Received: 27 November 2023 | Accepted: 10 April 2024

DOI: 10.1002/mma.10165

RESEARCH ARTICLE

WILEY

An age-structured SVEAIR epidemiological model

Vasiliki Bitsouni[1] | **Nikolaos Gialelis**[2,3] | **Vasilis Tsilidis**[1]

[1]Department of Mathematics, University of Patras, Rio Patras, Greece

[2]Department of Mathematics, National and Kapodistrian University of Athens, Athens, Greece

[3]School of Medicine, National and Kapodistrian University of Athens, Athens, Greece

Correspondence
Vasiliki Bitsouni, Department of Mathematics, University of Patras, GR-26504 Rio Patras, Greece.
Email: vbitsouni@math.upatras.gr

Communicated by: G. Barbatis

In this paper, we introduce and study an age-structured epidemiological compartment model and its respective problem, applied but not limited to the COVID-19 pandemic, in order to investigate the role of the age of the individuals in the evolution of epidemiological phenomena. We investigate the well-posedness of the model, as well as the global dynamics of it in the sense of basic reproduction number, via constructing Lyapunov functions.

KEYWORDS

age-structured epidemiological model, asymptomatic infectious, basic reproductive number, global stability, Lyapunov function, stability analysis

MSC CLASSIFICATION

35B35, 35Q92, 37N25, 92D30

1 | INTRODUCTION

Epidemiological mathematical models have played a crucial role in understanding and predicting the spread of infectious diseases, as well as informing public health policies and measures (see the literature [1–5] and many references therein). With the emergence of the COVID-19 pandemic, the importance of these models has been highlighted as they have been used to assess the anticipated spread of the virus and inform strategies to mitigate its impact [6–8].

One of the key aspects of modern epidemiological models is the incorporation of age-structured models, which take into account the differences in susceptibility, transmission, and disease progression across various age groups (such as previous works [2, 9]). This approach allows for a more accurate representation of disease dynamics and enables better targeting of interventions and resource allocation.

The aim of the present paper is to investigate the role of the age of the individuals in the evolution of epidemiological phenomena. Using as a case study the COVID-19 outbreak, we aim to address the following questions:

- How does the age of individuals affect the spread of the epidemic?
- What is the effect of the asymptomatic infectious individuals on the basic reproduction number, $\mathcal{R}_0$, of COVID-19?

We address the above questions by deriving an age-structured epidemiological compartment model that incorporates the important role of both asymptomatic and symptomatic individuals.

This study is organized as follows. In Section 2, we develop a novel age-structured SVEAIR model that incorporates, among others, the ambiguous (see Section 2.1) variable of asymptomaticity of infectious individuals for the spread of COVID-19 disease. We show its global well-posedness, we derive the basic reproductive number, $\mathcal{R}_0$, of the model, and we study the global stability of its steady states. In Section 3, we undertake numerical simulations to confirm the behavior of the solution of the problem. We conclude in Section 4 with a summary and discussion of the results.

2 | THE EPIDEMIOLOGICAL MODEL

Here, we introduce an epidemiological model, $\mathscr{M}$, along with the respective problem, $\mathscr{P}$, as a means of investigating the main questions of the present paper.

2.1 Derivation and analysis of the model

One of the most critical facts about COVID-19, is that a significant number of cases, mainly those of young age, have been reported as asymptomatic (see Gao et al. [10] and many references therein), leading to the fast spread of the infection. Although the asymptomatic cases have a shorter duration of viral shedding and lower viral load [11, 12], their proportion can range from 4% to 90% (see previous works [13, 14] and many references therein), and most of the time, they play a key role in infection transmission. Therefore, we incorporate not only both symptomatic and asymptomatic cases in our model (as it is done in, e.g., Bitsouni et al. [15]), but also the age of the infected/infectious individuals.

In particular, the proposed $\mathscr{M}$ is based on the following hypotheses.

1. The *total population*, N, is classified into six non-negative-valued compartments, *susceptible*, S, *vaccinated-with-a-prophylactic-vaccine*, V, *latent/exposed*, E, *asymptomatic infectious*, A, *symptomatic infectious*, I, and *recovered/removed*, R, *individuals*; thus,
$$N = S + V + E + A + I + R.$$
All of the above epidemiological variables depend on non-negative *time*, t.
2.
   i. There is also another independent non-negative "*age*"-variable, θ, which measures the time elapsed since, for example, birth or infection. The two time-variables have different scales, that is, they are measured in different units, and the parameter $\omega \in \mathbb{R}^+$ stands for the *conversion factor* from the units of θ to the units of t.
   ii. Only the non-negative-valued *age-densities* of E, A and I, that is, e, a and i, respectively, contribute to our $\mathscr{M}$. Those densities should vanish at (or have already vanished before) $\theta \to \infty$, hence it is natural for them to be considered as elements of $L^1\left(\mathbb{R}_0^+\right)$, for every fixed t. In the light of the above assumption, the expressions
$$E = \int_0^\infty e(\cdot,\theta)\,\mathrm{d}\theta,\ A = \int_0^\infty a(\cdot,\theta)\,\mathrm{d}\theta \text{ and } I = \int_0^\infty i(\cdot,\theta)\,\mathrm{d}\theta$$
are well-posed.
3.
   i. The vaccine is considered to be *purely prophylactic*.
   ii. Only a part of population is vaccinated and $p \in [0,1]$ stands for the *vaccine coverage*. Since the vaccine is supposed to be purely prophylactic, the only source for the vaccinees concerns the pool of the susceptible individuals. That source is considered to be linear.
   iii. The vaccine is likely to be imperfect (at providing prophylaxis) and $\epsilon \in [0,1]$ stands for its *effectiveness*.
   iv. The *vaccine-induced immunity*, that is, the process of vaccinees obtaining immunity and moving into the recovered population, is considered to be linear, and the letter $\zeta \in \mathbb{R}_0^+$ is employed for the vaccine-induced immunity rate.
4. The *transmission*, that is, the process of susceptible individuals and failed-to-be-immune vaccinees becoming latent, is considered to be exclusively *horizontal* and to be governed by the *Holling-type-I functional response*. The parameters $\beta_A, \beta_I \in L^\infty\left(\mathbb{R}_0^+;\mathbb{R}_0^+\right)$ stand for the transmission rates of asymptomatic and symptomatic, respectively, infectious individuals.
5. The *incubation*, that is, the process of latent individuals becoming infectious, is considered to be linear and $k \in L^\infty\left(\mathbb{R}_0^+;\mathbb{R}_0^+\right)$ is the incubation rate. That rate is the same for both asymptomatic and symptomatic classes, but those classes are different from each other in terms of magnitude of their sources. In particular, $q \in L^\infty\left(\mathbb{R}_0^+;[0,1]\right)$ stands for the proportion of latent individuals that become asymptomatic infectious ones.
6. The *recovery*, that is, the process of infectious individuals moving into the recovered population, is considered to be linear and $\gamma_A, \gamma_I \in L^\infty\left(\mathbb{R}_0^+;\mathbb{R}_0^+\right)$ stand for the recovery rates of asymptomatic and symptomatic, respectively, infectious ones.
7.
   i. Some asymptomatic infectious individuals never develop symptoms, and thus move directly into the recovered/removed class, with the letter $\xi \in L^\infty\left(\mathbb{R}_0^+;[0,1]\right)$ being employed for the proportion of those asymptomatic infectious individuals.
   ii. The *symptomatic transition*, that is, the process of asymptomatic infectious individuals turning into symptomatic ones, is considered to be linear and $\chi \in L^\infty\left(\mathbb{R}_0^+;\mathbb{R}_0^+\right)$ stands for the symptomatic transition rate.
8. *Demographic terms* are taken into account, and they are considered to be linear, with $\mu \in \mathbb{R}^+$ being the universal birth/death rate. We note that μ is considered to be the only strictly positive constant of $\mathscr{M}$.

9. No *reinfections* are taken into account; hence, no movement from the pool of the removed individuals to the pool of the susceptible ones is considered.

The respective *initial-boundary value* $\mathscr{P}$ has the following form: For a given

$$(S_0, V_0, e_0, a_0, i_0, R_0) \in \left(\mathbb{R}_0^+\right)^2 \times \left(L^1\left(\mathbb{R}_0^+;\mathbb{R}_0^+\right)\right)^3 \times \mathbb{R}_0^+,$$

we search for $T > 0$ and smooth enough

$$(S, V, e, a, i, R) : [0, T) \to \left(\mathbb{R}_0^+\right)^2 \times \left(L^1\left(\mathbb{R}_0^+;\mathbb{R}_0^+\right)\right)^3 \times \mathbb{R}_0^+,$$

such that

$$\begin{cases} \dfrac{\mathrm{d}S}{\mathrm{d}t} = \mu N - \left(p + \displaystyle\int_0^\infty \beta_A(\theta) a(\cdot,\theta) + \beta_I(\theta) i(\cdot,\theta)\,\mathrm{d}\theta + \mu \right) S \\ S(0) = S_0, \end{cases} \tag{1a}$$

$$\begin{cases} \dfrac{\mathrm{d}V}{\mathrm{d}t} = pS - \left(\zeta\epsilon + \displaystyle\int_0^\infty \beta_A(\theta) a(\cdot,\theta) + \beta_I(\theta) i(\cdot,\theta)\,\mathrm{d}\theta\,(1-\epsilon) + \mu \right) V \\ V(0) = V_0, \end{cases} \tag{1b}$$

$$\begin{cases} \dfrac{\partial e}{\partial t} + \dfrac{1}{\omega}\dfrac{\partial e}{\partial \theta} = -(k+\mu)\,e \\ e(\cdot,0) = \omega \displaystyle\int_0^\infty \beta_A(\theta) a(\cdot,\theta) + \beta_I(\theta) i(\cdot,\theta)\,\mathrm{d}\theta\,(S + (1-\epsilon)V) \\ e(0,\cdot) = e_0, \end{cases} \tag{1c}$$

$$\begin{cases} \dfrac{\partial a}{\partial t} + \dfrac{1}{\omega}\dfrac{\partial a}{\partial \theta} = -(\gamma_A \xi + \chi(1-\xi) + \mu)\,a \\ a(\cdot,0) = \omega \displaystyle\int_0^\infty k(\theta) q(\theta) e(\cdot,\theta)\,\mathrm{d}\theta \\ a(0,\cdot) = a_0, \end{cases} \tag{1d}$$

$$\begin{cases} \dfrac{\partial i}{\partial t} + \dfrac{1}{\omega}\dfrac{\partial i}{\partial \theta} = -(\gamma_I + \mu)\,i \\ i(\cdot,0) = \omega \displaystyle\int_0^\infty k(\theta)(1-q(\theta))\,e(\cdot,\theta) + \chi(\theta)(1-\xi(\theta))\,a(\cdot,\theta)\,\mathrm{d}\theta \\ i(0,\cdot) = i_0, \end{cases} \tag{1e}$$

$$\begin{cases} \dfrac{\mathrm{d}R}{\mathrm{d}t} = \zeta\epsilon V + \displaystyle\int_0^\infty \gamma_A(\theta)\xi(\theta) a(\cdot,\theta) + \gamma_I(\theta) i(\cdot,\theta)\,\mathrm{d}\theta - \mu R \\ R(0) = R_0. \end{cases} \tag{1f}$$

The dimensional units of all variables and parameters appeared in $\mathscr{P}$ (1) are gathered in Table 1.

We notice that by integration (with respect to θ over $\mathbb{R}_0^+$) and summation of the left and right-hand side of the derived ordinary differential equations, one gets

$$\frac{\mathrm{d}N}{\mathrm{d}t} = 0 \Longleftrightarrow N = N_0 := S_0 + V_0 + E_0 + A_0 + I_0 + R_0, \tag{2}$$

TABLE 1 Description of the independent and dependent variables as well as parameters of $\mathscr{M}$, along with their units.

Independent variables	**Description**	**Units**
t	Time	T
θ	Age, that is, time elapsed since, for example, birth or infection	Θ
Conversion factor	**Description**	**Units**
ω	Conversion factor from the units of θ to the units of t	$\mathrm{T}\Theta^{-1}$
Dependent variables	**Description**	**Units**
N	Number of total population of individuals	#
S	Number of susceptible individuals	#
V	Number of vaccinated-with-a-prophylactic-vaccine individuals	#
e	Age-density of latent/exposed individuals	$\#\Theta^{-1}$
E	Number of latent/exposed individuals	#
a	Age-density of asymptomatic infectious individuals	$\#\Theta^{-1}$
A	Number of asymptomatic infectious individuals	#
i	Age-density of symptomatic infectious	$\#\Theta^{-1}$
I	Number of symptomatic infectious individuals	#
R	Number of recovered/removed individuals	#
Parameters	**Description**	**Units**
N_0	Population size	#
μ	Birth/death rate	T^{-1}
β_A	Transmission rate of asymptomatic infectious individuals	$\#^{-1}\mathrm{T}^{-1}$
β_I	Transmission rate of symptomatic infectious individuals	$\#^{-1}\mathrm{T}^{-1}$
p	Vaccination rate	T^{-1}
ϵ	Vaccine effectiveness	-
ζ	Vaccine-induced immunity rate	T^{-1}
k	Latent rate (rate of susceptible individuals becoming infectious)	T^{-1}
q	Proportion of the latent/exposed individuals becoming asymptomatic infectious	-
ξ	Proportion of the asymptomatic infectious individuals becoming recovered/removed (without developing any symptoms)	-
χ	Incubation rate (rate of a part of asymptomatic infectious individuals developing symptoms)	T^{-1}
γ_A	Recovery rate of asymptomatic infectious individuals	T^{-1}
γ_I	Recovery rate of symptomatic infectious individuals	T^{-1}

where

$$E_0 := \int_0^\infty e_0(\theta)\ \mathrm{d}\theta,\ A_0 := \int_0^\infty a_0(\theta)\ \mathrm{d}\theta \text{ and } I_0 := \int_0^\infty i_0(\theta)\ \mathrm{d}\theta.$$

Hence, an additional hypothesis made is as follows.

1. The total population remains constant. This is a practical (yet not necessary) assumption and makes sense when the time-span of the modeled epidemiological phenomenon is way shorter than the time needed for observable changes of the total population (whether they are caused by the epidemic or not).

Equations (1a)–(1e) are independent of R, hence the problem is reduced to the aforementioned subsystem itself. In fact, with (2) at hand, R can be easily calculated by

$$R = N_0 - S - V - E - A - I.$$

2.1.1 Scaling of age

In order to simplify the analysis of (1a)–(1e), we eliminate the factor ω. We do so by the *scaling* of the independent age-variable, θ, and turning it to another time-variable measured in the same units as t.

Hence, while keeping the same notation, we change the variables as follows:

$$\begin{aligned} \omega\theta &\mapsto \theta, \\ \frac{1}{\omega} f \circ \frac{1}{\omega}\,\mathrm{id} &\mapsto f, \\ g \circ \frac{1}{\omega}\,\mathrm{id} &\mapsto g, \end{aligned}$$

for $(f, g) \in \left\{ e(t,\cdot), a(t,\cdot), i(t,\cdot) \,\middle|\, t \in \mathbb{R}_0^+ \right\} \times \{\beta_A, \beta_I, k, q, \gamma_A, \xi, \chi, \gamma_I\}$, and (1a)–(1e) then becomes

$$\begin{cases} \dfrac{\mathrm{d}S}{\mathrm{d}t} = \mu N_0 - \left(p + \displaystyle\int_0^\infty \beta_A(\theta) a(\cdot,\theta) + \beta_I(\theta) i(\cdot,\theta)\, \mathrm{d}\theta + \mu \right) S \\ S(0) = S_0, \end{cases} \tag{3a}$$

$$\begin{cases} \dfrac{\mathrm{d}V}{\mathrm{d}t} = pS - \left(\zeta\epsilon + \displaystyle\int_0^\infty \beta_A(\theta) a(\cdot,\theta) + \beta_I(\theta) i(\cdot,\theta)\, \mathrm{d}\theta\, (1-\epsilon) + \mu \right) V \\ V(0) = V_0, \end{cases} \tag{3b}$$

$$\begin{cases} \dfrac{\partial e}{\partial t} + \dfrac{\partial e}{\partial \theta} = -(k+\mu)\, e \\ e(\cdot,0) = \displaystyle\int_0^\infty \beta_A(\theta) a(\cdot,\theta) + \beta_I(\theta) i(\cdot,\theta)\, \mathrm{d}\theta\, (S + (1-\epsilon) V) \\ e(0,\cdot) = e_0, \end{cases} \tag{3c}$$

$$\begin{cases} \dfrac{\partial a}{\partial t} + \dfrac{\partial a}{\partial \theta} = -(\gamma_A \xi + \chi(1-\xi) + \mu)\, a \\ a(\cdot,0) = \displaystyle\int_0^\infty k(\theta) q(\theta) e(\cdot,\theta)\, \mathrm{d}\theta \\ a(0,\cdot) = a_0, \end{cases} \tag{3d}$$

$$\begin{cases} \dfrac{\partial i}{\partial t} + \dfrac{\partial i}{\partial \theta} = -(\gamma_I + \mu)\, i \\ i(\cdot,0) = \displaystyle\int_0^\infty k(\theta)(1-q(\theta))\, e(\cdot,\theta) + \chi(\theta)(1-\xi(\theta))\, a(\cdot,\theta)\, \mathrm{d}\theta \\ i(0,\cdot) = i_0, \end{cases} \tag{3e}$$

where t and (the new) θ are now measured in the same time-units.

The flow diagram of the differential equations in (1) is shown in Figure 1.

2.1.2 | Global well-posedness

We set

$$\beta := \int_0^\infty \beta_A(\theta) a(\cdot,\theta) + \beta_I(\theta) i(\cdot,\theta)\, \mathrm{d}\theta, \tag{4a}$$

$$\varepsilon := e(\cdot,0) = \beta\,(S + (1-\epsilon) V), \tag{4b}$$

$$\alpha := a(\cdot,0) = \int_0^\infty k(\theta) q(\theta) e(\cdot,\theta)\, \mathrm{d}\theta, \tag{4c}$$

$$\iota := i(\cdot,0) = \int_0^\infty k(\theta)(1-q(\theta))\, e(\cdot,\theta) + \chi(\theta)(1-\xi(\theta))\, a(\cdot,\theta)\, \mathrm{d}\theta. \tag{4d}$$

Integrating the independent variables of (3a) and (3b) along $[0,T)$, as well as the independent variables of (3c)–(3e) along the *characteristic straight-line paths*

$$\left\{ (t,\theta) \in [0,T) \times \mathbb{R}_0^+ \,\middle|\, t - \theta = c \right\}, \forall c \in \mathbb{R},$$

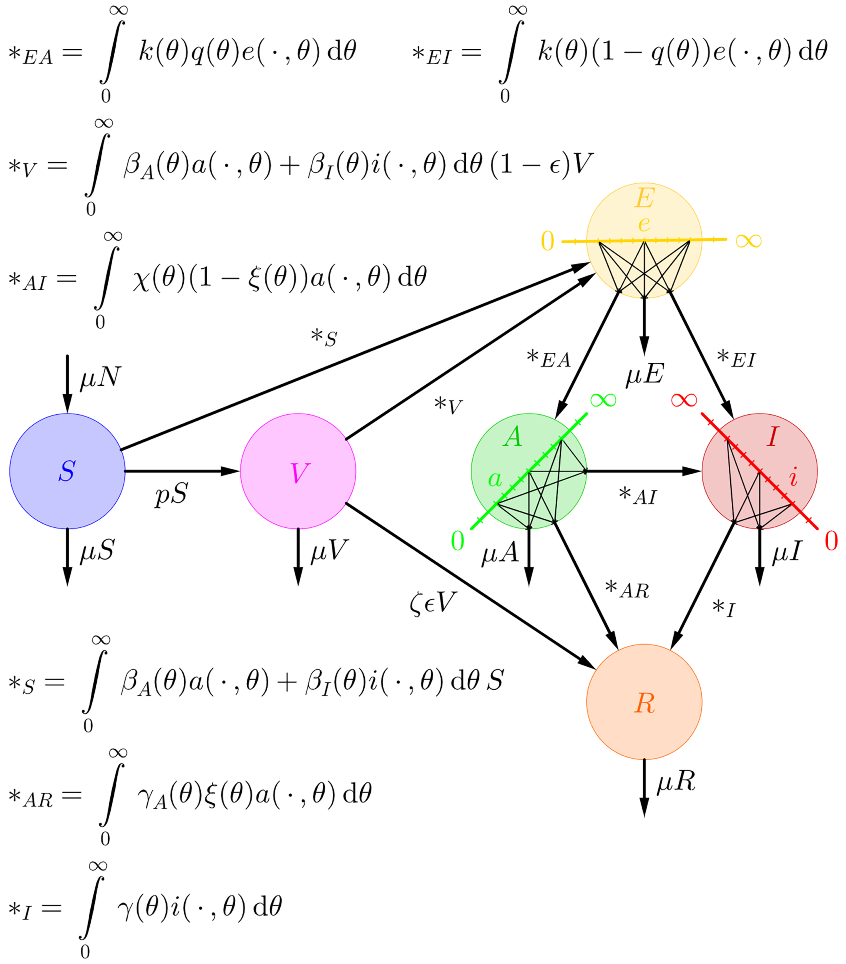

FIGURE 1 Flow diagram of $\mathscr{P}$ (3). The increase/decrease of A and I reflects the outbreak/attenuation of the epidemic, while E is the only source of the aforementioned compartments. [Colour figure can be viewed at wileyonlinelibrary.com]

we deduce that

$$S(t) = S_0 \mathrm{e}^{-\int_0^t p+\beta(s)+\mu\,\mathrm{d}s} + \mu N_0 \int_0^t \mathrm{e}^{-\int_s^t p+\beta(\tau)+\mu\,\mathrm{d}\tau}\,\mathrm{d}s,\ \forall t \in [0,T), \tag{5a}$$

$$V(t) = V_0 \mathrm{e}^{-\int_0^t \zeta\epsilon+\beta(s)(1-\epsilon)+\mu\,\mathrm{d}s} + p\int_0^t S(s)\mathrm{e}^{-\int_s^t \zeta\epsilon+\beta(\tau)(1-\epsilon)+\mu\,\mathrm{d}\tau}\,\mathrm{d}s,\ \forall t \in [0,T), \tag{5b}$$

$$e(t,\theta) = \begin{cases} e_0(\theta-t)\,\mathrm{e}^{-\int_0^t k(\theta-t+s)+\mu\,\mathrm{d}s}, & \text{if } t \in [0,\theta) \subsetneq [0,T) \\ \varepsilon(t-\theta)\,\mathrm{e}^{-\int_0^\theta k(s)+\mu\,\mathrm{d}s}, & \text{if } \theta \in [0,t) \subsetneq [0,T), \end{cases} \tag{5c}$$

$$a(t,\theta) = \begin{cases} a_0(\theta-t)\,\mathrm{e}^{-\int_0^t \gamma_A(\theta-t+s)\xi(\theta-t+s)+\chi(\theta-t+s)(1-\xi(\theta-t+s))+\mu\,\mathrm{d}s}, & \text{if } t \in [0,\theta) \subsetneq [0,T) \\ \alpha(t-\theta)\,\mathrm{e}^{-\int_0^\theta \gamma_A(s)\xi(s)+\chi(s)(1-\xi(s))+\mu\,\mathrm{d}s}, & \text{if } \theta \in [0,t) \subsetneq [0,T). \end{cases} \tag{5d}$$

$$i\,(t,\theta)=\begin{cases} i_0\,(\theta-t)\,\mathrm{e}^{-\int\limits_0^t \gamma_I(\theta-t+s)+\mu\,\mathrm{d}s}, & \text{if } t\in[0,\theta)\subsetneq[0,T) \\ \imath\,(t-\theta)\,\mathrm{e}^{-\int\limits_0^\theta \gamma_I(s)+\mu\,\mathrm{d}s}, & \text{if } \theta\in[0,t)\subsetneq[0,T). \end{cases} \tag{5e}$$

We then plug system (5) into system (4) to obtain

$$\beta(t)=\int\limits_0^t \beta_1(t,s)\,\mathrm{d}s+\int\limits_0^\infty \beta_2(t,s)\,\mathrm{d}s,\ \forall t\in[0,T), \tag{6a}$$

$$\varepsilon(t)=\beta(t)\,(S(t)+(1-\epsilon)\,V(t))\,,\ \forall t\in[0,T), \tag{6b}$$

$$\alpha(t)=\int\limits_0^t \alpha_1(t,s)\,\mathrm{d}s+\int\limits_0^\infty \alpha_2(t,s)\,\mathrm{d}s,\ \forall t\in[0,T), \tag{6c}$$

$$\imath(t)=\int\limits_0^t \imath_1(t,s)\,\mathrm{d}s+\int\limits_0^\infty \imath_2(t,s)\,\mathrm{d}s,\ \forall t\in[0,T), \tag{6d}$$

where

$$\begin{aligned} \beta_1(t,s)\ &:=\beta_A\,(t-s)\,\alpha(s)\mathrm{e}^{-\int\limits_0^{t-s} \gamma_A(\tau)\xi(\tau)+\chi(\tau)(1-\xi(\tau))+\mu\,\mathrm{d}\tau}+\beta_I\,(t-s)\,\imath(s)\mathrm{e}^{-\int\limits_0^{t-s} \gamma_I(\tau)+\mu\,\mathrm{d}\tau}, \\ \beta_2(t,s)\ &:=\beta_A(t+s)a_0(s)\mathrm{e}^{-\int\limits_0^{t} \gamma_A(\tau+s)\xi(\tau+s)+\chi(\tau+s)(1-\xi(\tau+s))+\mu\,\mathrm{d}\tau}+\beta_I(t+s)i_0(s)\mathrm{e}^{-\int\limits_0^{t} \gamma_I(\tau+s)+\mu\,\mathrm{d}\tau}, \end{aligned}$$

S and V have already been calculated in terms of β in (5a) and (5b), respectively,

$$\begin{aligned} \alpha_1(t,s)\ &:=k\,(t-s)\,q\,(t-s)\,\beta(s)\,(S(s)+(1-\epsilon)\,V(s))\,\mathrm{e}^{-\int\limits_0^{t-s} k(\tau)+\mu\,\mathrm{d}\tau}, \\ \alpha_2(t,s)\ &:=k(t+s)q(t+s)e_0(s)\mathrm{e}^{-\int\limits_0^{t} k(\tau+s)+\mu\,\mathrm{d}\tau} \end{aligned}$$

and

$$\begin{aligned} \imath_1(t,s)\ &:=k\,(t-s)\,(1-q\,(t-s))\,\beta(s)\,(S(s)+(1-\varepsilon)\,V(s))\,\mathrm{e}^{-\int\limits_0^{t-s} k(\tau)+\mu\,\mathrm{d}\tau}+ \\ &\quad+\chi\,(t-s)\,(1-\xi\,(t-s))\,\alpha(s)\mathrm{e}^{-\int\limits_0^{t-s} \gamma_A(\tau)\xi(\tau)+\chi(\tau)(1-\xi(\tau))+\mu\,\mathrm{d}\tau}, \\ \imath_2(t,s)\ &:=k(t+s)\,(1-q(t+s))\,e_0(s)\mathrm{e}^{-\int\limits_0^{t} k(\tau+s)+\mu\,\mathrm{d}\tau}+ \\ &\quad+\chi(t+s)\,(1-\xi(t+s))\,a_0(s)\mathrm{e}^{-\int\limits_0^{t} \gamma_A(t+s)\xi(t+s)+\chi(t+s)(1-\xi(t+s))+\mu\,\mathrm{d}\tau}. \end{aligned}$$

Equations (6a), (6c), and (6d) can be considered as an auxiliary problem (in integral form) for the unknown functions β, α and ι. A direct application of the *classic theory of integral equations* provides us with the following preliminary result, the standard proof of which is omitted (see, e.g., the literature [2, 16, 17]).

Theorem 1. *For every* $(S_0, V_0, e_0, a_0, i_0, R_0) \in \mathbb{R}^2 \times \left(L^1\left(\mathbb{R}_0^+; \mathbb{R}\right)\right)^3 \times \mathbb{R}$, *the problem (6a), (6c), (6d) is globally (i.e.,* $T = \infty$*) well-posed, with* $(\beta, \alpha, \iota) \in \left(C\left(\mathbb{R}_0^+; \mathbb{R}\right)\right)^3$.

Moreover, it is straightforward to check that if $(S_0, V_0, e_0, a_0, i_0, R_0) = (0, 0, 0, 0, 0, N_0)$, then the solution of (6a), (6c), (6d) is the constant $(\beta, \alpha, \iota) = (0, 0, 0)$. Hence, from the uniqueness of solution, we derive the next result.

Proposition 1. *If* $(S_0, V_0, e_0, a_0, i_0, R_0) \in \left(\mathbb{R}_0^+\right)^2 \times \left(L^1\left(\mathbb{R}_0^+; \mathbb{R}_0^+\right)\right)^3 \times \mathbb{R}_0^+$, *then* $(\beta, \alpha, \iota) \in \left(C\left(\mathbb{R}_0^+; \mathbb{R}_0^+\right)\right)^3$.

The global well-posedness of the main problem then follows.

Corollary 1. *For every* $(S_0, V_0, e_0, a_0, i_0, R_0) \in \left(\mathbb{R}_0^+\right)^2 \times \left(L^1\left(\mathbb{R}_0^+; \mathbb{R}_0^+\right)\right)^3 \times \mathbb{R}_0^+$, *the* $\mathscr{P}$ *(3) is globally well-posed, with* $(S, V, e, a, i) \in \left(C^1\left(\mathbb{R}_0^+; \mathbb{R}_0^+\right)\right)^2 \times \left(C\left(\mathbb{R}_0^+; L^1\left(\mathbb{R}_0^+\right)\right)\right)^3$. *In particular, the differential equations in (3a) and (3b) are satisfied* $\forall t \in \mathbb{R}_0^+$, *while the subsystem (3c)–(3e) is satisfied in the following sense:*

$$\begin{cases} \lim\limits_{h \to 0} \dfrac{e(t+h,\ \theta+h) - e(t,\ \theta)}{h} = -(k(\theta) + \mu)\, e(t, \theta), \textit{ for a.e. } (t, \theta) \in \left(\mathbb{R}_0^+\right)^2 \\ e(t, 0) = \varepsilon(t), \forall t \in \mathbb{R}^+ \\ e(0, \theta) = e_0(\theta), \textit{ for a.e. } \theta \in \mathbb{R}_0^+, \end{cases}$$

$$\begin{cases} \lim\limits_{h \to 0} \dfrac{a(t+h,\ \theta+h) - a(t,\ \theta)}{h} = -(\gamma_A(\theta)\xi(\theta) + \chi(\theta)(1 - \xi(\theta)) + \mu)\, a(t, \theta), \textit{ for a.e. } (t, \theta) \in \left(\mathbb{R}_0^+\right)^2 \\ a(t, 0) = \alpha(t), \forall t \in \mathbb{R}^+ \\ a(0, \theta) = a_0(\theta), \textit{ for a.e. } \theta \in \mathbb{R}_0^+, \end{cases}$$

$$\begin{cases} \lim\limits_{h \to 0} \dfrac{i(t+h,\ \theta+h) - i(t,\ \theta)}{h} = -(\gamma_I(\theta) + \mu)\, i(t, \theta), \textit{ for a.e. } (t, \theta) \in \left(\mathbb{R}_0^+\right)^2 \\ i(t, 0) = \iota(t), \forall t \in \mathbb{R}^+ \\ i(0, \theta) = i_0(\theta), \textit{ for a.e. } \theta \in \mathbb{R}_0^+. \end{cases}$$

We also note that we can obtain certain *regularity results* by strengthening the assumptions regarding the data of the problem, but this lies beyond the scope of the present work.

2.1.3 | Steady states and basic reproductive number

A *steady state*, $(S^*, V^*, e^*, a^*, i^*)$, of $\mathscr{P}$ (3) is a constant-with-respect-to-t solution, that is, it is defined to satisfy

$$0 = \mu N_0 - (p + \beta^* + \mu)\, S^*, \tag{7a}$$

$$0 = pS^* - (\zeta\epsilon + \beta^*(1 - \epsilon) + \mu)\, V^*, \tag{7b}$$

$$\begin{cases} \dfrac{\mathrm{d}e^*}{\mathrm{d}\theta} = -(k + \mu)\, e^* \\ e^*(0) = \varepsilon^*, \end{cases} \tag{7c}$$

$$\begin{cases} \dfrac{\mathrm{d}a^*}{\mathrm{d}\theta} = -(\gamma_A\xi + \chi(1 - \xi) + \mu)\, a^* \\ a^*(0) = \alpha^*, \end{cases} \tag{7d}$$

$$\begin{cases} \dfrac{\mathrm{d}i^*}{\mathrm{d}\theta} = -(\gamma_I + \mu)\, i^* \\ i^*(0) = \iota^*, \end{cases} \tag{7e}$$

where

$$\beta^* := \int_0^\infty \beta_A(\theta)a^*(\theta) + \beta_I(\theta)i^*(\theta)\,\mathrm{d}\theta, \tag{8a}$$

$$\varepsilon^* := \beta^*\left(S^* + (1-\epsilon)\,V^*\right), \tag{8b}$$

$$\alpha^* := \int_0^\infty k(\theta)q(\theta)e^*(\theta)\,\mathrm{d}\theta, \tag{8c}$$

$$\iota^* := \int_0^\infty k(\theta)\,(1-q(\theta))\,e^*(\theta) + \chi(\theta)\,(1-\xi(\theta))\,a^*(\theta)\,\mathrm{d}\theta; \tag{8d}$$

hence,

$$S^* = \frac{\mu N_0}{p + \beta^* + \mu}, \tag{9a}$$

$$V^* = \frac{pS^*}{\zeta\epsilon + \beta^*\,(1-\epsilon) + \mu}, \tag{9b}$$

$$e^*(\theta) = \varepsilon^*\mathrm{e}^{-\int_0^\theta k(s)+\mu\,\mathrm{d}s}, \forall\theta \in \mathbb{R}_0^+, \tag{9c}$$

$$a^*(\theta) = \alpha^*\mathrm{e}^{-\int_0^\theta \gamma_A(s)\xi(s)+\chi(s)(1-\xi(s))+\mu\,\mathrm{d}s}, \forall\theta \in \mathbb{R}_0^+, \tag{9d}$$

$$i^*(\theta) = \iota^*\mathrm{e}^{-\int_0^\theta \gamma_I(s)+\mu\,\mathrm{d}s}, \forall\theta \in \mathbb{R}_0^+. \tag{9e}$$

By plugging (8b)–(8d) into (9) and expressing the components of a steady state exclusively in terms of the constant parameter β^*, we get

$$S^* = \frac{\mu N_0}{p + \beta^* + \mu}, \tag{10a}$$

$$V^* = \frac{p\mu N_0}{(p + \beta^* + \mu)\,(\zeta\epsilon + \beta^*\,(1-\epsilon) + \mu)}, \tag{10b}$$

$$e^*(\theta) = \beta^*\frac{\mu N_0}{p + \beta^* + \mu}\left(1 + \frac{p\,(1-\epsilon)}{\zeta\epsilon + \beta^*\,(1-\epsilon) + \mu}\right)\mathrm{e}^{-\int_0^\theta k(s)+\mu\,\mathrm{d}s}, \forall\theta \in \mathbb{R}_0^+, \tag{10c}$$

$$\begin{aligned} a^*(\theta) = \beta^*\frac{\mu N_0}{p + \beta^* + \mu}\left(1 + \frac{p\,(1-\epsilon)}{\zeta\epsilon + \beta^*\,(1-\epsilon) + \mu}\right)\int_0^\infty k(s)q(s)\mathrm{e}^{-\int_0^s k(\tau)+\mu\,\mathrm{d}\tau}\,\mathrm{d}s\times \\ \times\,\mathrm{e}^{-\int_0^\theta \gamma_A(s)\xi(s)+\chi(s)(1-\xi(s))+\mu\,\mathrm{d}s}, \forall\theta \in \mathbb{R}_0^+, \end{aligned} \tag{10d}$$

$$
\begin{aligned}
i^*(\theta) = \beta^* \frac{\mu N_0}{p+\beta^*+\mu}\left(1+\frac{p\,(1-\epsilon)}{\zeta\epsilon+\beta^*\,(1-\epsilon)+\mu}\right)\times \\
\times\left(\begin{array}{l} \displaystyle\int_0^\infty k(s)\,(1-q(s))\,\mathrm{e}^{-\int_0^s k(\tau)+\mu\,\mathrm{d}\tau}\,\mathrm{d}s+ \\ \displaystyle +\int_0^\infty k(s)q(s)\mathrm{e}^{-\int_0^s k(\tau)+\mu\,\mathrm{d}\tau}\,\mathrm{d}s\int_0^\infty \chi(s)\,(1-\xi(s))\,\mathrm{e}^{-\int_0^s \gamma_A(\tau)\xi(\tau)+\chi(\tau)(1-\xi(\tau))+\mu\,\mathrm{d}\tau}\,\mathrm{d}s \end{array}\right)\times \\
\times\,\mathrm{e}^{-\int_0^\theta \gamma_I(s)+\mu\,\mathrm{d}s},\ \forall\theta\in\mathbb{R}_0^+.
\end{aligned}
\tag{10e}
$$

We now set

$$
\boxed{\mathbb{R}_0^+ \ni \mathcal{R}_0 := \frac{\mu N_0}{p+\mu}\left(1+\frac{p\,(1-\epsilon)}{\zeta\epsilon+\mu}\right)(\mathcal{R}_A+\mathcal{R}_I),}
\tag{11}
$$

where

$$
\boxed{\mathbb{R}_0^+ \ni \mathcal{R}_A := \int_0^\infty k(s)q(s)\mathrm{e}^{-\int_0^s k(\tau)+\mu\,\mathrm{d}\tau}\,\mathrm{d}s\int_0^\infty \beta_A(s)\mathrm{e}^{-\int_0^s \gamma_A(\tau)\xi(\tau)+\chi(\tau)(1-\xi(\tau))+\mu\,\mathrm{d}\tau}\,\mathrm{d}s}
$$

and

$$
\boxed{\begin{aligned}
\mathbb{R}_0^+ \ni \mathcal{R}_I := \left(\begin{array}{l} \displaystyle\int_0^\infty k(s)\,(1-q(s))\,\mathrm{e}^{-\int_0^s k(\tau)+\mu\,\mathrm{d}\tau}\,\mathrm{d}s+ \\ \displaystyle +\int_0^\infty k(s)q(s)\mathrm{e}^{-\int_0^s k(\tau)+\mu\,\mathrm{d}\tau}\,\mathrm{d}s\int_0^\infty \chi(s)\,(1-\xi(s))\,\mathrm{e}^{-\int_0^s \gamma_A(\tau)\xi(\tau)+\chi(\tau)(1-\xi(\tau))+\mu\,\mathrm{d}\tau}\,\mathrm{d}s \end{array}\right)\times \\
\times\int_0^\infty \beta_I(s)\mathrm{e}^{-\int_0^s \gamma_I(\tau)+\mu\,\mathrm{d}\tau}\,\mathrm{d}s,
\end{aligned}}
$$

for the *basic reproductive number* of the aforementioned problem. Its definition emerges naturally from the following result.

Proposition 2. *Concerning* $\beta^* \in \mathbb{R}_0^+$,

1. *if* $\mathcal{R}_0 \le 1$, *then* $\beta^* = 0$,
2. *if* $\mathcal{R}_0 > 1$, *then*
   (a) *either* $\beta^* = 0$,
   (b) *or* $\beta^* > 0$, *such that*

$$
b_2{\beta^*}^2 + b_1\beta^* + b_0 = 0,
$$

where

$$
b_2 = (1-\epsilon)\,,\ b_1 = (p+\mu)(1-\epsilon)+\zeta\epsilon+\mu-\mu N_0\,(1-\epsilon)(\mathcal{R}_A+\mathcal{R}_I)\,,\ b_0 = (p+\mu)(\epsilon\zeta+\mu)(1-\mathcal{R}_0)\,.
$$

Proof. We substitute a^* and i^* of (10d) and (10e), respectively, into (8a) to deduce that

$$
\beta^* = \beta^* \frac{\mu N_0}{p+\beta^*+\mu}\left(1+\frac{p\,(1-\epsilon)}{\zeta\epsilon+\beta^*\,(1-\epsilon)+\mu}\right)(\mathcal{R}_A+\mathcal{R}_I)\,.
$$

There are only two discrete cases, either $\beta^* = 0$, or $\beta^* > 0$. If $\beta^* > 0$, then, equivalently,

$$1 = \frac{\mu N_0}{p + \beta^* + \mu}\left(1 + \frac{p(1-\epsilon)}{\zeta\epsilon + \beta^* + (1-\epsilon) + \mu}\right)(\mathcal{R}_A + \mathcal{R}_I),$$

or else

$$b_2 {\beta^*}^2 + b_1\beta^* + b_0 = 0.$$

We observe that

a. if $\epsilon = 1$ then $b_2 = 0$ and $b_1 > 0$,
b. if $\epsilon \neq 1$ then $b_2 > 0$.

Therefore, in any case, there exists $\beta^* > 0$ satisfying the above equation iff $b_3 < 0$, that is, $\mathcal{R}_0 > 1$, and of course, such β^* is unique. ☐

The following result is now straightforward.

Corollary 2. *Concerning* $(S^*, V^*, e^*, a^*, i^*)$,

1. *if* $\mathcal{R}_0 \leq 1$ *then* $(\mathrm{e}^*, a^*, i^*) = (0, 0, 0)$,
2. *if* $\mathcal{R}_0 > 1$ *then*
   (a) *either* $(\mathrm{e}^*, a^*, i^*) = (0, 0, 0)$,
   (b) *or* $(\mathrm{e}^*, a^*, i^*) > (0, 0, 0)$.

The solution $(S^*, V^*, e^*, a^*, i^*)$ is called *disease-free steady state* if $(\mathrm{e}^*, a^*, i^*) = (0, 0, 0)$, as well as *endemic steady state* if $(\mathrm{e}^*, a^*, i^*) > (0, 0, 0)$.

2.1.4 | Global stability

We are interested in the longer-time dynamics of the modeled epidemiological phenomenon, globally with respect to the set of initial data, $\left(\mathbb{R}_0^+\right)^2 \times \left(L^1\left(\mathbb{R}_0^+; \mathbb{R}_0^+\right)\right)^3 \times \mathbb{R}_0^+$. Below, we check the *global stability* of the steady state of $\mathscr{P}$ (3) by finding a *Lyapunov function*. Since the steady state changes with respect to the sign of $1 - \mathcal{R}_0$, we check each such case separately.

Theorem 2. *If* $\mathcal{R}_0 \leq 1$, *then the disease-free steady state,*

$$(S^*, V^*, e^*, a^*, i^*) = \left(\frac{\mu N_0}{p + \mu}, \frac{p\mu N_0}{(p+\mu)(\zeta\epsilon + \mu)}, 0, 0, 0\right),$$

is globally asymptotically stable.

Proof. Step I:

We define the following functions:

$$f : \mathbb{R}^+ \to \mathbb{R}_0^+$$

$$x \mapsto f(x) := x - 1 - \ln x,$$

and

$$L : \mathbb{R}_0^+ \to \mathbb{R}_0^+$$

$$t \mapsto L(t; S, V, e, a, i) := L_{SV} + L_E + L_A + L_I,$$

where

$$L_{SV} := S^* f\left(\frac{S}{S^*}\right) + V^* f\left(\frac{V}{V^*}\right), \tag{12}$$

$$L_E := \int_0^\infty f_E(\theta) e(\cdot, \theta)\, \mathrm{d}\theta \tag{13}$$

$$L_A := \int_0^\infty f_A(\theta) a(\cdot, \theta)\, \mathrm{d}\theta \tag{14}$$

$$L_I := \int_0^\infty f_I(\theta) i(\cdot, \theta)\, \mathrm{d}\theta, \tag{15}$$

and f_E, f_A and f_I are left to be defined.

Step II:

We differentiate L_{SV}, L_E, L_A and L_I. From (3a) and (3b), we get

$$\begin{aligned}
\frac{\mathrm{d}L_{SV}}{\mathrm{d}t} &= \left(1 - \frac{S^*}{S}\right)\frac{\mathrm{d}S}{\mathrm{d}t} + \left(1 - \frac{V^*}{V}\right)\frac{\mathrm{d}V}{\mathrm{d}t} = \\
&= \mu S^*\left(2 - \frac{S}{S^*} - \frac{S^*}{S}\right) + pS^*\left(3 - \frac{V}{V^*} - \frac{S^*}{S} - \frac{SV^*}{S^*V}\right) - \beta\left(S + (1-\epsilon)V\right) + \beta\left(S^* + (1-\epsilon)V^*\right).
\end{aligned}$$

With (5c) at hand, we also calculate

$$\begin{aligned}
\frac{\mathrm{d}L_E}{\mathrm{d}t} &= \frac{\mathrm{d}}{\mathrm{d}t}\left(\int_0^t f_E(\theta)\varepsilon(t-\theta)\,\mathrm{e}^{-\int_0^\theta k(s)+\mu\,\mathrm{d}s}\,\mathrm{d}\theta + \int_t^\infty f_E(\theta)e_0(\theta - t)\,\mathrm{e}^{-\int_0^t k(\theta-t+s)+\mu\,\mathrm{d}s}\,\mathrm{d}\theta\right) = \\
&= f_E(0)\varepsilon + \int_0^\infty \left(\frac{\mathrm{d}f_E}{\mathrm{d}\theta}(\theta) - f_E(\theta)\left(k(\theta)+\mu\right)\right) e(\cdot,\theta)\,\mathrm{d}\theta.
\end{aligned}$$

Similarly, from (5d) and (5e), we deduce the following expressions:

$$\frac{\mathrm{d}L_A}{\mathrm{d}t} = f_A(0)\alpha + \int_0^\infty \left(\frac{\mathrm{d}f_A}{\mathrm{d}\theta}(\theta) - f_A(\theta)\left(\gamma_A(\theta)\xi(\theta) + \chi(\theta)\left(1 - \xi(\theta)\right) + \mu\right)\right) a(\cdot,\theta)\,\mathrm{d}\theta$$

and

$$\frac{\mathrm{d}L_I}{\mathrm{d}t} = f_I(0)\imath + \int_0^\infty \left(\frac{\mathrm{d}f_I}{\mathrm{d}\theta}(\theta) - f_I(\theta)\left(\gamma_I(\theta) + \mu\right)\right) i(\cdot,\theta)\,\mathrm{d}\theta.$$

Therefore, we have

$$\begin{aligned}
\frac{\mathrm{d}L}{\mathrm{d}t} &= \frac{\mathrm{d}L_{SV}}{\mathrm{d}t} + \frac{\mathrm{d}L_E}{\mathrm{d}t} + \frac{\mathrm{d}L_A}{\mathrm{d}t} + \frac{\mathrm{d}L_I}{\mathrm{d}t} = \\
&= -\mu S^*\left(\frac{S}{S^*} + \frac{S^*}{S} - 1\right) - pS^*\left(\frac{V}{V^*} + \frac{S^*}{S} + \frac{SV^*}{S^*V} - 3\right) - \left(1 - f_E(0)\right)\varepsilon + \\
&\quad + \left(S^* + (1-\epsilon)V^*\right)\int_0^\infty \beta_A(\theta)a(\cdot,\theta) + \beta_I(\theta)i(\cdot,\theta)\,\mathrm{d}\theta + \\
&\quad + \int_0^\infty \left(\frac{\mathrm{d}f_E}{\mathrm{d}\theta}(\theta) - f_E(\theta)\left(k(\theta)+\mu\right) + f_A(0)k(\theta)q(\theta) + f_I(0)k(\theta)\left(1 - q(\theta)\right)\right) e(\cdot,\theta)\,\mathrm{d}\theta + \\
&\quad + \int_0^\infty \left(\frac{\mathrm{d}f_A}{\mathrm{d}\theta}(\theta) - f_A(\theta)\left(\gamma_A(\theta)\xi(\theta) + \chi(\theta)\left(1-\xi(\theta)\right) + \mu\right) + f_I(0)\chi(\theta)\left(1 - \xi(\theta)\right)\right) a(\cdot,\theta)\,\mathrm{d}\theta + \\
&\quad + \int_0^\infty \left(\frac{\mathrm{d}f_I}{\mathrm{d}\theta}(\theta) - f_I(\theta)\left(\gamma_I(\theta)+\mu\right)\right) i(\cdot,\theta)\,\mathrm{d}\theta.
\end{aligned}$$

Step III:

We choose f_E, f_A, and f_I such that the latter terms in the last equation to be zero, that is,

$$\frac{\mathrm{d}f_E}{\mathrm{d}\theta} = f_E\,(k+\mu) - f_A(0)kq - f_I(0)k\,(1-q)\,,$$

$$\frac{\mathrm{d}f_A}{\mathrm{d}\theta} = f_A\,(\gamma_A\xi + \chi\,(1-\xi) + \mu) - f_I(0)\chi\,(1-\xi) - (S^* + (1-\epsilon)\,V^*)\,\beta_A,$$

$$\frac{\mathrm{d}f_I}{\mathrm{d}\theta} = f_I\,(\gamma_I + \mu) - (S^* + (1-\epsilon)\,V^*)\,\beta_I.$$

Hence, $\forall\theta \in \mathbb{R}_0^+$, we set

$$f_E(\theta) := f_A(0)\int\limits_0^\infty k(s)q(s)\mathrm{e}^{-\int\limits_\theta^s k(\tau)+\mu\,\mathrm{d}\tau}\mathrm{d}s + f_I(0)\int\limits_0^\infty k(s)\,(1-q(s))\,\mathrm{e}^{-\int\limits_\theta^s k(\tau)+\mu\,\mathrm{d}\tau}\mathrm{d}s, \tag{16}$$

$$\begin{aligned} f_A(\theta) := (S^* + (1-\epsilon)\,V^*)\int\limits_\theta^\infty \beta_A(s)\mathrm{e}^{-\int\limits_\theta^s \gamma_A(\tau)\xi(\tau)+\chi(\tau)(1-\xi(\tau))+\mu\,\mathrm{d}\tau}\mathrm{d}s+ \\ + f_I(0)\int\limits_\theta^\infty \chi(s)\,(1-\xi(s))\,\mathrm{e}^{-\int\limits_\theta^s \gamma_A(\tau)\xi(\tau)+\chi(\tau)(1-\xi(\tau))+\mu\,\mathrm{d}\tau}\mathrm{d}s, \end{aligned} \tag{17}$$

$$f_I(\theta) := (S^* + (1-\epsilon)\,V^*)\int\limits_\theta^\infty \beta_I(s)\mathrm{e}^{-\int\limits_\theta^s \gamma_I(\tau)+\mu\,\mathrm{d}\tau}\mathrm{d}s. \tag{18}$$

For f_E, f_A, and f_I defined as such, we have

$$\frac{\mathrm{d}L}{\mathrm{d}t} = -\mu S^*\left(\frac{S}{S^*} + \frac{S^*}{S} - 1\right) - pS^*\left(\frac{V}{V^*} + \frac{S^*}{S} + \frac{SV^*}{S^*V} - 3\right) - (1-\mathcal{R}_0)\,\varepsilon.$$

Step IV:

Due to the arithmetic-geometric mean inequality, we derive

$$\mathcal{R}_0 \leq 1 \Rightarrow \frac{\mathrm{d}L}{\mathrm{d}t} \leq 0,\ \forall t \in \mathbb{R}_0^+$$

and the equality holds only for the disease-free steady state, that is, when

$$(S, V, e, a, i) = (S^*, V^*, e^*, a^*, i^*)\,.$$

Hence, the singleton $\{(S^*, V^*, e^*, a^*, i^*)\}$ is the largest invariant set for which

$$\frac{\mathrm{d}L}{\mathrm{d}t} = 0.$$

Then, from the LaSalle in-variance principle, it follows that the disease-free steady state is globally asymptotically stable. □

Theorem 3. *If $\mathcal{R}_0 > 1$, then the endemic steady state,*

$$(S^*, V^*, e^*, a^*, i^*) \neq (S^*, V^*, 0, 0, 0)\,,$$

is globally asymptotically stable.

Proof. Step I:

Based on (16)–(18), we now define

$$\begin{aligned} L \,:\, & \mathbb{R}_0^+ \to \mathbb{R}_0^+ \\ & t \mapsto L\left(t; S, V, e, a, i\right) := L_{SV} + L_E + L_A + L_I, \end{aligned}$$

with

$$\begin{aligned} L_{SV} &:= S^* f\left(\frac{S}{S^*}\right) + V^* f\left(\frac{V}{V^*}\right), \\ L_E &:= f_A(0) \int_0^\infty \int_\theta^\infty k(s) q(s) e^*(s) \, \mathrm{d}s \, f\left(\frac{e\left(\cdot, \theta\right)}{e^*(\theta)}\right) \mathrm{d}\theta + \\ &\quad + f_I(0) \int_0^\infty \int_\theta^\infty k(s) \left(1 - q(s)\right) e^*(s) \, \mathrm{d}s \, f\left(\frac{e\left(\cdot, \theta\right)}{e^*(\theta)}\right) \mathrm{d}\theta, \\ L_A &:= \left(S^* + \left(1 - \epsilon\right) V^*\right) \int_0^\infty \int_\theta^\infty \beta_A(s) a^*(s) \, \mathrm{d}s \, f\left(\frac{a\left(\cdot, \theta\right)}{a^*(\theta)}\right) \mathrm{d}\theta + \\ &\quad + f_I(0) \int_0^\infty \int_\theta^\infty \chi(s) \left(1 - \xi(s)\right) a^*(s) \, \mathrm{d}s \, f\left(\frac{a\left(\cdot, \theta\right)}{a^*(\theta)}\right) \mathrm{d}\theta, \\ L_I &:= \left(S^* + \left(1 - \epsilon\right) V^*\right) \int_0^\infty \int_\theta^\infty \beta_I(s) i^*(s) \, \mathrm{d}s \, f\left(\frac{i\left(\cdot, \theta\right)}{i^*(\theta)}\right) \mathrm{d}\theta \end{aligned}$$

and

$$\begin{aligned} f \,:\, & \mathbb{R}^+ \to \mathbb{R}_0^+ \\ & x \mapsto f(x) := x - 1 - \ln x. \end{aligned}$$

Step IIa:
We differentiate L_{SV}, L_E, L_A, and L_I. From (3a) and (3b), we get

$$\begin{aligned} \frac{\mathrm{d}L_{SV}}{\mathrm{d}t} &= \left(1 - \frac{S^*}{S}\right) \frac{\mathrm{d}S}{\mathrm{d}t} + \left(1 - \frac{V^*}{V}\right) \frac{\mathrm{d}V}{\mathrm{d}t} = \\ &= -\mu S^* \left(\frac{S}{S^*} + \frac{S^*}{S} - 2\right) - p S^* \left(\frac{V}{V^*} + \frac{S^*}{S} + \frac{S V^*}{S^* V} - 3\right) + \\ &\quad + S^* \int_0^\infty \beta_A(\theta) a^*(\theta) \left(1 - \frac{S a\left(\cdot, \theta\right)}{S^* a^*(\theta)} - \frac{S^*}{S} + \frac{a\left(\cdot, \theta\right)}{a^*(\theta)}\right) \mathrm{d}\theta + \\ &\quad + S^* \int_0^\infty \beta_I(\theta) i^*(\theta) \left(1 - \frac{S i\left(\cdot, \theta\right)}{S^* i^*(\theta)} - \frac{S^*}{S} + \frac{i\left(\cdot, \theta\right)}{i^*(\theta)}\right) \mathrm{d}\theta + \\ &\quad + \left(1 - \epsilon\right) V^* \int_0^\infty \beta_A(\theta) a^*(\theta) \left(-1 - \frac{V a\left(\cdot, \theta\right)}{V^* a^*(\theta)} + \frac{V}{V^*} + \frac{a\left(\cdot, \theta\right)}{a^*(\theta)}\right) \mathrm{d}\theta + \\ &\quad + \left(1 - \epsilon\right) V^* \int_0^\infty \beta_I(\theta) i^*(\theta) \left(-1 - \frac{V i\left(\cdot, \theta\right)}{V^* i^*(\theta)} + \frac{V}{V^*} + \frac{i\left(\cdot, \theta\right)}{i^*(\theta)}\right) \mathrm{d}\theta. \end{aligned}$$

From the differential equation in (3c) along with (7c), we have

$$\frac{\partial}{\partial t} f\left(\frac{e(t,\theta)}{e^*(\theta)}\right) = -\frac{\partial}{\partial \theta} f\left(\frac{e(t,\theta)}{e^*(\theta)}\right),$$

thus,

$$\begin{aligned}\frac{\mathrm{d}L_E}{\mathrm{d}t} = & -f_A(0)\int_0^{\infty}\int_{\theta}^{\infty} k(s)q(s)e^*(s)\,\mathrm{d}s\,\frac{\partial}{\partial\theta} f\left(\frac{e(\cdot,\theta)}{e^*(\theta)}\right)\mathrm{d}\theta - \\ & - f_I(0)\int_0^{\infty}\int_{\theta}^{\infty} k(s)\left(1-q(s)\right)e^*(s)\,\mathrm{d}s\,\frac{\partial}{\partial\theta} f\left(\frac{e(\cdot,\theta)}{e^*(\theta)}\right)\mathrm{d}\theta = \\ & = f_A(0)\int_0^{\infty} k(\theta)q(\theta)e^*(\theta)\left(\frac{\varepsilon}{\varepsilon^*} - \frac{e(\cdot,\theta)}{e^*(\theta)} + \ln\frac{e(\cdot,\theta)}{e^*(\theta)} - \ln\frac{\varepsilon}{\varepsilon^*}\right)\mathrm{d}\theta + \\ & + f_I(0)\int_0^{\infty} k(\theta)\left(1-q(\theta)\right)e^*(\theta)\left(\frac{\varepsilon}{\varepsilon^*} - \frac{e(\cdot,\theta)}{e^*(\theta)} + \ln\frac{e(\cdot,\theta)}{e^*(\theta)} - \ln\frac{\varepsilon}{\varepsilon^*}\right)\mathrm{d}\theta.\end{aligned}$$

Similarly, from (3d) along with (7d), as well as (3e) along with (7e), we deduce

$$\begin{aligned}\frac{\mathrm{d}L_A}{\mathrm{d}t} = & \left(S^* + (1-\epsilon)V^*\right)\int_0^{\infty}\beta_A(\theta)a^*(\theta)\left(\frac{\alpha}{\alpha^*} - \frac{a(\cdot,\theta)}{a^*(\theta)} + \ln\frac{a(\cdot,\theta)}{a^*(\theta)} - \ln\frac{\alpha}{\alpha^*}\right)\mathrm{d}\theta + \\ & + f_I(0)\int_0^{\infty}\chi(\theta)\left(1-\xi(\theta)\right)a^*(\theta)\left(\frac{\alpha}{\alpha^*} - \frac{a(\cdot,\theta)}{a^*(\theta)} + \ln\frac{a(\cdot,\theta)}{a^*(\theta)} - \ln\frac{\alpha}{\alpha^*}\right)\mathrm{d}\theta\end{aligned}$$

and

$$\frac{\mathrm{d}L_I}{\mathrm{d}t} = \left(S^* + (1-\epsilon)V^*\right)\int_0^{\infty}\beta_I(\theta)i^*(\theta)\left(\frac{\imath}{\imath^*} - \frac{i(\cdot,\theta)}{i^*(\theta)} + \ln\frac{i(\cdot,\theta)}{i^*(\theta)} - \ln\frac{\imath}{\imath^*}\right)\mathrm{d}\theta,$$

respectively. Therefore, we have

$$\begin{aligned}\frac{\mathrm{d}L}{\mathrm{d}t} = & \frac{\mathrm{d}L_{SV}}{\mathrm{d}t} + \frac{\mathrm{d}L_E}{\mathrm{d}t} + \frac{\mathrm{d}L_A}{\mathrm{d}t} + \frac{\mathrm{d}L_I}{\mathrm{d}t} = \\ = & -\mu S^*\left(\frac{S}{S^*} + \frac{S^*}{S} - 2\right) - pS^*\left(\frac{V}{V^*} + \frac{S^*}{S} + \frac{SV^*}{S^*V} - 3\right) + \\ & + S^*\int_0^{\infty}\beta_A(\theta)a^*(\theta)\left(1 - \frac{S^*}{S} + \ln\frac{a(\cdot,\theta)}{a^*(\theta)} - \ln\frac{\alpha}{\alpha^*}\right)\mathrm{d}\theta + \\ & + S^*\int_0^{\infty}\beta_I(\theta)i^*(\theta)\left(1 - \frac{S^*}{S} + \ln\frac{i(\cdot,\theta)}{i^*(\theta)} - \ln\frac{\imath}{\imath^*}\right)\mathrm{d}\theta +\end{aligned}$$

$$+ (1-\epsilon)\, V^* \int_0^\infty \beta_A(\theta) a^*(\theta) \left(-1 + \frac{V}{V^*} + \ln \frac{a\,(\cdot,\theta)}{a^*(\theta)} - \ln \frac{\alpha}{\alpha^*} \right) \mathrm{d}\theta +$$

$$+ (1-\epsilon)\, V^* \int_0^\infty \beta_I(\theta) i^*(\theta) \left(-1 + \frac{V}{V^*} + \ln \frac{i\,(\cdot,\theta)}{i^*(\theta)} - \ln \frac{\iota}{\iota^*} \right) \mathrm{d}\theta +$$

$$+ f_A(0) \int_0^\infty k(\theta) q(\theta) e^*(\theta) \left(\ln \frac{e\,(\cdot,\theta)}{e^*(\theta)} - \ln \frac{\varepsilon}{\varepsilon^*} \right) \mathrm{d}\theta +$$

$$+ f_I(0) \int_0^\infty k(\theta)\, (1-q(\theta))\, e^*(\theta) \left(\ln \frac{e\,(\cdot,\theta)}{e^*(\theta)} - \ln \frac{\varepsilon}{\varepsilon^*} \right) \mathrm{d}\theta +$$

$$+ f_I(0) \int_0^\infty \chi(\theta)\, (1-\xi(\theta))\, a^*(\theta) \left(\ln \frac{a\,(\cdot,\theta)}{a^*(\theta)} - \ln \frac{\alpha}{\alpha^*} \right) \mathrm{d}\theta + \sum_{i=1}^{6} D_i,$$

where

$$D_1 := (S^* + (1-\epsilon)\, V^*) \int_0^\infty \beta_A(\theta) a^*(\theta) \frac{\alpha}{\alpha^*} + \beta_I(\theta) i^*(\theta) \frac{\iota}{\iota^*} \,\mathrm{d}\theta,$$

$$D_2 := -(S^* + (1-\epsilon)\, V^*) \int_0^\infty \beta_A(\theta) \mathrm{e}^{-\int_0^\theta \gamma_A(s)\xi(s)+\chi(s)(1-\xi(s))+\mu \,\mathrm{d}s} \mathrm{d}\theta \int_0^\infty k(\theta) q(\theta) e^*(\theta) \frac{e\,(\cdot,\theta)}{e^*(\theta)} \,\mathrm{d}\theta -$$

$$- f_I(0) \left(\int_0^\infty k(\theta)\, (1-q(\theta))\, e^*(\theta) \frac{e\,(\cdot,\theta)}{e^*(\theta)} \,\mathrm{d}\theta + \int_0^\infty \chi(\theta)\, (1-\xi(\theta))\, a^*(\theta) \frac{a\,(\cdot,\theta)}{a^*(\theta)} \,\mathrm{d}\theta \right),$$

$$D_3 := -S^* \int_0^\infty \beta_A(\theta) a^*(\theta) \frac{S a\,(\cdot,\theta)}{S^* a^*(\theta)} + \beta_I(\theta) i^*(\theta) \frac{S i\,(\cdot,\theta)}{S^* i^*(\theta)} \,\mathrm{d}\theta -$$

$$- (1-\epsilon)\, V^* \int_0^\infty \beta_A(\theta) a^*(\theta) \frac{V a\,(\cdot,\theta)}{V^* a^*(\theta)} + \beta_I(\theta) i^*(\theta) \frac{V i\,(\cdot,\theta)}{V^* i^*(\theta)} \,\mathrm{d}\theta,$$

$$D_4 := \frac{\varepsilon}{\varepsilon^*} \int_0^\infty (f_A(0) k(\theta) q(\theta) + f_I(0) k(\theta)\, (1-q(\theta)))\, e^*(\theta) \,\mathrm{d}\theta,$$

$$D_5 := -f_I(0) \int_0^\infty \chi(\theta)\, (1-\xi(\theta))\, \mathrm{e}^{-\int_0^\theta \gamma_A(s)\xi(s)+\chi(s)(1-\xi(s))+\mu \,\mathrm{d}s} \mathrm{d}\theta \int_0^\infty k(\theta) q(\theta) e^*(\theta) \frac{e\,(\cdot,\theta)}{e^*(\theta)} \,\mathrm{d}\theta,$$

$$D_6 := f_I(0) \int_0^\infty \chi(\theta)\, (1-\xi(\theta))\, a^*(\theta) \frac{\alpha}{\alpha^*} \,\mathrm{d}\theta.$$

Step IIb:

From (4c) and (9d), we see that

$$D_5 + D_6 = 0.$$

Moreover, by (8) and (9), along with (4a) and (4b), we observe that

$$\begin{aligned}D_4 = {} & \frac{\varepsilon}{\varepsilon^*}\left(S^* + (1-\epsilon)\,V^*\right)\int_0^\infty \beta_A(\theta)\mathrm{e}^{-\int_0^\theta \gamma_A(s)\xi(s)+\chi(s)(1-\xi(s))+\mu\,\mathrm{d}s}\,\mathrm{d}\theta \int_0^\infty k(\theta)q(\theta)e^*(\theta)\,\mathrm{d}\theta + \\ & + \frac{\varepsilon}{\varepsilon^*} f_I(0)\left(\int_0^\infty k(\theta)\left(1-q(\theta)\right)e^*(\theta) + \chi(\theta)\left(1-\xi(\theta)\right)a^*(\theta)\,\mathrm{d}\theta\right) = \\ & = \frac{\varepsilon}{\varepsilon^*}\left(S^* + (1-\epsilon)\,V^*\right)\left(\alpha^*\int_0^\infty \beta_A(\theta)\mathrm{e}^{-\int_0^\theta \gamma_A(s)\xi(s)+\chi(s)(1-\xi(s))+\mu\,\mathrm{d}s}\,\mathrm{d}\theta + \iota^*\int_0^\infty \beta_I(\theta)\mathrm{e}^{-\int_0^\theta \gamma_I(s)+\mu\,\mathrm{d}s}\,\mathrm{d}\theta\right) = \\ & = \frac{\varepsilon}{\varepsilon^*}\left(S^* + (1-\epsilon)\,V^*\right)\beta^* = \frac{\varepsilon}{\varepsilon^*}\varepsilon^* = \beta\left(S + (1-\epsilon)\,V\right) = \\ & = \left(S + (1-\epsilon)\,V\right)\int_0^\infty \beta_A(\theta)a\left(\cdot,\theta\right) + \beta_I(\theta)i\left(\cdot,\theta\right)\,\mathrm{d}\theta = -D_3.\end{aligned}$$

Additionally, from (8) and (9), we have that

$$\begin{aligned}-D_2 = {} & \alpha\left(S^* + (1-\epsilon)\,V^*\right)\int_0^\infty \beta_A(\theta)\mathrm{e}^{-\int_0^\theta \gamma_A(s)\xi(s)+\chi(s)(1-\xi(s))+\mu\,\mathrm{d}s}\,\mathrm{d}\theta + \iota f_I(0) = \\ & = \frac{\alpha}{\alpha^*}\alpha^*\left(S^* + (1-\epsilon)\,V^*\right)\int_0^\infty \beta_A(\theta)\mathrm{e}^{-\int_0^\theta \gamma_A(s)\xi(s)+\chi(s)(1-\xi(s))+\mu\,\mathrm{d}s}\,\mathrm{d}\theta + \frac{\iota}{\iota^*}\iota^* f_I(0) = \\ & = \frac{\alpha}{\alpha^*}\left(S^* + (1-\epsilon)\,V^*\right)\int_0^\infty \beta_A(\theta)\mathrm{e}^{-\int_0^\theta \gamma_A(s)\xi(s)+\chi(s)(1-\xi(s))+\mu\,\mathrm{d}s}\,\mathrm{d}\theta\int_0^\infty k(\theta)q(\theta)e^*(\theta)\,\mathrm{d}\theta + \\ & + \frac{\iota}{\iota^*} f_I(0)\left(\int_0^\infty k(\theta)\left(1-q(\theta)\right)e^*(\theta)\,\mathrm{d}\theta + \int_0^\infty \chi(\theta)\left(1-\xi(\theta)\right)a^*(\theta)\,\mathrm{d}\theta\right) = D_1.\end{aligned}$$

Consequently,

$$\sum_{i=1}^{6} D_i = 0$$

and with (7b) at hand, we deduce that

$$\begin{aligned}\frac{\mathrm{d}L}{\mathrm{d}t} = {} & -\mu S^*\left(\frac{S}{S^*} + \frac{S^*}{S} - 2\right) - \left(\zeta\epsilon + \beta^*\left(1-\epsilon\right) + \mu\right)V^*\left(\frac{V}{V^*} + \frac{S^*}{S} + \frac{SV^*}{S^*V} - 3\right) + \\ & + S^*\int_0^\infty \beta_A(\theta)a^*(\theta)\left(1 - \frac{S^*}{S} + \ln\frac{a\left(\cdot,\theta\right)}{a^*(\theta)} - \ln\frac{\alpha}{\alpha^*}\right)\mathrm{d}\theta + \\ & + S^*\int_0^\infty \beta_I(\theta)i^*(\theta)\left(1 - \frac{S^*}{S} + \ln\frac{i\left(\cdot,\theta\right)}{i^*(\theta)} - \ln\frac{\iota}{\iota^*}\right)\mathrm{d}\theta + \\ & + (1-\epsilon)\,V^*\int_0^\infty \beta_A(\theta)a^*(\theta)\left(-1 + \frac{V}{V^*} + \ln\frac{a\left(\cdot,\theta\right)}{a^*(\theta)} - \ln\frac{\alpha}{\alpha^*}\right)\mathrm{d}\theta + \\ & + (1-\epsilon)\,V^*\int_0^\infty \beta_I(\theta)i^*(\theta)\left(-1 + \frac{V}{V^*} + \ln\frac{i\left(\cdot,\theta\right)}{i^*(\theta)} - \ln\frac{\iota}{\iota^*}\right)\mathrm{d}\theta +\end{aligned}$$

$$+ f_A(0)\int_0^\infty k(\theta)q(\theta)e^*(\theta)\left(\ln\frac{e(\cdot,\theta)}{e^*(\theta)} - \ln\frac{\varepsilon}{\varepsilon^*}\right)\mathrm{d}\theta +$$

$$+ f_I(0)\int_0^\infty k(\theta)\left(1-q(\theta)\right)e^*(\theta)\left(\ln\frac{e(\cdot,\theta)}{e^*(\theta)} - \ln\frac{\varepsilon}{\varepsilon^*}\right)\mathrm{d}\theta +$$

$$+ f_I(0)\int_0^\infty \chi(\theta)\left(1-\xi(\theta)\right)a^*(\theta)\left(\ln\frac{a(\cdot,\theta)}{a^*(\theta)} - \ln\frac{\alpha}{\alpha^*}\right)\mathrm{d}\theta.$$

Step IIc:

We then proceed by adding some useful zero terms in the above equation. First, from (4b), along with (8a) and (8b), we have the following useful expression for

$$\left(S^* + (1-\epsilon)V^*\right)\int_0^\infty \beta_A(\theta)a^*(\theta) + \beta_I(\theta)i^*(\theta)\,\mathrm{d}\theta = \varepsilon^*$$

as follows:

$$\varepsilon^* = \frac{\varepsilon^*}{\varepsilon}\varepsilon = \frac{\varepsilon^*}{\varepsilon}\left(S + (1-\epsilon)V\right)\int_0^\infty \beta_A(\theta)a(\cdot,\theta) + \beta_I(\theta)i(\cdot,\theta)\,\mathrm{d}\theta =$$

$$= S^*\int_0^\infty \beta_A(\theta)a^*(\theta)\frac{S\,a(\cdot,\theta)\,\varepsilon^*}{S^*a^*(\theta)\varepsilon} + \beta_I(\theta)i^*(\theta)\frac{S\,i(\cdot,\theta)\,\varepsilon^*}{S^*i^*(\theta)\varepsilon}\,\mathrm{d}\theta +$$

$$+ (1-\epsilon)V^*\int_0^\infty \beta_A(\theta)a^*(\theta)\frac{V\,a(\cdot,\theta)\,\varepsilon^*}{V^*a^*(\theta)\varepsilon} + \beta_I(\theta)i^*(\theta)\frac{V\,i(\cdot,\theta)\,\varepsilon^*}{V^*i^*(\theta)\varepsilon}\,\mathrm{d}\theta.$$

Second, by (4c) and (4d), along with (8c) and (8d), we have

$$0 = \left(S^* + (1-\epsilon)V^*\right)\int_0^\infty \beta_A(\theta)\mathrm{e}^{-\int_0^\theta \gamma_A(s)\xi(s)+\chi(s)(1-\xi(s))+\mu\,\mathrm{d}s}\,\mathrm{d}\theta\left(\alpha^* - \frac{\alpha^*}{\alpha}\alpha\right) + f_I(0)\left(\iota^* - \frac{\iota^*}{\iota}\iota\right) =$$

$$= \left(S^* + (1-\epsilon)V^*\right)\int_0^\infty \beta_A(\theta)\mathrm{e}^{-\int_0^\theta \gamma_A(s)\xi(s)+\chi(s)(1-\xi(s))+\mu\,\mathrm{d}s}\,\mathrm{d}\theta\int_0^\infty k(\theta)q(\theta)e^*(\theta)\left(1 - \frac{e(\cdot,\theta)\,\alpha^*}{e^*(\theta)\alpha}\right)\mathrm{d}\theta +$$

$$+ f_I(0)\left(\int_0^\infty k(\theta)\left(1-q(\theta)\right)e^*(\theta)\left(1 - \frac{e(\cdot,\theta)\,\iota^*}{e^*(\theta)\iota}\right)\mathrm{d}\theta + \int_0^\infty \chi(\theta)\left(1-\xi(\theta)\right)a^*(\theta)\left(1 - \frac{a(\cdot,\theta)\,\iota^*}{a^*(\theta)\iota}\right)\mathrm{d}\theta\right).$$

In view of the above, we now write

$$\frac{\mathrm{d}L}{\mathrm{d}t} = -\mu S^*\left(\frac{S}{S^*} + \frac{S^*}{S} - 2\right) - (\zeta\epsilon + \mu)V^*\left(\frac{V}{V^*} + \frac{S^*}{S} + \frac{SV^*}{S^*V} - 3\right) +$$

$$+ \left(S^* + (1-\epsilon)V^*\right)\int_0^\infty \left(\beta_A(\theta)a^*(\theta) + \beta_I(\theta)i^*(\theta)\right)\left(1 - \frac{S^*}{S} + \ln\frac{S^*}{S}\right)\mathrm{d}\theta +$$

$$+ S^* \int_0^\infty \beta_A(\theta) a^*(\theta) \left(\ln \frac{S a(\cdot,\theta)}{S^* a^*(\theta)} - \ln \frac{\alpha}{\alpha^*} + 1 - \frac{S a(\cdot,\theta)\,\varepsilon^*}{S^* a^*(\theta)\varepsilon} \right) \mathrm{d}\theta +$$

$$+ S^* \int_0^\infty \beta_I(\theta) i^*(\theta) \left(\ln \frac{S i(\cdot,\theta)}{S^* i^*(\theta)} - \ln \frac{\imath}{\imath^*} + 1 - \frac{S i(\cdot,\theta)\,\varepsilon^*}{S^* i^*(\theta)\varepsilon} \right) \mathrm{d}\theta +$$

$$+ (1-\epsilon)\, V^* \int_0^\infty \beta_A(\theta) a^*(\theta) \left(1 - \frac{SV^*}{S^*V} + \ln \frac{S a(\cdot,\theta)}{S^* a^*(\theta)} - \ln \frac{\alpha}{\alpha^*} + 1 - \frac{V a(\cdot,\theta)\,\varepsilon^*}{V^* a^*(\theta)\varepsilon} \right) \mathrm{d}\theta +$$

$$+ (1-\epsilon)\, V^* \int_0^\infty \beta_I(\theta) i^*(\theta) \left(1 - \frac{SV^*}{S^*V} + \ln \frac{S i(\cdot,\theta)}{S^* i^*(\theta)} - \ln \frac{\imath}{\imath^*} + 1 - \frac{V i(\cdot,\theta)\,\varepsilon^*}{V^* i^*(\theta)\varepsilon} \right) \mathrm{d}\theta +$$

$$+ (1-\epsilon)\, V^* \int_0^\infty \beta_A(\theta) a^*(\theta) \left(\ln \frac{SV^*}{S^*V} - \ln \frac{SV^*}{S^*V} + \ln \frac{V a(\cdot,\theta)\,\varepsilon^*}{V^* a^*(\theta)\varepsilon} - \ln \frac{V a(\cdot,\theta)\,\varepsilon^*}{V^* a^*(\theta)\varepsilon} \right) \mathrm{d}\theta +$$

$$+ (1-\epsilon)\, V^* \int_0^\infty \beta_I(\theta) i^*(\theta) \left(\ln \frac{SV^*}{S^*V} - \ln \frac{SV^*}{S^*V} + \ln \frac{V i(\cdot,\theta)\,\varepsilon^*}{V^* i^*(\theta)\varepsilon} - \ln \frac{V i(\cdot,\theta)\,\varepsilon^*}{V^* i^*(\theta)\varepsilon} \right) \mathrm{d}\theta +$$

$$+ f_A(0) \int_0^\infty k(\theta) q(\theta) e^*(\theta) \left(\ln \frac{e(\cdot,\theta)}{e^*(\theta)} - \ln \frac{\varepsilon}{\varepsilon^*} \right) \mathrm{d}\theta +$$

$$+ f_I(0) \int_0^\infty k(\theta)\,(1-q(\theta))\,e^*(\theta) \left(\ln \frac{e(\cdot,\theta)}{e^*(\theta)} - \ln \frac{\varepsilon}{\varepsilon^*} \right) \mathrm{d}\theta +$$

$$+ f_I(0) \int_0^\infty \chi(\theta)\,(1-\xi(\theta))\,a^*(\theta) \left(\ln \frac{a(\cdot,\theta)}{a^*(\theta)} - \ln \frac{\alpha}{\alpha^*} \right) \mathrm{d}\theta +$$

$$+ (S^* + (1-\epsilon)\, V^*) \int_0^\infty \beta_A(\theta) \mathrm{e}^{-\int_0^\theta \gamma_A(s)\xi(s)+\chi(s)(1-\xi(s))+\mu\,\mathrm{d}s}\, \mathrm{d}\theta \int_0^\infty k(\theta) q(\theta) e^*(\theta) \left(1 - \frac{e(\cdot,\theta)\,\alpha^*}{e^*(\theta)\alpha} \right) \mathrm{d}\theta +$$

$$+ f_I(0) \left(\int_0^\infty k(\theta)\,(1-q(\theta))\,e^*(\theta) \left(1 - \frac{e(\cdot,\theta)\,\imath^*}{e^*(\theta)\imath} \right) \mathrm{d}\theta + \int_0^\infty \chi(\theta)\,(1-\xi(\theta))\,a^*(\theta) \left(1 - \frac{a(\cdot,\theta)\,\imath^*}{a^*(\theta)\imath} \right) \mathrm{d}\theta \right).$$

Step IId:
From the definition of f and the equation

$$D_1 = \frac{\alpha}{\alpha^*} (S^* + (1-\epsilon)\, V^*) \int_0^\infty \beta_A(\theta) \mathrm{e}^{-\int_0^\theta \gamma_A(s)\xi(s)+\chi(s)(1-\xi(s))+\mu\,\mathrm{d}s}\, \mathrm{d}\theta \int_0^\infty k(\theta) q(\theta) e^*(\theta)\, \mathrm{d}\theta +$$

$$+ \frac{\imath}{\imath^*} f_I(0) \left(\int_0^\infty k(\theta)\,(1-q(\theta))\,e^*(\theta)\, \mathrm{d}\theta + \int_0^\infty \chi(\theta)\,(1-\xi(\theta))\,a^*(\theta)\, \mathrm{d}\theta \right),$$

the expression can eventually be simplified as follows:

$$
\begin{aligned}
\frac{\mathrm{d}L}{\mathrm{d}t} = & -\mu S^* \left(\frac{S}{S^*} + \frac{S^*}{S} - 2\right) - (\zeta\epsilon + \mu)\, V^* \left(\frac{V}{V^*} + \frac{S^*}{S} + \frac{SV^*}{S^*V} - 3\right) - \\
& - (S^* + (1-\epsilon)\, V^*) \int_0^\infty (\beta_A(\theta) a^*(\theta) + \beta_I(\theta) i^*(\theta))\, f\left(\frac{S^*}{S}\right) \mathrm{d}\theta - \\
& - S^* \int_0^\infty \beta_A(\theta) a^*(\theta) f\left(\frac{S a(\cdot,\theta)\, \varepsilon^*}{S^* a^*(\theta)\varepsilon}\right) \mathrm{d}\theta - S^* \int_0^\infty \beta_I(\theta) i^*(\theta) f\left(\frac{S i(\cdot,\theta)\, \varepsilon^*}{S^* i^*(\theta)\varepsilon}\right) \mathrm{d}\theta - \\
& - (1-\epsilon)\, V^* \int_0^\infty \beta_A(\theta) a^*(\theta) f\left(\frac{V a(\cdot,\theta)\, \varepsilon^*}{V^* a^*(\theta)\varepsilon}\right) \mathrm{d}\theta - (1-\epsilon)\, V^* \int_0^\infty \beta_I(\theta) i^*(\theta) f\left(\frac{V i(\cdot,\theta)\, \varepsilon^*}{V^* i^*(\theta)\varepsilon}\right) \mathrm{d}\theta - \\
& - (1-\epsilon)\, V^* \int_0^\infty (\beta_A(\theta) a^*(\theta) + \beta_I(\theta) i^*(\theta))\, f\left(\frac{SV^*}{S^*V}\right) \mathrm{d}\theta - \\
& - (S^* + (1-\epsilon)\, V^*) \int_0^\infty \beta_A(\theta) \mathrm{e}^{-\int_0^\theta \gamma_A(s)\xi(s) + \chi(s)(1-\xi(s)) + \mu \,\mathrm{d}s} \mathrm{d}\theta \int_0^\infty k(\theta) q(\theta) e^*(\theta) f\left(\frac{e(\cdot,\theta)\, \alpha^*}{e^*(\theta)\alpha}\right) \mathrm{d}\theta - \\
& - f_I(0) \int_0^\infty k(\theta)\, (1 - q(\theta))\, e^*(\theta) f\left(\frac{e(\cdot,\theta)\, \iota^*}{e^*(\theta)\iota}\right) \mathrm{d}\theta - f_I(0) \int_0^\infty \chi(\theta)\, (1 - \xi(\theta))\, a^*(\theta) f\left(\frac{a(\cdot,\theta)\, \iota^*}{a^*(\theta)\iota}\right) \mathrm{d}\theta.
\end{aligned}
$$

Step III:
Employing the arithmetic-geometric mean inequality, we get

$$
\mathcal{R}_0 \le 1 \Rightarrow \frac{\mathrm{d}L}{\mathrm{d}t} \le 0, \forall t \in \mathbb{R}_0^+,
$$

and the equality holds only for the endemic steady state, that is, when

$$
(S, V, e, a, i) = (S^*, V^*, e^*, a^*, i^*)\,.
$$

Hence, the singleton $\{(S^*, V^*, e^*, a^*, i^*)\}$ is the largest invariant set for which

$$
\frac{\mathrm{d}L}{\mathrm{d}t} = 0.
$$

Then, from the LaSalle in-variance principle, it follows that the endemic steady state is globally asymptotically stable. ☐

3 | NUMERICAL SIMULATIONS

In this section, we numerically solve $\mathscr{P}$ (3) in order to verify the validity of the analysis performed in Section 2.1 and to further investigate the behavior of its solution.

3.1 | Numerical scheme

Here, we present the temporal discretization used to numerically solve $\mathscr{P}$ (3) and the code used to implement it.

3.1.1 | Temporal discretization

We assume that the maximum age of the population, $\theta_\dagger$, is equal to $90\cdot 360$ days. Furthermore, we study $\mathscr{P}$ (3) for a time of up to 1500 days. Hence, we solve $\mathscr{P}$ (3) in the interval $(t,\theta)\in[0,\ 1500]\times[0,\ 90\cdot 360]\ \cdot$ days. The time-age step we chose is $h=0.05$. Let $\mathcal{N}$ be the number of time-age steps needed to reach the maximum age, that is, $\theta_\dagger$, and $\mathcal{J}$ be the number of time-age steps needed to reach the maximum time, that is, 1500 days.

To discretize the time derivative, we use the following first-order forward difference scheme:

$$\frac{\partial}{\partial t}\left(u(t^n)\right)=\lim_{h\to 0^+}\frac{u(t^n+h)-u(t^n)}{h}\approx\frac{u^{n+1}-u^n}{h},\ 0\le n\le\mathcal{N}-1\,,$$

for $u\in\{S(t),\ V(t)\,|\,t\in[0,\ 1500]\ \cdot\text{ days}\}$.

To discretize the temporal directional derivative, we use the following first-order approximation:

$$\left(\frac{\partial}{\partial t}+\frac{\partial}{\partial\theta}\right)\left(u(t^n,\theta_j)\right)=\lim_{h\to 0^+}\frac{u(t^n+h,\theta_j+h)-u(t^n,\theta_j)}{h}\approx\frac{u_{j+1}^{n+1}-u_j^n}{h},\ 0\le n\le\mathcal{N}-1,\ 0\le j\le\mathcal{J}-1\,,$$

for $u\in\{e\,(t,\theta)\,,a\,(t,\theta)\,,i\,(t,\theta)\,|\,(t,\ \theta)\in[0,\ 1500]\times[0,\ 90\cdot 360]\ \cdot\text{ days}\}$.

To discretize the integrals, we use the following quadrature formula:

$$\int_0^\infty g(\theta)u\left(t^n,\theta\right)\,\mathrm{d}\theta\approx h\sum_{j=0}^{\mathcal{J}}g\left(\theta_j\right)u\left(t^n,\theta_j\right)=h\sum_{j=0}^{\mathcal{J}}g_ju_j^n,\ 0\le n\le\mathcal{N}-1\,,$$

for

$$(u,g)\in\{e\,(t,\theta)\,,a\,(t,\theta)\,,i\,(t,\theta)\,|\,(t,\ \theta)\in[0,\ 1500]\times[0,\ 90\cdot 360]\ \cdot\text{ days}\}\times$$

$$\times\{\,\beta_A(\theta),\beta_I(\theta),k(\theta),q(\theta),\gamma_A(\theta),\xi(\theta),\chi(\theta),\gamma_I(\theta)\,|\,\theta\in[0,\ 90\cdot 360]\ \cdot\text{ days}\}\ .$$

3.1.2 | Code implementation

To implement the aforementioned discretization schemes, we use Julia (v1.8.5) [18]. The code can be found at https://github.com/TsilidisV/age-structured-SVeaiR-model. To plot the numerical solution of $\mathscr{P}$ (3), we use Makie.jl [19]. To save and load the results, we use JLD2.jl and CodecZlib.jl. To calculate $\mathcal{R}_0$, we use QuadGK.jl [20] and Integrals.jl [21]. To create faster Julia structs for the parameters and initial conditions, we use FunctionWrappers.jl. Finally, we use Dierckx.jl to interpolate, as well as CSV.jl and DataFrames.jl [22] to load the data for the parameter values.

3.2 | Parameter values

Here, we give a description of the parameter values chosen to represent the case of SARS-CoV-2. A summary of the parameter values, can be found in Table 2.

TABLE 2 A list of parameters of $\mathscr{P}$ (3), along with their value, units, value, and source.

Parameters	Value	Units	Source
N_0	$80\cdot 10^6$	Individuals	Estimated from Mathieu et al. [23]
μ	$4.38356\cdot 10^{-5}$	day $^{-1}$	Estimated from Mathieu et al.[23]
β_A	Figure 2	Individual$^{-1}\cdot$day $^{-1}$	Estimated from Del Valle et al. [24]
β_I	Figure 2	Individual$^{-1}\cdot$day^{-1}	Estimated from Del Valle et al. [24]
p	10^{-3}	day^{-1}	Estimated from Mathieu et al. [23]
ϵ	0.7	-	Estimated from Grant et al. [25]
ζ	$\frac{1}{14}$	day^{-1}	Estimated from Chau et al. [26]
k	Equation (20)	day^{-1}	Estimated from the literature [27, 28]
q	Figure 3	-	Estimated from Sah et al. [14]
ξ	0.5	-	Estimated from the literature [29, 30]
χ	Equation (21)	day^{-1}	Estimated from the literature [29, 30]
γ_A	$\frac{1}{8}$	day^{-1}	Estimated from Byrne et al. [31]
γ_I	$\frac{1}{14}$	day^{-1}	Estimated from Byrne et al. [31]

- $N_0 = 80 \cdot 10^6$, the size of the population, is chosen to be that of a relative large country [23].
- $\mu = 4.38356 \cdot 10^{-5}$ day^{-1}, the birth/death rate, is converted from the average birth/death rate of the world for the year 2021, 16 per 1000 individuals per year, found in Mathieu et al. [23].
- β_A and β_I are functions of age and are estimated from Del Valle et al. [24]. As can be seen from fig. 2 of Del Valle et al. [24], the average contacts an individual makes each day regardless of their epidemiological status is about 16.71 contacts per day. In order to examine the effect of age in the dynamics of $\mathscr{P}$ (3), we assume the following two functions to respectively model two extreme cases of the average number of contacts an individual makes:

$$c_1(\theta) = \frac{16.71}{0.38} \exp\left(\left(\frac{\theta - 80\omega}{10^4}\right)^2\right), \quad \theta \in [0,\ 90 \cdot 360] \ \cdot \ \text{days} \tag{19a}$$

$$c_2(\theta) = \frac{16.71}{0.38} \exp\left(\left(\frac{\theta - 10\omega}{10^4}\right)^2\right), \quad \theta \in [0,\ 90 \cdot 360] \ \cdot \ \text{days} . \tag{19b}$$

  Both c_1 and c_2 have the same mean value of 16.71 contacts per day in the interval $[0,\ 90 \cdot 360] \ \cdot$ days. We additionally assume that the probability of an exposed individual passing to the compartments of asymptomatic and symptomatic individuals to be $\varpi_{E \to A} = \frac{1}{5}$ and $\varpi_{E \to I} = \frac{2}{5}$, respectively. Finally, assuming the transmission rates to be defined as $\beta_{A_i} = \frac{c_i \cdot \varpi_{E \to A}}{N_0}$ and $\beta_{I_i} = \frac{c_i \cdot \varpi_{E \to I}}{N_0}$, for $i = 1, 2$, we get Figure 2.
- $p = 10^{-3}$ day^{-1}, the vaccination rate, is assumed to be that during the summer of 2021 in the United States [23].
- $\epsilon = 0.7$, the vaccine effectiveness, is assumed to be an average effectiveness of the BNT162b2 and ChAdOx1 nCoV-19 vaccine [25].
- $\zeta = \frac{1}{14}$, the vaccine-induced immunity rate, is taken from Chau et al. [26].
- k, the latent rate, is a function of age and is taken by assuming that the latent and incubation period differ by one day [27, 28]. It is given by

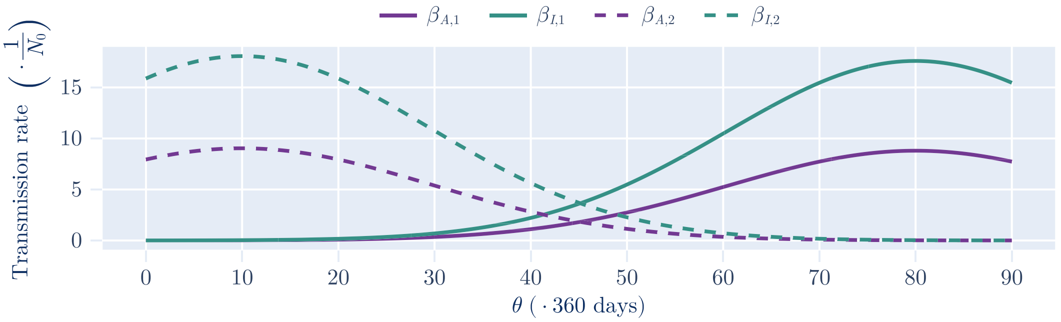

FIGURE 2 Two extreme types of transmission rates for the symptomatic infectious and asymptomatic infectious individuals. The transmission rates corresponding to the contact function of c_1 peak at individuals of 10 years of age, whereas the transmission rates corresponding to the contact function of c_2 peak at individuals of 80 years of age. [Colour figure can be viewed at wileyonlinelibrary.com]

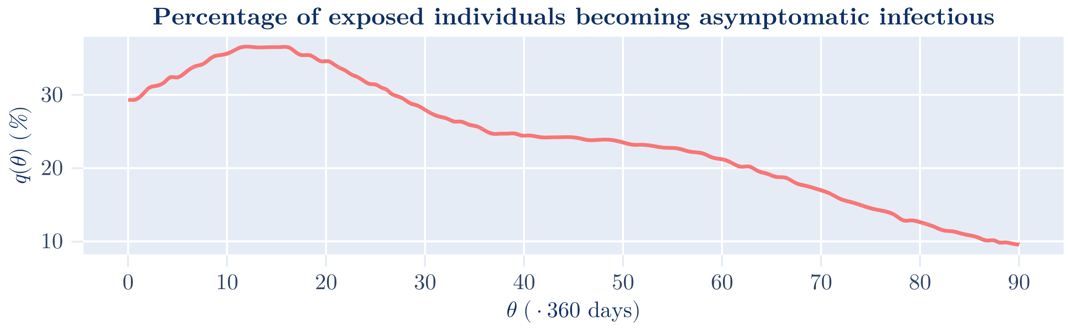

FIGURE 3 Percentage of asymptomatic COVID-19 infection, by age (in days), taken from Sah et al. [14]. [Colour figure can be viewed at wileyonlinelibrary.com]

$$k(\theta) = \begin{cases} \frac{1}{4}\ \text{day}^{-1}, & \theta < 30 \cdot 360 \\ \frac{1}{4.8}\ \text{day}^{-1}, & 30 \cdot 360 \leq \theta < 40 \cdot 360 \\ \frac{1}{4.8}\ \text{day}^{-1}, & 40 \cdot 360 \leq \theta < 50 \cdot 360 \\ \frac{1}{5.5}\ \text{day}^{-1}, & 50 \cdot 360 \leq \theta < 60 \cdot 360 \\ \frac{1}{3.1}\ \text{day}^{-1}, & 60 \cdot 360 \leq \theta < 70 \cdot 360 \\ \frac{1}{6}\ \text{day}^{-1}, & 70 \cdot 360 \leq \theta\ . \end{cases} \tag{20}$$

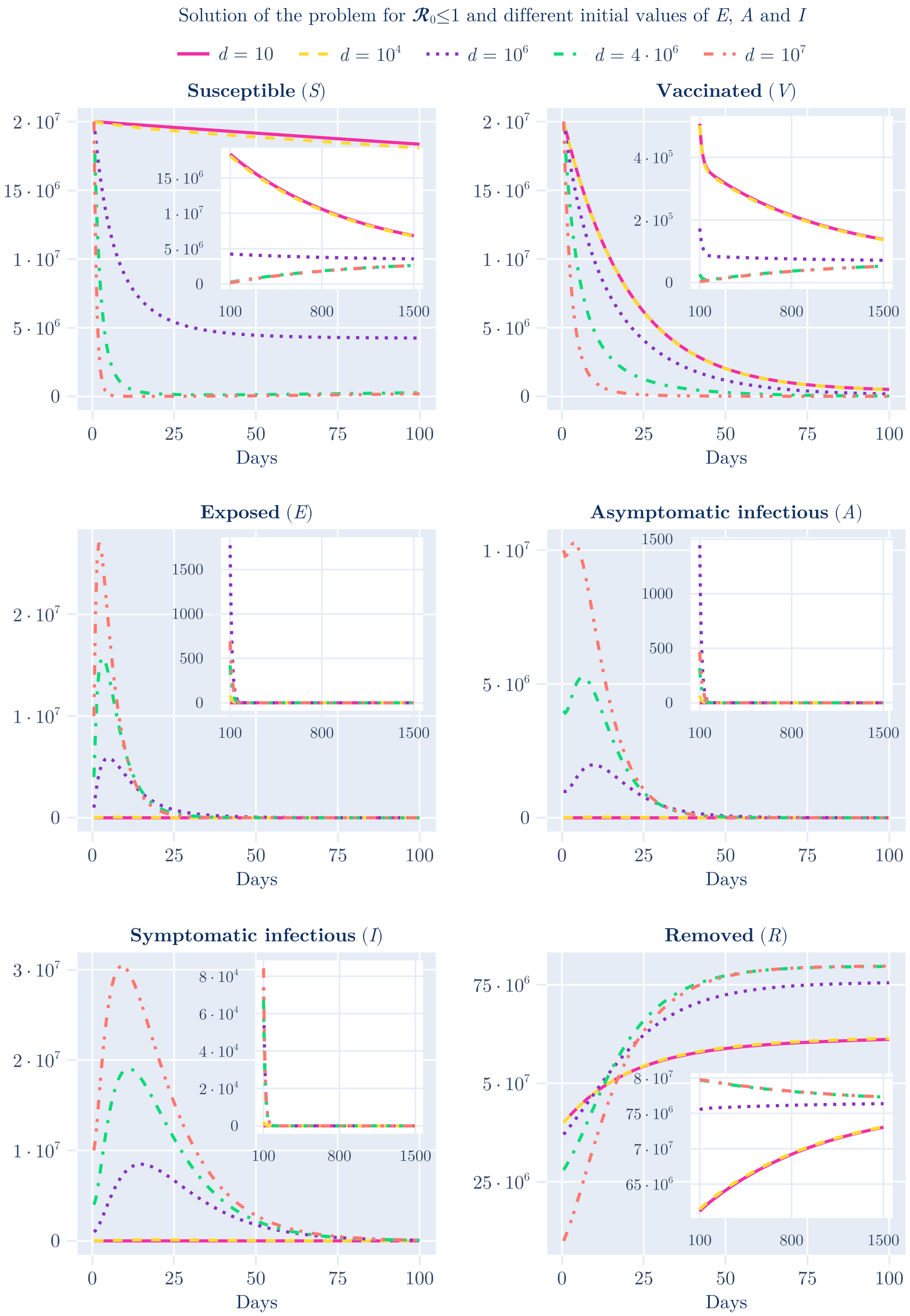

FIGURE 4 Solution of $\mathscr{P}$ (3) for $t \in [0, 1500]\cdot$ days. The time in each large diagram is in the range $[0, 100]\cdot$ days, whereas in each inserted small diagram, in the range of $[100,1500]\cdot$ days. The parameter values are as in Table 2, with $c = c_1$, and the initial conditions for S and V are $S_0 = V_0 = 2 \cdot 10^7$. The time-related initial conditions E_0, A_0 and I_0 for E, A and I, respectively, are all equal, that is, $E_0 = A_0 = I_0 = d$. The value of d takes the values of $10, 10^4, 10^6, 4 \cdot 10^6$ and 10^7. We see that for all initial conditions the solutions converge toward the disease-free steady state, since $(E,\ A,\ I) \to (0,\ 0,\ 0)$, as $t \to \infty$. Hence, the global stability of the disease-free steady state for $\mathcal{R}_0 \leq 1$ is numerically confirmed. [Colour figure can be viewed at wileyonlinelibrary.com]

- q, the proportion of the latent/exposed individuals becoming asymptomatic infectious is taken from Sah et al. [14] and can be seen in Figure 3. To digitize the data from Sah et al. [14], we use WebPlotDigitizer 4.6 [32].
- $\xi = 0.5$, the proportion of the asymptomatic infectious individuals becoming recovered/removed without developing any symptoms, is estimated from the literature [29, 30].

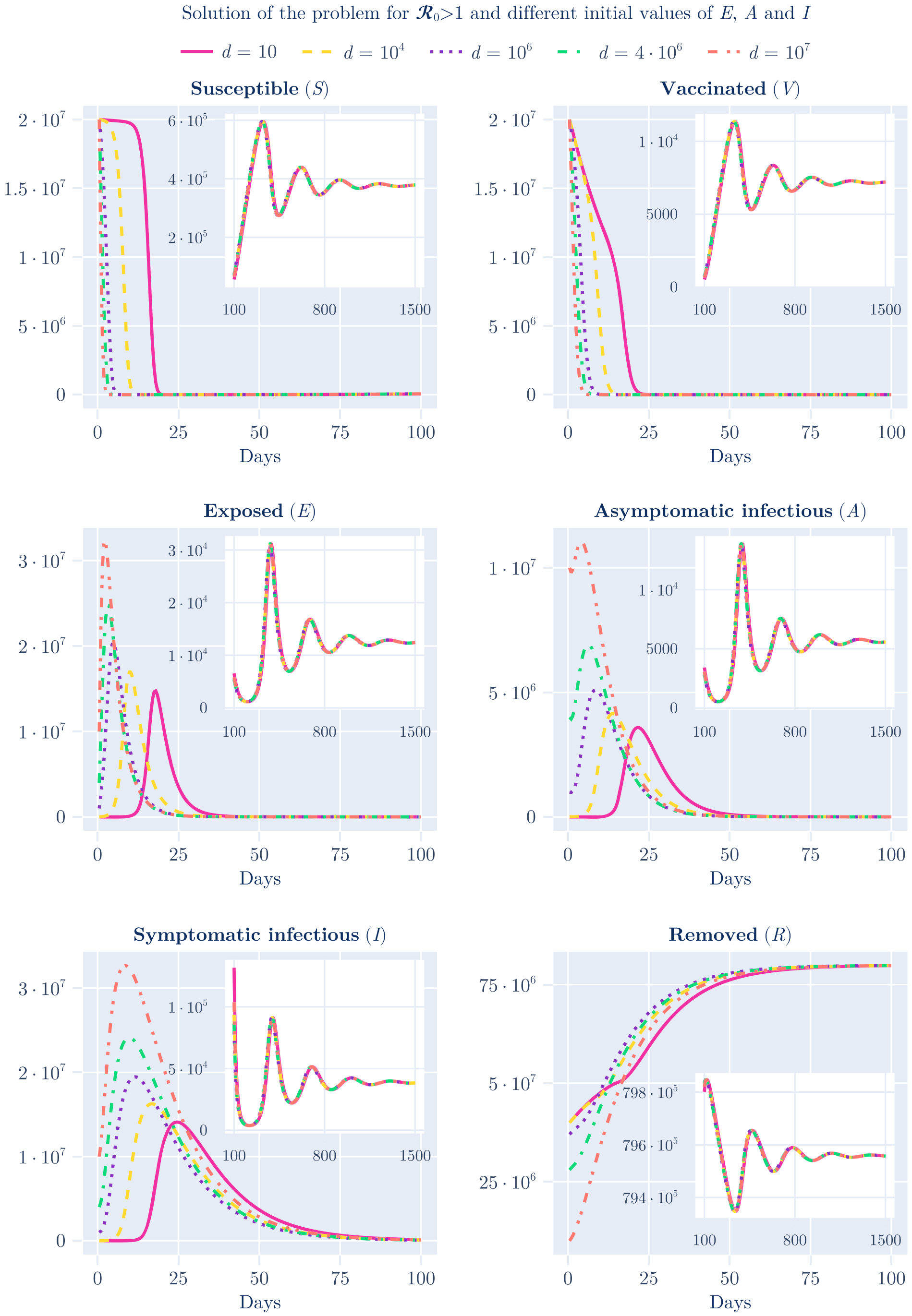

FIGURE 5 Solution of $\mathscr{P}$ (3) for $t \in [0, 1500]\cdot$ days. The time in each large diagram is in the range $[0, 100]\cdot$ days, whereas in each inserted small diagram, in the range of $[100{,}1500]\cdot$ days. The parameter values are as in Table 2, with $c = c_2$, and the initial conditions for S and V are $S_0 = V_0 = 2\cdot 10^7$. The time-related initial conditions E_0, A_0 and I_0 for E, A and I, respectively, are all equal, that is, $E_0 = A_0 = I_0 = d$. The value of d takes the values of $10,\ 10^4,\ 10^6, 4\cdot 10^6$ and 10^7. We see that for all initial conditions the solutions converge toward the endemic steady state, since $(E,\ A,\ I)$ converges to a nonzero value, as $t \to \infty$. Interestingly, the convergence to the endemic steady state is oscillatory. Hence, the global stability of the endemic steady state for $\mathcal{R}_0 > 1$ is numerically confirmed. [Colour figure can be viewed at wileyonlinelibrary.com]

- χ, the incubation rate, is a function of age and is taken from data from Tan et al. [33]. It is given by

$$\chi(\theta) = \begin{cases} \frac{1}{5}\ \text{day}^{-1}, & \theta < 30 \cdot 360 \\ \frac{1}{5.8}\ \text{day}^{-1}, & 30 \cdot 360 \leq \theta < 40 \cdot 360 \\ \frac{1}{5.8}\ \text{day}^{-1}, & 40 \cdot 360 \leq \theta < 50 \cdot 360 \\ \frac{1}{6.5}\ \text{day}^{-1}, & 50 \cdot 360 \leq \theta < 60 \cdot 360 \\ \frac{1}{4.1}\ \text{day}^{-1}, & 60 \cdot 360 \leq \theta < 70 \cdot 360 \\ \frac{1}{7}\ \text{day}^{-1}, & 70 \cdot 360 \leq \theta\ . \end{cases} \tag{21}$$

- $\gamma_A = \frac{1}{8}$ day^{-1}, the recovery rate of the asymptomatic infectious individuals, is a function of age, but it is taken as a constant due to lack of available data. It is estimated from Byrne et al. [31].
- $\gamma_I = \frac{1}{14}$ day^{-1}, the recovery rate of the symptomatic infectious individuals, is a function of age, but it is taken as a constant due to lack of available data. It is estimated from Byrne et al. [31].

3.3 | Results

Throughout our simulations, we assume that $S_0 = V_0 = 2 \cdot 10^7$ individuals. In order to study $\mathscr{P}$ (3) in a global scale, we vary the rest of the initial conditions. In particular, we assume that $E_0 = A_0 = I_0 = d$ and let d take the values of $10,\ 10^4,\ 10^6,\ 4 \cdot 10^6,\ 10^7$.

3.3.1 | The case of $\mathcal{R}_0 \leq 1$

Here, we assume the average number of contacts of each individual, c, to be as in (19a), that is, $c = c_1$. In such a case, $\mathcal{R}_0 = 5.95 \cdot 10^{-5}$. As we see in Figure 4, for every initial condition, we have that $(E,\ A,\ I) \to (0,\ 0,\ 0)$, as $t \to \infty$. This confirms the global stability analysis performed in Section 2.1, since the solutions converge to the disease-free steady state for every initial condition when $\mathcal{R}_0 \leq 1$.

3.3.2 | The case of $\mathcal{R}_0 > 1$

Here, we assume the average number of contacts of each individual, c, to be as in (19b), that is, $c = c_2$. In such a case, $\mathcal{R}_0 = 9.14$. As we see in Figure 5, for every initial condition we have that $(E,\ A,\ I)$ converges to a nonzero value, as $t \to \infty$. This confirms the global stability analysis performed in Section 2.1, since the solutions converge, in an oscillatory way, to the endemic steady state for every initial condition when $\mathcal{R}_0 > 1$.

4 | CONCLUSIONS AND DISCUSSION

In this paper, we derived an age-structured epidemiological compartment problem and we studied it in terms of global well-posedness and stability analysis. From this analysis we deduced the basic reproductive number, $\mathcal{R}_0$, of the model, a critical measurement of the transmission potential of a disease.

The model presented in this paper focused on the age structure of a population. A straightforward generalization includes the consideration of more independent variables, such as a spatial one. Moreover, it would be essential to include additional, potentially important factors of the evolution of the epidemiological phenomenon, such as waning immunity gained by both infected and vaccinated individuals.

AUTHOR CONTRIBUTIONS

Vasiliki Bitsouni: Conceptualization; writing—original draft. **Nikolaos Gialelis:** Conceptualization; writing—original draft. **Vasilis Tsilidis:** Conceptualization; writing—original draft.

ACKNOWLEDGEMENTS

The publication of the article in Open Access was financially supported by HEAL-Link.

CONFLICT OF INTEREST STATEMENT

This work does not have any conflicts of interest.

ORCID

Vasiliki Bitsouni https://orcid.org/0000-0002-0684-0583
Nikolaos Gialelis https://orcid.org/0000-0002-6465-7242
Vasilis Tsilidis https://orcid.org/0000-0001-5868-4984

REFERENCES

1. M. Iannelli and A. Pugliese, *An Introduction to Mathematical Population Dynamics: Along the Trail of Volterra and Lotka*, Springer, 2014.
2. M. Iannelli and F. Milner, *The Basic Approach to Age-Structured Population Dynamics: Models, Methods and Numerics*, Lecture Notes on Mathematical Modelling in the Life Sciences, Springer, 2017.
3. F. R. Sharpe and A. J. Lotka, *A problem in age-distribution*, The London, Edinburgh, Dublin Philosop. Mag. J. Sci. **21** (1911), no. 124, 435–438.
4. A. G. M'kendrick, *Applications of mathematics to medical problems*, Proc. Edinb. Math. Soc. **44** (1925), 98–130.
5. Y. Xiang, Y. Jia, L. Chen, L. Guo, B. Shu, and E. Long, *COVID-19 epidemic prediction and the impact of public health interventions: a review of COVID-19 epidemic models*, Infect. Dis. Model **6** (2021), 324–342.
6. A. Adiga, D. Dubhashi, B. Lewis, M. Marathe, S. Venkatramanan, and A. Vullikanti, *Mathematical models for COVID-19 pandemic: a comparative analysis*, J. Indian. Inst. Sci. **100** (2020), no. 4, 793–807.
7. N. P. Jewell, J. A. Lewnard, and B. L. Jewell, *Predictive mathematical models of the COVID-19 pandemic: underlying principles and value of projections*, JAMA **323** (2020), no. 19, 1893–1894.
8. O. J. Watson, G. Barnsley, J. Toor, A. B. Hogan, P. Winskill, and A. C. Ghani, *Global impact of the first year of COVID-19 vaccination: a mathematical modelling study*, Lancet Infect. Dis. **22** (2022), no. 9, 1293–1302.
9. H. Inaba, *Threshold and stability results for an age-structured epidemic model*, J. Math. Biol. **28** (1990), 411–434.
10. Z. Gao, Y. Xu, C. Sun, X. Wang, Y. Guo, S. Qiu, and K. Ma, *A systematic review of asymptomatic infections with COVID-19*, J. Microbiol. Immunol. Infect. **54** (2021), no. 1, 12–16.
11. R. Li, S. Pei, B. Chen, Y. Song, T. Zhang, W. Yang, and J. Shaman, *Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV-2)*, Science **368** (2020), no. 6490, 489–493.
12. R. Yang, X. Gui, and Y. Xiong, *Comparison of clinical characteristics of patients with asymptomatic vs symptomatic coronavirus disease 2019 in Wuhan, China*, JAMA Netw. Open **3** (2020), e2010182.
13. C. Heneghan, J. Brassey, and T. Jefferson, *COVID-19: what proportion are asymptomatic?*. CEBM. 2020.
14. P. Sah, M. C. Fitzpatrick, C. F. Zimmer, E. Abdollahi, L. Juden-Kelly, S. M. Moghadas, B. H. Singer, and A. P. Galvani, *Asymptomatic SARS-CoV-2 infection: a systematic review and meta-analysis*, Proc. Natl. Acad. Sci. **118** (2021), no. 34, e2109229118.
15. V. Bitsouni, N. Gialelis, and I. G. Stratis, A model for the outbreak of COVID-19: vaccine effectiveness in a case study of Italy, *Operator theory and harmonic analysis - part ii: probability- analytical models, methods and applications*, A. Karapetyants, I. V. Pavlov, and A. N. Shiryaev, (eds.), Springer Proc. in Math. & Stat., Vol. **358**, Springer, 2021, pp. 91–107.
16. H. Inaba, *Age-Structured Population Dynamics in Demography and Epidemiology*, Springer, 2017.
17. G. F. Webb, *Theory of Nonlinear Age-Dependent Population Dynamics*, Monographs and Textbooks in Pure and Applied Mathematics, Marcel Dekker, 1985.
18. J. Bezanson, A. Edelman, S. Karpinski, and V. B. Shah, *Julia: a fresh approach to numerical computing*, SIAM Review **59** (2017), no. 1, 65–98, DOI 10.1137/141000671.
19. S. Danisch and J. Krumbiegel, *Makie.jl: flexible high-performance data visualization for Julia*, J. Open Source Softw. **6** (2021), no. 65, 3349, DOI 10.21105/joss.03349.
20. S. G. Johnson, *QuadGK.jl: Gauss–Kronrod integration in Julia*, 2013. https://github.com/JuliaMath/QuadGK.jl
21. C. Rackauckas and Q. Nie, *Differentialequations.jl a performant and feature-rich ecosystem for solving differential equations in Julia*, J. Open Source Softw. **5** (2017), no. 1. Exported from https://app.dimensions.ai on 2019/05/05
22. M. Bouchet-Valat and B. Kamiski, *DataFrames.jl: flexible and fast tabular data in Julia*, J. Stat. Softw. **107** (2023), no. 4, 1–32. https://www.jstatsoft.org/index.php/jss/article/view/v107i04
23. E. Mathieu, H. Ritchie, L. Rods-Guirao, C. Appel, C. Giattino, J. Hasell, B. Macdonald, S. Dattani, D. Beltekian, E. Ortiz-Ospina, and M. Roser, *Coronavirus pandemic (COVID-19)*, Our World in Data (2020). https://ourworldindata.org/coronavirus
24. S. Y. Del Valle, J. M. Hyman, H. W. Hethcote, and S. G. Eubank, *Mixing patterns between age groups in social networks*, Soc. Netw. **29** (2007), no. 4, 539–554. https://linkinghub.elsevier.com/retrieve/ pii/S0378873307000330
25. R. Grant, T. Charmet, L. Schaeffer, S. Galmiche, Y. Madec, C. Von Platen, O. Chény, F. Omar, C. David, and A. Rogoff, *Impact of SARS-CoV-2 Delta variant on incubation, transmission settings and vaccine effectiveness: results from a nationwide case-control study in France*, Lancet Reg. Health Eur. **13** (2022), 100278.
26. N. V. V. Chau, L. A. Nguyet, N. T. Truong, N. T. Dung, M. T. Nhan, D. N. H. Man, N. M. Ngoc, H. P. Thao, T. N. H. Tu, and H. K. Mai, *Immunogenicity of Oxford-AstraZeneca COVID-19 vaccine in Vietnamese health-care workers*, Am. J. Trop. Med. Hyg. **106** (2022), no. 2, 556.

27. M. Kang, H. Xin, J. Yuan, S. T. Ali, Z. Liang, J. Zhang, T. Hu, E. ricH. Y. Lau, Y. Zhang, and M. Zhang, *Transmission dynamics and epidemiological characteristics of SARS-CoV-2 Delta variant infections in Guangdong, China, May to June 2021*, Eurosurveillance **27** (2022), no. 10, 2100815.
28. Y. Wu, L. Kang, Z. Guo, J. Liu, M. Liu, and W. Liang, *Incubation period of COVID-19 caused by unique SARS-CoV-2 strains: a systematic review and meta-analysis*, JAMA Netw. Open **5** (2022), no. 8, e2228008–e2228008.
29. J. He, Y. Guo, R. Mao, and J. Zhang, *Proportion of asymptomatic coronavirus disease 2019: a systematic review and meta-analysis*, J. Med. Virol. **93** (2021), no. 2, 820–830.
30. D. Buitrago-Garcia, A. M. Ipekci, L. Heron, H. Imeri, L. Araujo-Chaveron, I. Arevalo-Rodriguez, A. Ciapponi, M. Cevik, A. Hauser, and M. I. Alam, *Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: update of a living systematic review and meta-analysis*, PLOS Medicine **19** (2022), no. 5, e1003987.
31. A. W. Byrne, D. McEvoy, A. B. Collins, K. Hunt, M. Casey, A. Barber, F. Butler, J. Griffin, E. A. Lane, and C. McAloon, *Inferred duration of infectious period of SARS-CoV-2: rapid scoping review and analysis of available evidence for asymptomatic and symptomatic COVID-19 cases*, BMJ Open **10** (2020), no. 8, e039856.
32. A. Rohatgi, *Webplotdigitizer: version 4.6*, 2022. https://automeris.io/WebPlotDigitizer
33. W. Y. T. Tan, L. Y. Wong, Y. S. Leo, and M. P. H. S. Toh, *Does incubation period of COVID-19 vary with age? A study of epidemiologically linked cases in Singapore*, Epidemiol. Infect. **148** (2020), e197.

How to cite this article: V. Bitsouni, N. Gialelis, and V. Tsilidis, *An age-structured SVEAIR epidemiological model*, Math. Meth. Appl. Sci. (2024), 1–27, DOI 10.1002/mma.10165.