 \end{pmatrix}, \quad \mathcal{V} = \begin{pmatrix} (\mu+\delta)E - (1-\theta)\gamma R \\ (\eta+\mu+d_1+k)I - \delta E - \theta\gamma R \\ (\mu+\nu)E_R \\ (\alpha+\mu+d_2)I_R - \eta I - \nu E_R \\ -kI - \alpha I_R + (\mu+\gamma)R \end{pmatrix}.$$

Calculating the Jacobi matrices of $\mathcal{F}$ and $\mathcal{V}$ at P_0, we obtain

$$\mathbf{F} = \begin{pmatrix} 0 & p\beta_1 S_0 & 0 & 0 & 0 \\ 0 & (1-p)\beta_1 S_0 & 0 & 0 & 0 \\ 0 & 0 & 0 & q\beta_2 S_0 & 0 \\ 0 & 0 & 0 & (1-q)\beta_2 S_0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$\mathbf{V} = \begin{pmatrix} \mu+\delta & 0 & 0 & 0 & -(1-\theta)\gamma \\ -\delta & \eta+\mu+k+d_1 & 0 & 0 & -\theta\gamma \\ 0 & 0 & \mu+\nu & 0 & 0 \\ 0 & -\eta & -\nu & \alpha+\mu+d_2 & 0 \\ 0 & -k & 0 & -\alpha & \mu+\gamma \end{pmatrix}.$$

From this, for the stochastic model (2.1) we further define the matrices as follows

$$\mathbf{F}^S = \begin{pmatrix} 0 & \frac{p\beta_1\Lambda}{\mu+\frac{1}{2}\sigma_1^2} & 0 & 0 & 0 \\ 0 & \frac{(1-p)\beta_1\Lambda}{\mu+\frac{1}{2}\sigma_1^2} & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{q\beta_2\Lambda}{\mu+\frac{1}{2}\sigma_1^2} & 0 \\ 0 & 0 & 0 & \frac{(1-q)\beta_2\Lambda}{\mu+\frac{1}{2}\sigma_1^2} & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$\mathbf{V}^S = \begin{pmatrix} \mu+\delta+\frac{1}{2}\sigma_2^2 & 0 & 0 & 0 & -(1-\theta)\gamma \\ -\delta & \eta+\mu+d_1+k+\frac{1}{2}\sigma_3^2 & 0 & 0 & -\theta\gamma \\ 0 & 0 & \mu+\nu+\frac{1}{2}\sigma_4^2 & 0 & 0 \\ 0 & -\eta & -\nu & \alpha+\mu+d_2+\frac{1}{2}\sigma_5^2 & 0 \\ 0 & -k & 0 & -\alpha & \mu+\gamma+\frac{1}{2}\sigma_6^2 \end{pmatrix}.$$

An interesting open problem is whether we can also obtain $\widetilde{\mathfrak{R}}_0^S = \max\{\widetilde{\mathfrak{R}}_{01}^S, \widetilde{\mathfrak{R}}_{02}^S\} = \rho\big(\mathbf{F}^S(\mathbf{V}^S)^{-1}\big)$, and if condition $\widetilde{\mathfrak{R}}_0^S = \rho\big(\mathbf{F}^S(\mathbf{V}^S)^{-1}\big)$ couldn't be met, then whether we can directly obtain that when spectral radius $\rho\big(\mathbf{F}^S(\mathbf{V}^S)^{-1}\big) > 1$ then solution $x(t)$ of model (2.1) with initial value $x(0) \in \mathbb{R}_+^6$ is ergodic and admits a stationary distribution.

4 Numerical simulations

In this section, we perform numerical simulations of model (2.1) to both validate theoretical results and explore the effect of prevention and control strategies on the nosocomial infection prevalence. Firstly, we fix most of our parameter values from literature (Hughes et al. 2017; Hurford et al. 2012; Juan et al. 2005; Melsen et al. 2013; Schumacher et al. 2013; Wolkewitz et al. 2014) and calibrate the transmission rates β_1 and β_2, based on a 9–37% health care associated infection acquisition percentage obtained from Toronto teaching hospitals (Hughes et al. 2017). Secondly, we numer-

ically verify the existence of ergodic stationary distribution by plotting the frequency histogram fitting curves of solutions for our model. Moreover, we conduct global sensitivity analysis to address the uncertainty of some key parameters by employing Latin Hypercube Sampling (LHS) (Iman et al. 1981) and partial rank correlation coefficients (PRCCs) Marino et al. (2008) methods. We then investigate impacts of key parameters on the infected population with different strains ($I(t)$ and $I_R(t)$) to more clearly illustrate the effect of prevention and control strategies on the prevalence of nosocomial infection. In addition, two numerical examples are provided to exhibit the stochastic extinction of nosocomial infection. By utilizing Milsteins higher-order method in Higham (2001), model (2.1) is discretized as the corresponding discretization system (where we set six independent the Gaussian random variables following $N(0, 1)$ distribution and the time increment $\Delta t = 0.01$). We use Matlab 2017 b software to run the discretization system and obtain the solution of model (2.1). The visualization of charts and partial results for statistical analysis is achieved by using R 4.0.5 software, (some specific libraries such as 'ggcorrplot', 'ggplot2' and 'scatterplot3d' etc.).

4.1 Calibrating the parameters β_1 and β_2

We perform simulations on a middle sized hospital with 100 beds (Wolkewitz et al. 2014). The length of stay and hazard rate of death vary significantly among patients, and for uninfected patients, we assume a discharge rate of 0.17 per day (Hurford et al. 2012) and a death rate of 0.02 per day (Wolkewitz et al. 2014). We thus have a baseline discharge and death rate $\mu = 0.19$ per day, and set the admission rate $\Lambda = \mu N$. An appropriate antibiotic treatment takes five to ten days, and may be even longer for patients infected by resistant bacteria - who would require treatment corrections when the 3-day lab results become available and confirm resistance. Therefore, we assume that the average time for patients infected by sensitive strains getting their infections under control is three days, where as that for those infected by resistant strains is six days. The hazard ratio of discharge for patients with nosocomial infection is estimated in between 1.0 and 2.3, and the hazard ratio of death to be in between 0.49 and 1.0 (Melsen et al. 2013; Schumacher et al. 2013). We thus parameterize the excess discharge and death rates as 1.65×0.17 and 0.745×0.02, respectively, by adopting the median values of hazard ratios in the estimated intervals. The uncertainties of the parameters on discharge and death will be ultimately reflected and modeled by the stochastic terms. Then the overall excess discharge and death rate is 0.29 per day. The description of fixed and calibrated parameters are summarized in Tables 1 and 2.

Here, we fix $\gamma = 0.15$, $\delta = \nu = 0.013$ and $\eta = 0.025$ and other parameters of model (2.1) are given in Tables 1 and 2. We set all variances $\sigma_i = 0.05$ ($i = 1, \ldots, 6$). And in the long run, the solution of model (2.1) with any positive initial values would approach to a stable state, so the influence of the changes of the initial values on solution curves will fade out. Thus we set the initial values as $S(0) = 85$, $E(0) = 10$, $I(0) = 1$, $E_R(0) = 2$, $I_R(0) = 5$ and $R(0) = 2$, and perform all simulations on a daily basis (Fig. 1).

We calibrate the transmission rates β_1 and β_2 by fitting the nosocomial infection acquisition percentage to the range of 9–37% Hughes et al. (2017). Specifically, we

Table 1 Parameter values on hospital settings

Parameter	Value	References
N—Number of beds	100	Assumed
μ—Baseline death and discharge rate	$0.17 + 0.02\ \text{day}^{-1}$	Hurford et al. (2012) and Wolkewitz et al. (2014))
Λ—Admission rate	μN	Assumed
η—Rate of resistance emergence	0.02–$0.03\ \text{day}^{-1}$	Juan et al. (2005)
γ—Termination rate of antibiotic treatment	0.1–$0.2\ \text{day}^{-1}$	Hughes et al. (2017)
θ—Reinfection probability after treatment termination	0.1	Assumed

first find that the model solution curves typically converge to the steady states after 50 days days (see Fig. 1). We thus calculate the average percentage of nosocomial infection acquisition between 100–200 days, Q, as below:

$$Q =: \frac{\int_{100}^{200}[\beta_1 S(t)I(t) + \beta_2 S_R(t)I_R(t)]dt}{\Lambda \cdot 100}.$$

Next, for each pair of (β_1, β_2), we run our model 100 times and calculate the number of times when the corresponding Q value falls within the range of 9–37%. We perform such simulation for a total of 380 value pairs and plot the number of times in Fig. 2. Figure 3a depicts the distributions of the Q value based on various (β_1, β_2) pairs. For instance, the values of the infection acquisition Q in 100 random simulations all fall into the range 9–37% for this case $\beta_1 = 0.022$ and $\beta_2 = 0.054$. There is 0 out of 100 times for the infection acquisition Q falling into 9–37% with the combinations of both $\beta_1 = 0.011$, $\beta_2 = 0.04$ and $\beta_1 = 0.026$, $\beta_2 = 0.072$. And in the rest of combinations ($\beta_1 = 0.016$, $\beta_2 = 0.044$ and $\beta_1 = 0.024$, $\beta_2 = 0.064$), only part of the Q values fall into the credible range.

In Fig. 2, the cells colored in red and labeled with 100 correspond to the best fitting scenario for the parameter set (β_1, β_2), i.e., $[0.018, 0.022] \times [0.05, 0.06]$ is the best credible range for (β_1, β_2). This also indicates that both larger and smaller values for β_1 and β_2 are unlikely to make the infection acquisition Q to fall into the known range 9–37%. Moreover, Fig. 3b further shows the medians of infection acquisition Q increase as β_1 and β_2 increase.

Figure 4 shows the basic reproductive numbers $\widetilde{\mathfrak{R}}_0^S$ based on each (β_1, β_2) pair, which fall between 1.15 and 1.5 under the credible transmission rates. By applying LHS to generate 10,000 random samples of the transmission rates (β_1, β_2) in the credible range, the box plots for $\widetilde{\mathfrak{R}}_{01}^S$, $\widetilde{\mathfrak{R}}_{02}^S$, and $\widetilde{\mathfrak{R}}_0^S$ are depicted in Fig. 5. We find that $\widetilde{\mathfrak{R}}_0^S$ is greater than one with the median 1.384 and interquartile range (IQR) 0.1197, which implies that nosocomial pathogens has been prevalent in the hospital for a long time. In addition, from Table 3 we know that the resistant bacteria stain might dominate the transmission.

Table 2 Parameter values on bacterial strains

Parameter	Notation	Value	References
Excess death and discharge rate due to infection	d_1	0.29	Melsen et al. (2013) and Schumacher et al. (2013)
	d_2	0.29	
Transmission rate	β_1		Calibrated
	β_2		
Colonization probability	p	0.5	Assumed
	q	0.9	
Infection development rate	δ	0.013–0.0203 day^{-1}	Hughes et al. (2017)
	ν	0.013–0.0203 day^{-1}	
Treatment enforcement rate	k	$1/3$ day^{-1}	Hughes et al. (2017)
	α	$1/6$ day^{-1}	

White rows refer to sensitive strains; gray row refer to resistant strains

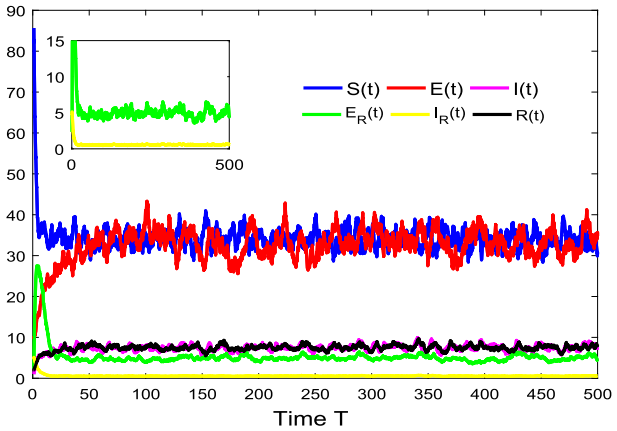


Fig. 1 The evolution of a single path of solutions for model (2.1) with initial values $(S(0), E(0), I(0), E_R(0), I_R(0), R(0)) = (85, 10, 1, 2, 5, 2)$, where $\beta_1 = 0.045$, $\beta_2 = 0.058$, $\gamma = 0.15$, $\delta = \nu = 0.013$, $\eta = 0.025$ and other parameters of model (2.1) are given in Tables 1 and 2

4.2 Stationary distribution

Theorem 3.2 indicates $\widetilde{\mathfrak{R}}_0^S > 1$ is a sufficient but not necessary condition ensuring the existence of a unique ergodic stationary distribution for the solutions of model (2.1). In what follows, we would select different values of β_1 and β_2, and then plot the frequency histogram fitting curves to verify this result by the following two situations:

(i) We choose $\beta_1 = 0.022$, $\beta_2 = 0.05$, $\gamma = 0.15$, $\delta = \nu = 0.013$, $\eta = 0.025$ and other parameters of model (2.1) are given in Tables 1 and 2, under which we calculate $\widetilde{\mathfrak{R}}_0^S = 1.4019 > 1$.
(ii) We choose $\beta_1 = 0.0155$ and $\beta_2 = 0.041$ but other parameter values remain unchanged, but we obtain $\widetilde{\mathfrak{R}}_0^S = 0.9929 < 1$.

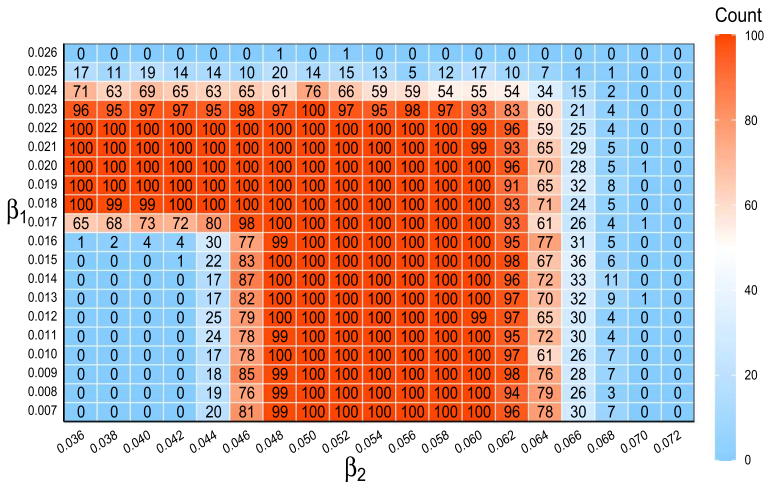
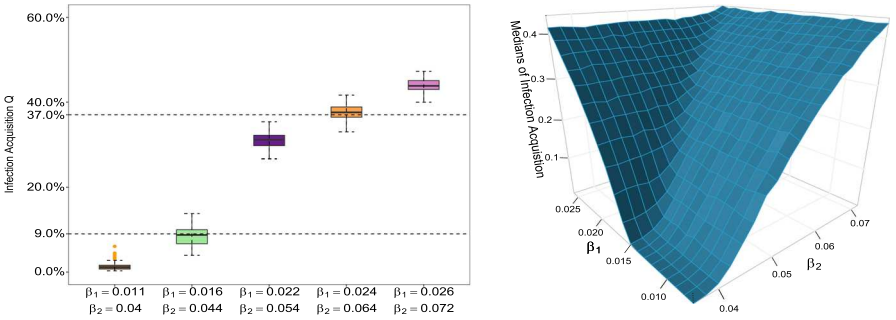


Fig. 2 The heatmap of the frequency which the values of the infection acquisition Q fall into the known range 9–37% in 100 random simulations. Simulations were carried out based on parameter values in Tables 1 and 2 and initial value $(S(0), E(0), I(0), E_R(0), I_R(0), R(0)) = (85, 10, 1, 2, 5, 2)$.



(a) Box plot of the infection acquisition Q (b) Medians of the infection acquisition Q

Fig. 3 Statistic graphs of the infection acquisition Q falling into the known range 9–37% in 100 random simulations under various combinations of β_1 and β_2

As shown in Figs. 6 and 7, both solutions of model (2.1) with different β_1 and β_2 could present good stationary properties no matter $\widetilde{\mathfrak{R}}_0^S > 1$ (see Fig. 6) or $\widetilde{\mathfrak{R}}_0^S < 1$ (see Fig. 7). Then, we separately implement 10,000 simulations with five different initial values for two different situations, (value 1: (85, 10, 1, 2, 5, 2); value 2: (35, 20, 40, 10, 25, 60); value 3: (50, 50, 100, 20, 35, 34); value 4: (10, 60, 51, 8, 15, 48); value 5: (100, 80, 60, 30, 45, 50)). Five groups of the frequency histogram fitting curves under two different situations are displayed in Figs. 8 and 9, respectively, which all clearly demonstrate that the density functions of the solution for model (2.1) separately converge to the same functions regardless of where the initial values start from. That is, there would exist a uniquely ergodic stationary distribution of solutions for model (2.1) when $\widetilde{\mathfrak{R}}_0^S > 1$ whereas it's also possible that the solution of model (2.1) is ergodic and admits a stationary distribution when $\widetilde{\mathfrak{R}}_0^S < 1$, as described in Remark 3.3.

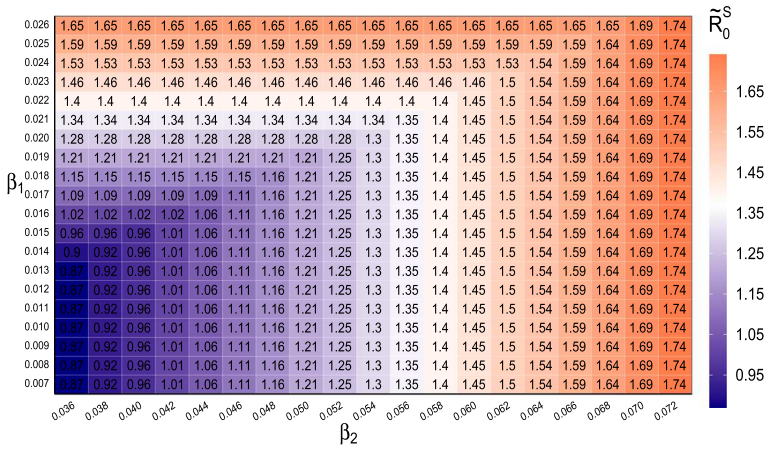


Fig. 4 The heatmap of the basic reproductive number for nosocomial outbreak $\widetilde{\mathfrak{R}}_0^S$ at various presumable values of β_1 and β_2

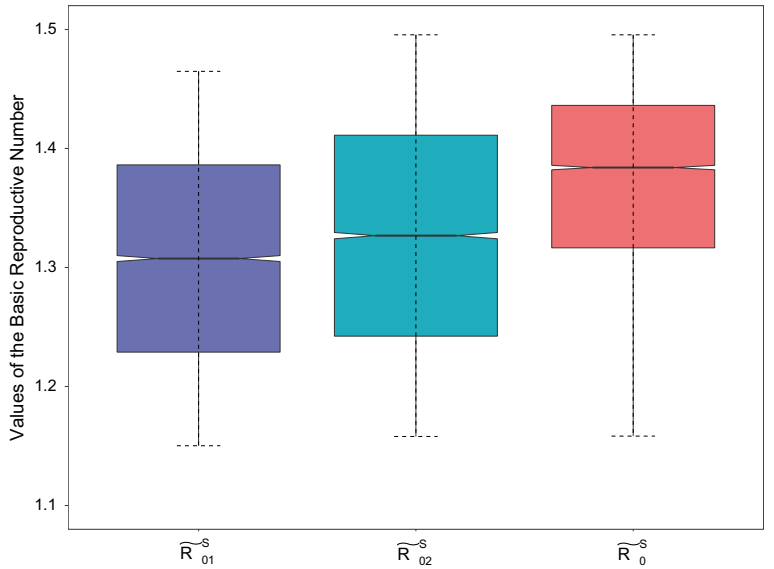


Fig. 5 Box plots of the basic reproductive number for nosocomial outbreaks of both stains, based on LHS method generating 10,000 samples for transmission rates (β_1 , β_2) in the best fitting scenario [0.018, 0.023]× [0.048, 0.062]

4.3 Sensitivity analysis

In the following, we perform global sensitivity analysis to investigate the influence of the parameters on the basic reproductive number for nosocomial outbreak $\widetilde{\mathfrak{R}}_0^S$ and infection acquisition Q. By using LHS method, we generate 2,000 random parameter combinations and evaluate the corresponding values of partial rank correlation

Table 3 Distribution characteristic of the basic reproductive number for nosocomial outbreaks of both stains

Item	Minimum	Median (P_{25}, P_{75})	Mean	Maximum
$\widetilde{\Re}_{01}^{S}$	1.150	1.308 (1.229, 1.386)	1.308	1.465
$\widetilde{\Re}_{02}^{S}$	1.158	1.327 (1.242, 1.411)	1.327	1.496
$\widetilde{\Re}_{0}^{S}$	1.158	1.384 (1.316, 1.436)	1.371	1.496

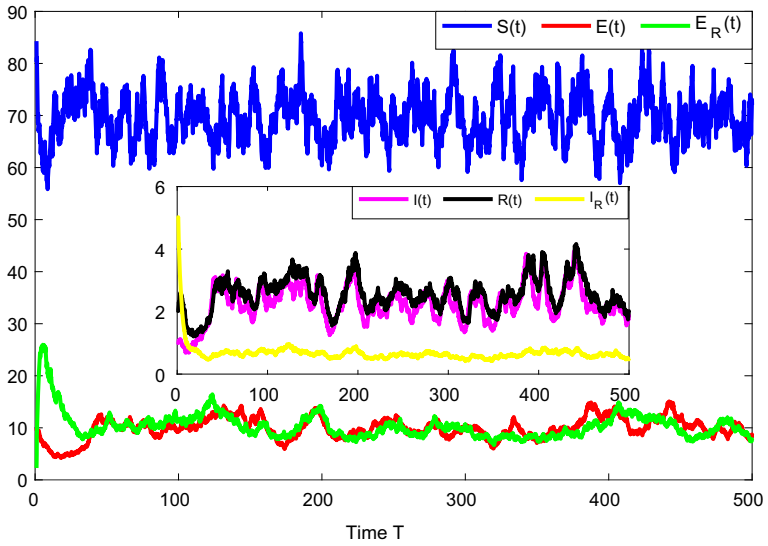


Fig. 6 The evolutions of a single path of solutions for model (2.1) with initial value $(S(0), E(0), I(0), E_R(0), I_R(0), R(0)) = (85, 10, 1, 2, 5, 2)$, where $\beta_1 = 0.022, \beta_2 = 0.05, \gamma = 0.15, \delta = \nu = 0.013$, $\eta = 0.025$ and other parameters of model (2.1) are given in Tables 1 and 2

coefficients (PRCCs) for the various input parameters (i.e., β_1, β_2, δ, γ, η, ν, k, θ, α and σ_i $(i = 1, \ldots, 6)$) against the output variables ($\widetilde{\Re}_0^S$ and Q). We assume that all model parameters are drawn based on uniform distributions, where η, γ, δ and ν are drawn based on the ranges in Tables 1 and 2, β_1 and β_2 are drawn from their calibrated ranges, and all other parameters are perturbed based on their fixed values. Specifically, $k \sim$ Uniform$(0.33, 0.34)$, $\alpha \sim$ Uniform$(0.16, 0.168)$, $\theta \sim$ Uniform$(0.08, 0.12)$, and $\sigma_i \sim$ Uniform$(0.04, 0.06)$ for $i = 1, \ldots, 6$.

Figure 10 shows that the values of $\widetilde{\Re}_0^S$ and Q are most sensitive to the transmission rats β_1 and β_2, and the infection development rates δ and ν. In particular, there is a strongest positive correlation between the transmission rate for resistant strain and $\widetilde{\Re}_0^S$ (with PRCCs value 0.9561), Q (with PRCCs value 0.7853). On the other hand, $\widetilde{\Re}_0^S$ and Q are negatively correlated with the treatment enforcement rates k and α. These suggest that reducing transmission rates, shortening infection progression rates, and enhancing treatment accuracy for infected patients are all effective strategies to avoid nosocomial infection outbreaks and prevalence.

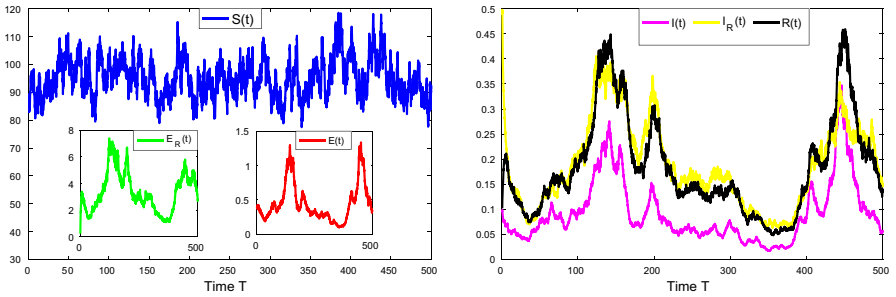
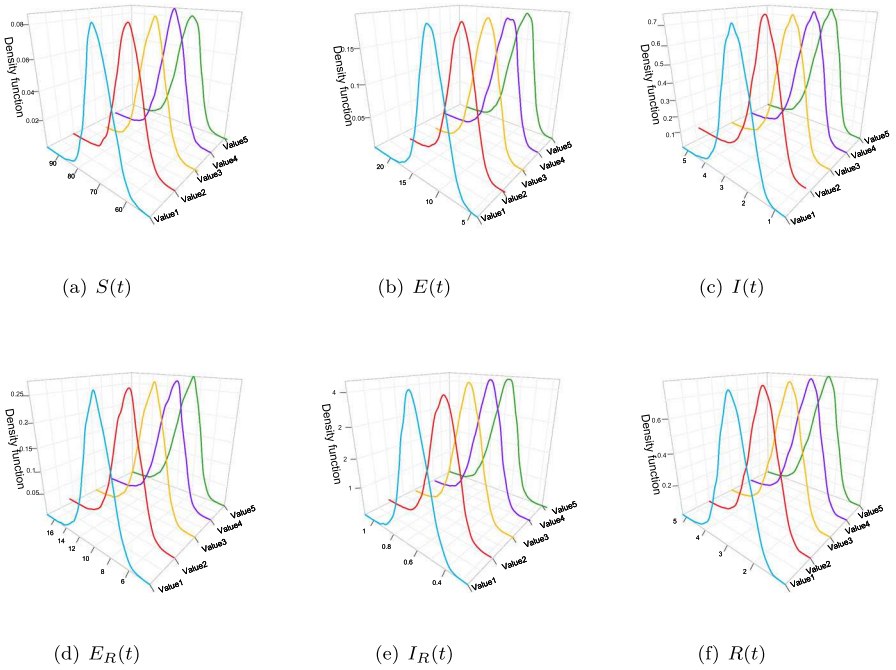


Fig. 7 The evolutions of a single path of solutions for model (2.1) with initial value $(S(0), E(0), I(0), E_R(0), I_R(0), R(0)) = (85, 0.4, 0.1, 0.2, 0.5, 0.1)$, where $\beta_1 = 0.0155$ and $\beta_2 = 0.041$ but other parameter values are same with the ones in Fig. 6



(a) $S(t)$ (b) $E(t)$ (c) $I(t)$

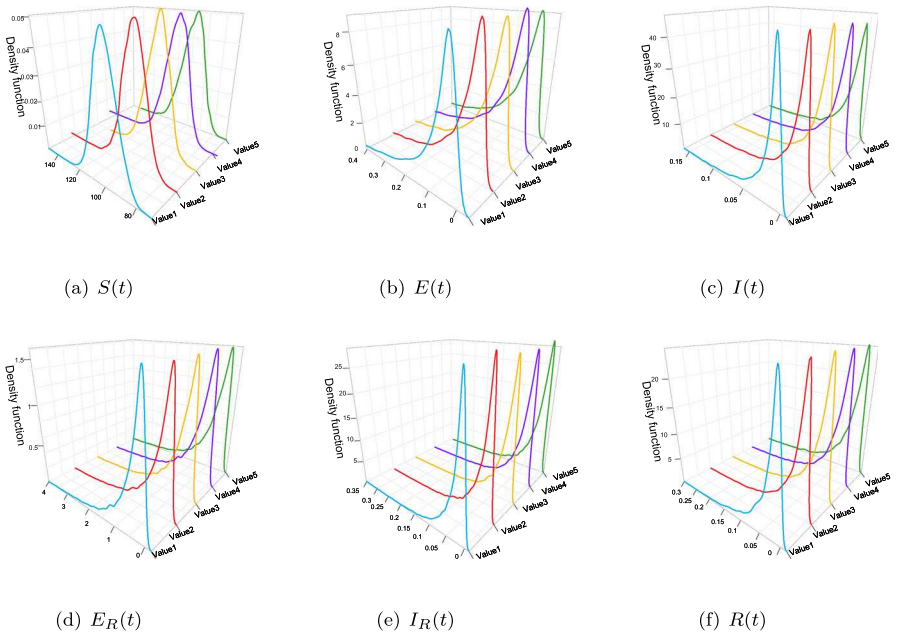
(d) $E_R(t)$ (e) $I_R(t)$ (f) $R(t)$

Fig. 8 The frequency histogram fitting curves of the solutions for model (2.1) under the parameters $\beta_1 = 0.022$ and $\beta_2 = 0.05$, with five different initial values based on the 10,000 sample paths

In addition, the above findings also indicate that the infection caused by resistant strain plays a vital role in the transmission of nosocomial bacteria. Moreover, the randomness resulted from discharge and death does not appear to impact the outbreak and transmission potential of nosocomial pathogens.

4.4 Control strategies analysis

(i) Reducing the transmission rate of sensitive/resistant strains.



(a) $S(t)$ (b) $E(t)$ (c) $I(t)$

(d) $E_R(t)$ (e) $I_R(t)$ (f) $R(t)$

Fig. 9 The frequency histogram fitting curves of the solutions for model (2.1) under the parameters $\beta_1 = 0.0155$ and $\beta_2 = 0.041$, with five different initial values based on the 10,000 sample paths

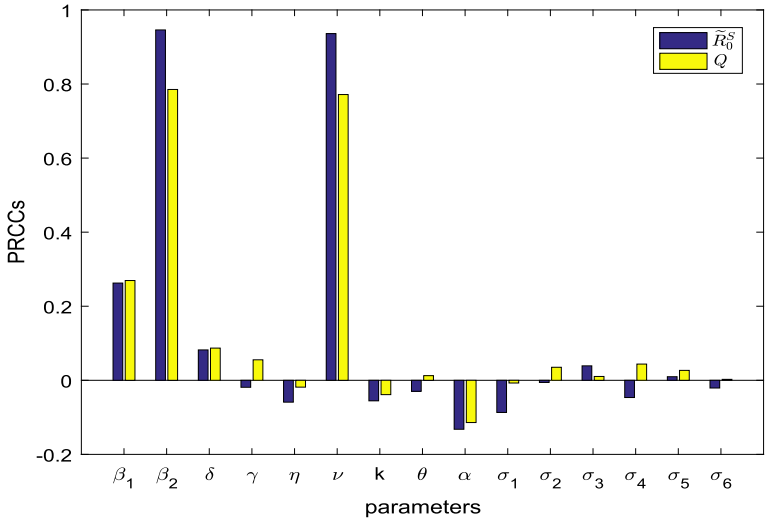


Fig. 10 The sensitivity analysis on $\widetilde{\mathfrak{R}}_0^S$ and Q with different parameters in model (2.1)

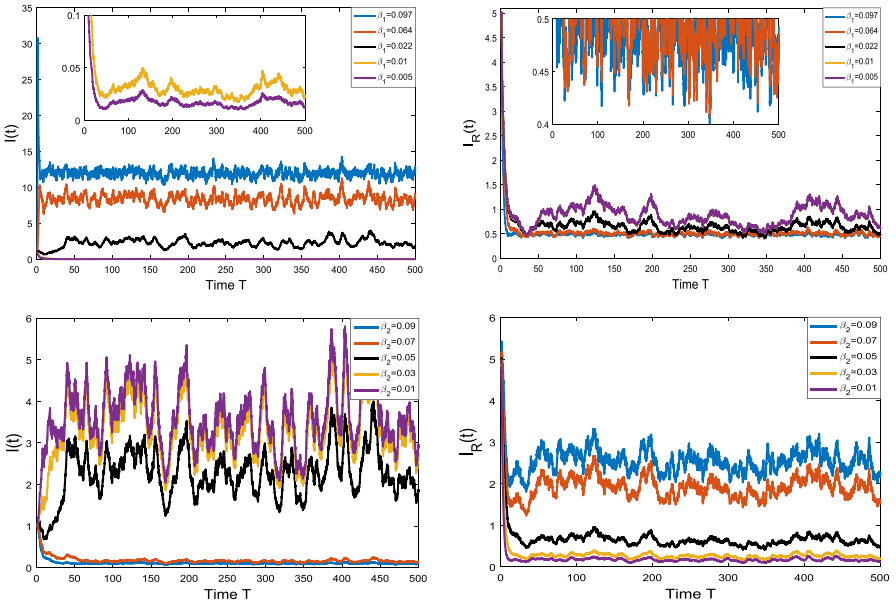


Fig. 11 The trend plots of $I(t)$ and $I_R(t)$ vary with parameters β_1 and β_2

The reduction of transmission rates can be achieved by strengthening the adherence of hand hygiene and disinfection policies on medical instruments. Figure 11 demonstrates that when the transmission rate of sensitive strain β_1 reduces, $I(t)$ markedly declines despite slight increase in $I_R(t)$. Such phenomenon can be explained by the competitive exclusion principle in ecology, and is observed as expected. The infected population for both strains would decrease significantly when both transmission rates are reduced. Hence, cutting off the transmission routes of pathogenic bacteria could effectively reduce the risk of nosocomial infection from these aspects together: medical staff, patients and the environment of hospital wards. For instance, sterile operation should be implemented at the course of surgeries and nursing care, precision instruments, syringes, catheters *etc*. would be regularly counted and disinfected, the compliance of hand hygiene for medical workers and volunteers should be strengthened. Washing hands for family members of patients would be encouraged and visiting hours should be shortened, patients' ward should be regularly decontaminated and the ward trash should be cleaned up in time, etc.

(ii) Extending latent period of patients colonized with sensitive/resistant strains.

Patients colonized with sensitive and resistant strains can develop infections after latent period $\frac{1}{\delta}$ and $\frac{1}{\nu}$, respectively. As shown in Fig. 12, both $I(t)$ and $I_R(t)$ distinctly decrease and keep themselves at a relatively low level. This shows that nosocomial infection could be controlled at a low level if it takes a longer time for colonized patients to develop infections. Strategies such as monitoring targeted infection cases, early diagnosis and therapy for patients, and strength exercise for improving immunity of patients may help with the prevention of infection development.

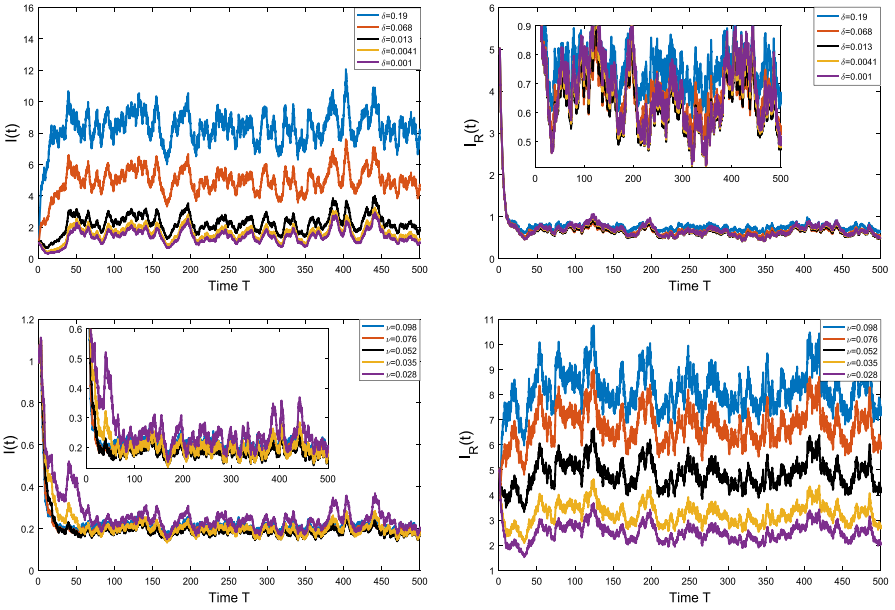


Fig. 12 The trend plots of $I(t)$ and $I_R(t)$ vary with parameters δ and ν

(iii) Improving treatment accuracy and preventing antibiotic resistance.

Figure 13 shows that improving the treatment efficiency for sensitive strain infections can significantly reduce the prevalence of sensitive strains where that of resistant strains are not crucially affected. Whereas improving the treatment efficiency for resistant strain infections could in turn promote the prevalence of sensitive strains. In reality, enhancing treatment accuracy for sensitive strain infections are relatively feasible, but this could be hindered by the fear of resulting in higher prevalence of resistant strains. Our simulation indicates that there would be no harm on the ecology of nosocomial pathogens if only treatment accuracy of sensitive strains can be improved. Further, our simulation of varying the value of resistance development rate η shows increases of resistant strains and decrease of sensitive strains, which are expected results.

4.5 Stochastic extinction for model (2.1)

In the following, we would provide the two numerical examples to exhibit the stochastic extinction of nosocomial infection.

First of all, we choose the following feasible parameters to verify Theorem 3.1: $\mu = 0.02$, $\Lambda = 0.8$, $p = 0.2$, $q = 0.5$, $\delta = 0.033$, $\theta = 0.01$, $\gamma = 0.05$, $\eta = 0.03$, $d_1 = 0.002$, $d_2 = 0.023$, $k = 0.04$, $\nu = 0.02$, $\alpha = 0.03$, $\beta_1 = 0.0018$, $\beta_2 = 0.0017$, $\sigma_1 = 0.02$, $\sigma_2 = 0.45$, $\sigma_3 = 0.56$, $\sigma_4 = 0.59$, $\sigma_5 = 0.49$ and $\sigma_6 = 0.39$, respectively. By calculation, we obtain the basic reproduction number $\mathcal{R}_0$ for the deterministic model (3.2) is 1.048 and a positive left eigenvector $(\xi_1, \xi_2, \xi_3, \xi_4, \xi_5)$ corresponding to $\mathcal{R}_0$ is (0.4937, 0.4252, 0.3936, 0.4853, 0.4303), and then $\sigma_1^2 - 2\mu = -0.0396 < 0$,

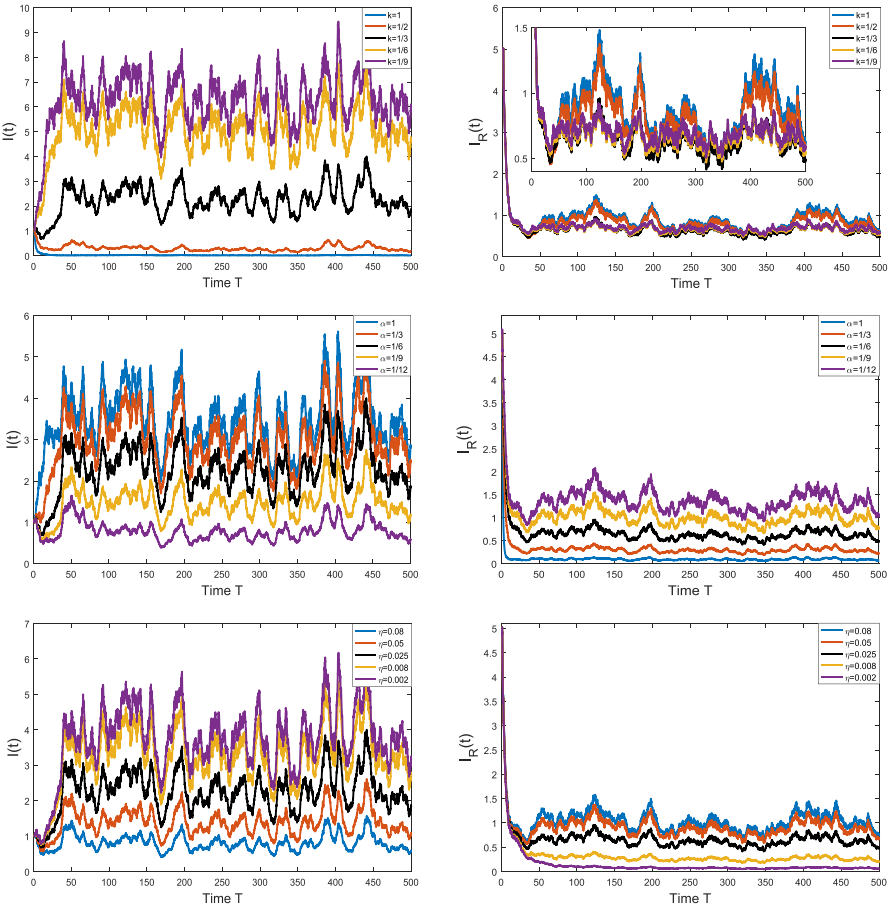


Fig. 13 The trend plots of $I(t)$ and $I_R(t)$ vary with parameters k, α and η

$m = -0.0014 < 0$, which are satisfied with the conditions of Theorem 3.1. As shown in Fig. 14, the solution of stochastic model (2.1) would become extinct while the solution of the deterministic system would be prevalent under the same parameter values.

Next, we would show the stochastic extinction of nosocomial infection in model (2.1) when $\widetilde{\mathfrak{R}}_0^S$ defined in Theorem 3.2 is less than one. Select these parameters in model (2.1): $\mu = 0.42$, $\Lambda = 1.4$, $p = 0.2$, $q = 0.5$, $\delta = 0.3$, $\theta = 0.51$, $\gamma = 0.35$, $\eta = 0.23$, $d_1 = 0.102$, $d_2 = 0.36$, $k = 0.74$, $\nu = 0.28$, $\alpha = 0.39$, $\beta_1 = 0.38$, $\beta_2 = 0.47$, $\sigma_1 = 0.42$, $\sigma_2 = 0.35$, $\sigma_3 = 0.26$, $\sigma_4 = 0.39$, $\sigma_5 = 0.59$ and $\sigma_6 = 0.39$, respectively. By computation, we obtain $\widetilde{\mathfrak{R}}_0^S \approx 0.7039 < 1$, which are not satisfied with the condition of Theorem 3.2. As shown in Fig. 15, the solution of stochastic model (2.1) would become extinct. Combining this example and the one in Sect. 4.2 (Fig. 7), it would be derived that condition $\widetilde{\mathfrak{R}}_0^S < 1$ does not guarantees the solution

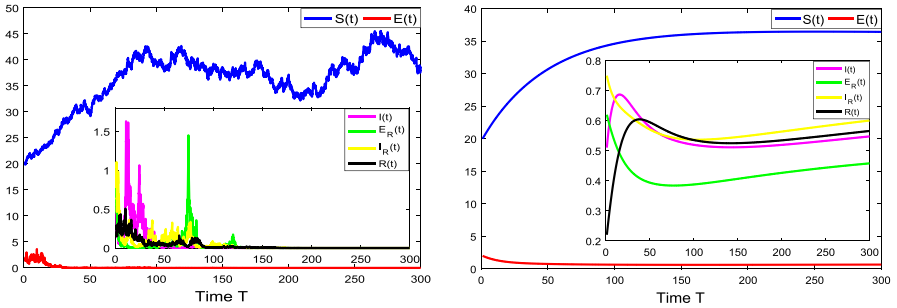


Fig. 14 The evolution of a single path of solutions for model (2.1) and its corresponding deterministic model (3.2). The initial value of all solutions is (20, 2, 0.51, 0.62, 0.75, 0.22)

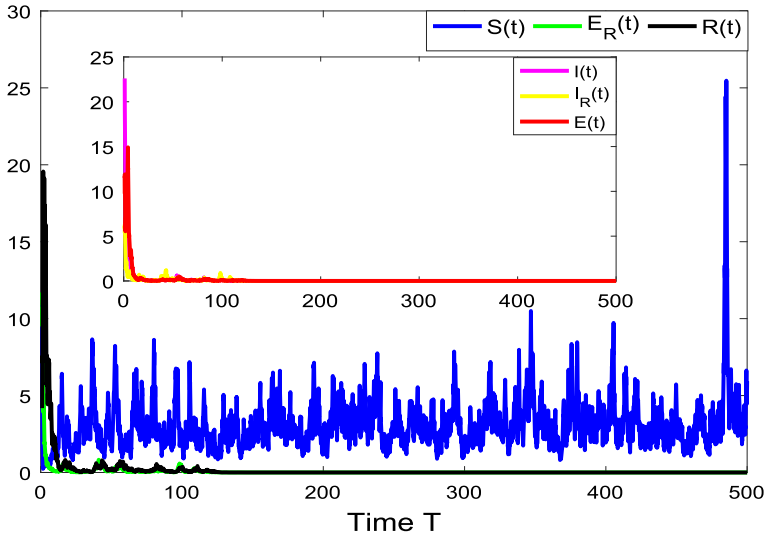


Fig. 15 The solution of model (2.1) becomes extinct when $\widetilde{\mathfrak{R}}_0^S \approx 0.7039 < 1$. The initial value of the solution is (13, 10, 21, 12, 5, 4)

of stochastic model (2.1) must be extinct, but there may be existed a uniquely ergodic stationary distribution of solutions for model (2.1).

5 Conclusion and discussion

In this paper, we derived a stochastic dynamical model about the transmission of bacterial strains among patients in a hospital setting, where the randomness of death and discharge for all patients is modeled by introducing linear functions of white noise. The dynamical behaviors for this model were analyzed. Firstly, we showed that large randomness of death and discharge in colonized and infected patients may rule out

the possibility of nosocomial outbreaks. This result is biologically sound because the significant variance in the length of stay will result in less transmission caused by the infectious patients while the uncolonized patient population are maintained at a reasonable amount ($\sigma_1^2 < 2\mu$ in Theorem 3.1). The spectral radius analysis method applied in the proof of the corresponding theorem is challenging and innovative because it could be extended from traditional deterministic models or stochastic models with only one infection route to sensitive and resistant strains infection routes in our paper. Another highlight of this paper is, we defined the stochastic threshold value for nosocomial outbreaks of both strains, and prove that when the model parameters exceed this threshold, the system admits a unique stationary distribution with solutions being ergodic by constructing suitable stochastic Lyapunov functions. However, this Lyapunov function is very complex since there are sensitive and resistant strains infection routes in this model, and we have obtained more general and milder conditions for the existence and ergodicity of the stationary distribution, which is different from the conditions related with the endemic equilibrium of the corresponding deterministic model in Fu (2019).

It is not hard to show that, without the stochastic terms, the endemic steady state of the corresponding deterministic system is globally stable when the basic reproductive number is larger than one (Mccluskey 2006). Our results show that variances in death and discharge will reduce the stochastic threshold value, and then reduce the potential of nosocomial outbreaks. It is worth mentioning that the spectral radius form of stochastic threshold value is provided in the special case of model (2.1), similarly with the corresponding deterministic system. We therefore conjecture that one can obtain ergodic solution that admits a stationary distribution when this spectral radius is larger than one, and will investigate it in our future work.

We performed numerical simulations to both validate the theoretical results and investigate the effect of prevention and control strategies on the prevalence of nosocomial infection. In particular, one of the highlights of numerical simulations is to select credible transmission rates by calibrating them to known range of the health-care associated infection acquisition, which is also different from stochastic simulations in the previous literature Wang et al. (2018, 2021). Additionally, based on the result of global sensitivity analysis, we explored the effect of prevention and control strategies on the prevalence of nosocomial infection. Our simulation results suggest a number of infection control strategies such as enhancing hygiene, preventing infections, improving treatment accuracy, shortening the treatment length, etc..

Last but not least, from the modeling point of view, there are more than one directions to formulate randomness in epidemiological models. Here we adopt the idea used mostly in financial modeling (Mao 2008; Lan et al. 2021). In some studies, stochastic models can be derived for each model parameters with random values (Allen 2016). In many other studies, the population compartments are first formulated as a continuous-time random variable with integer values by considering random transmission events (Allen 2008). In addition, from the perspective of genetic mechanism, gene transcription, translation and transportation in the process of co-circulation of antibiotic-sensitive and antibiotic-resistant bacterial strains are not completed instantaneously and will take some time (Monk 2003), therefore, studies on stochastic models

with consideration of time delays are potential future directions towards realistic applications of this modeling framework (Xu et al. 2021).

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Data availability Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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