Dealing with different types of population heterogeneity in epidemiological models

Andreas Widder

Research Report 2013-03

March 2013

Operations Research and Control Systems
Institute of Mathematical Methods in Economics
Vienna University of Technology

Research Unit ORCOS
Argentinierstraße 8/E105-4,
1040 Vienna, Austria
E-mail: orcos@tuwien.ac.at

Dealing with different types of population heterogeneity in epidemiological models*

Andreas Widder†

Abstract

We take as a starting point an ODE model for the spreading of a disease in a homogeneous population. We extend this model by introducing heterogeneities in the population, which yields a model including a PDE or an infinite dimensional system of ODEs. We show how these models can be reduced to a system of integro-differential equations and show a comparison of this system to the original ODE model. Furthermore, we suggest a way to deal with the practically unknown boundary conditions that arise in heterogeneous models.

1 Introduction

Differences between individuals in a population can be important when trying to study the spread of an epidemic in that population. Many factors, e.g. social behaviour or strength of the immune system, play a role in this process, for example by influencing the amount of contacts between individuals or the likelihood that a contact between a susceptible and infected individual leads to an infection. Consequently, epidemiological models that include heterogeneities in the population have been studied (e.g. Couthino et al. [1], Dushoff [2], Novozhilov [9], and Veliov [10]). In this context the study of dynamics of heterogeneous populations is important, as done e.g. by Karev [6], [7].

Starting from a model for a homogeneous population, we introduce two different kinds of heterogeneity. First we consider a time dependent heterogeneity, i.e. the parameter assigned to a single individual undergoes changes as the system evolves. This turns the system of ordinary differential equations (ODEs) describing the evolution of the disease in a homogeneous population into a system containing partial differential equations (PDEs). Second, we consider a semi-static heterogeneity, i.e. each individual is assigned a fixed parameter, which may change, however, when the health status of the individual changes. This will yield an infinite dimensional system of ODEs.

In both cases we face the problem that the initial and the boundary conditions require distributed data that are not available in reality. Therefore, our main goal is to reduce these systems to a finite dimensional systems with at most a few unknown parameters. These simpler systems will turn out to consist of integro-differential equations.

*This research was supported by the Austrian Science Foundation under Grant No. P24125-N13

†Institute of Mathematical Methods in Economics, Vienna University of Technology, Austria, andreas.widder@tuwien.ac.at

The starting point for our considerations is the usual SIS model in the general form considered by Veliov in [10]. It models the spreading of a disease in a homogeneous population. The dynamics is

$$\begin{aligned}\dot{S}(t) &= -\sigma\frac{I(t)}{S(t)+I(t)}S(t)+\lambda(S,I)S(t)+\gamma(S,I)I(t), \quad S(0)=S_0,\\ \dot{I}(t) &= \sigma\frac{I(t)}{S(t)+I(t)}S(t)-\delta(S,I)I(t), \quad I(0)=I_0.\end{aligned}$$

Here, $S(t)$ and $I(t)$ denote susceptible and infected individuals, respectively. The parameter $\lambda(S,I)$ is defined as the difference between the birth rate and mortality rate of susceptible individuals while $\gamma(S,I)$ denotes the inflow rate of susceptible individuals resulting from recovery of the infected population. The parameter $\delta(S,I)$, on the other hand, denotes the net outflow rate of infected individuals. Furthermore, σ represents the infectiousness (strength of infection).

This model is versatile, since we allow the demographic parameters to depend on S and I. The evolution of a disease, however, depends on many more factors (variables). Clearly, every additional variable introduces new complications into the dynamics of the system. We restrict ourselves here to introducing a single new variable representing a specific heterogeneity in the population.

The first heterogeneity we consider is the infection age, i.e. the time since an individual has become infected. This heterogeneity obviously only applies to the infected part of the population. Also, infection age is clearly a characteristic that changes with time. Models containing infection age have been considered before (see for example Feichtinger et al. [3] or Inaba [4]).

Static heterogeneities have been considered in various interpretations, see e.g. Kretzschmar [8], Novozhilov [9], and Veliov [10]. We will leave the interpretation of the heterogeneity open, although our heterogeneous model is taken from Veliov [10], where it is interpreted behaviourally, as habits or vulnerability to risks, rather then biologically.

The rest of this paper is split into two parts, one of which deals with time dependent, the second one with static heterogeneities. Both parts are structured in the same way. After introducing the heterogeneous model and its dynamics, we give, as much as possible, an analytical solution to the equations. This in turn will be used to reduce the PDE system or infinite dimensional ODE system to a finite dimensional system of integro-differential equations. Next we will study how these system corresponds to the basic model introduced above. In particular we will see that in absence of any heterogeneity these models do indeed coincide. Finally we will suggest ways to deal with unknown initial data that is needed to fully determine the dynamics of the model.

2 A time dependent heterogeneity

We enhance the presented model by introducing a second variable α for infected individuals that denotes the infection age, i.e. the time since the individual has become infected.

In order to incorporate this variable into our model, we decompose $\delta = \mu(\alpha) - (1-\epsilon)\eta(S,I)$, where $\mu(\alpha)$ is the mortality of infected individuals dependent on age of infection and η is the fertility rate of infected individuals. By ϵ we denote the fraction of newborns that are susceptible. So conversely, we set $\gamma(S, I) = \epsilon\eta(S, I)$. Furthermore, we introduce a function $i(\alpha)$ that indicates the infectivity of an individual with infection age α. This results in the following model:

$$\begin{aligned}
\dot{S}(t) &= -\sigma \frac{J(t)}{S(t) + I(t)} S(t) + \lambda(S, I)S(t) + \epsilon\eta(S, I)I(t), \\
\left(\frac{\partial}{\partial t} + \frac{\partial}{\partial \alpha}\right) \bar{I}(t, \alpha) &= -\mu(\alpha)\bar{I}(t, \alpha), \\
S(0) &= S_0, \\
\bar{I}(0, \alpha) &= I_0(\alpha), \\
\bar{I}(t, 0) &= \sigma \frac{J(t)}{S(t) + I(t)} S(t) + (1 - \epsilon)\eta(S, I)I(t), \\
I(t) &= \int_0^\infty \bar{I}(t, \alpha) d\alpha, \\
J(t) &= \int_0^\infty i(\alpha)\bar{I}(t, \alpha) d\alpha.
\end{aligned}$$

Note that except for $\mu(\alpha)$ and $i(\alpha)$ we allow all parameters to be dependent on population sizes.

The biggest problem with this model is that we can not expect to know the boundary condition $\bar{I}_0(\alpha)$, so we are unable to compute a solution for this model. Furthermore, no information about $\bar{I}(t, \alpha)$ is available for any later time, which also makes data fitting more difficult.
Our goal is therefore to reduce this system to a solely time-dependent system for I, S, and J.

2.1 Reducing the heterogeneous model

We use the simple structure of the PDE for $\bar{I}(t, \alpha)$ and solve it analytically using the method of characteristics. The characteristic equations for $\bar{I}(t, \alpha)$ are

$$\begin{aligned}
\frac{dt(r, s)}{dr} &= 1, \\
\frac{d\alpha(r, s)}{dr} &= 1, \\
\frac{d\bar{I}(r, s)}{dr} &= -\mu(\alpha)\bar{I}(r, s),
\end{aligned}$$

with the initial conditions

$$\begin{aligned}
t(0, s) &= s, \\
\alpha(0, s) &= 0, \\
\bar{I}(0, s) &= \sigma \frac{J(s)}{S(s) + I(s)} S(s) + (1 - \epsilon)\eta(S(s), I(s))I(s).
\end{aligned}$$

This yields

$$\bar{I}(t,\alpha) = e^{-\int_0^\alpha \mu(a)da}\left(\sigma\frac{J(t-\alpha)}{S(t-\alpha)+I(t-\alpha)}S(t-\alpha) + (1-\epsilon)\tilde{\eta}(S(t-\alpha), I(t-\alpha))I(t-\alpha)\right).$$

This solution obviously only makes sense for $t \geq \alpha$. However, if we use the initial conditions

$$\begin{aligned} t(0,s) &= 0, \\ \alpha(0,s) &= s, \\ \bar{I}(0,s) &= I_0(s). \end{aligned}$$

for the characteristic equations, we get

$$\bar{I}(t,\alpha) \quad = \quad e^{-\int_{\alpha-t}^\alpha \mu(a)da} I_0(\alpha - t),$$

which makes sense for $\alpha \geq t$. We get

$$\bar{I}(t,\alpha) \quad = \quad \begin{cases} e^{-\int_0^\alpha \mu(a)da}\left(\sigma\frac{J(t-\alpha)}{S(t-\alpha)+I(t-\alpha)}S(t-\alpha) + (1-\epsilon)\eta(S(t-\alpha), I(t-\alpha))I(t-\alpha)\right) & t > \alpha, \\ e^{-\int_{\alpha-t}^\alpha \mu(a)da} I_0(\alpha - t) & t \leq \alpha. \end{cases}$$

This function is continuous, provided that

$$I_0(0) = \sigma\frac{J(0)}{S(0)+I(0)}S(0) + (1-\epsilon)\eta(S(0), I(0))I(0).$$

We now can derive a formula for $I(t)$ by integrating $\bar{I}(t,\alpha)$ over the parameter α. We get

$$\begin{aligned} I(t) \quad = \quad & \int_0^\infty \bar{I}(t,\alpha)d\alpha = \\ & \int_0^t e^{-\int_0^\alpha \mu(a)da}\left(\sigma\frac{J(t-\alpha)}{S(t-\alpha)+I(t-\alpha)}S(t-\alpha) + (1-\epsilon)\eta(S(t-\alpha), I(t-\alpha))I(t-\alpha)\right)d\alpha + \\ & \int_t^\infty e^{-\int_{\alpha-t}^\alpha \mu(a)da} I_0(\alpha - t)d\alpha = \\ & \int_0^t e^{-\int_0^{t-x} \mu(a)da}\left(\sigma\frac{J(x)}{S(x)+I(x)}S(x) + (1-\epsilon)\eta(S,I)I(x)\right)dx + \int_0^\infty e^{-\int_x^{x+t} \mu(a)da} I_0(x)dx \end{aligned}$$

by substitution. Using the formula

$$\frac{d}{dt}\int_{a(t)}^{b(t)} f(t,x)dx \quad = \quad f(t,b(t))b'(t) - f(t,a(t))a'(t) + \int_{a(t)}^{b(t)} \frac{\partial}{\partial t} f(t,x)dx$$

we get

$$
\begin{aligned}
\frac{d}{dt}I(t) &= \sigma\frac{J(t)}{S(t)+I(t)}S(t)+(1-\epsilon)\eta(S,I)I(t)- \\
&\int\limits_0^t \mu(t-x)e^{-\int_0^{t-x}\mu(a)da}\left(\sigma\frac{J(x)}{S(x)+I(x)}S(x)+(1-\epsilon)\eta(S,I)I(x)\right)dx- \\
&\int\limits_0^\infty \mu(x+t)e^{-\int_x^{x+t}\mu(a)da}I_0(x)dx.
\end{aligned}
$$

We also need an equation to determine $J(t)$. As is to be suspected by its definition, these equation is very similar to that for $I(t)$ and can be derived analogically.

$$
\begin{aligned}
J(t) &= \int\limits_0^\infty i(\alpha)\bar{I}(t,\alpha)d\alpha = \\
&\int\limits_0^t i(t-x)e^{-\int_0^{t-x}\mu(a)da}\left(\sigma\frac{J(x)}{S(x)+I(x)}S(x)+(1-\epsilon)\eta(S,I)I(x)\right)dx+ \\
&\int\limits_0^\infty i(x+t)e^{-\int_x^{x+t}\mu(a)da}I_0(x)dx
\end{aligned}
$$

and

$$
\begin{aligned}
\frac{d}{dt}J(t) &= i(0)\left(\sigma\frac{J(t)}{S(t)+I(t)}S(t)+(1-\epsilon)\eta(S,I)I(t)\right)+ \\
&\int_0^t (i'(t-x)-i(t-x)\mu(t-x))e^{-\int_0^{t-x}\mu(a)da}\left(\sigma\frac{J(x)}{S(x)+I(x)}S(x)+(1-\epsilon)\eta(S,I)I(x)\right)dx+ \\
&\int_0^\infty (i'(x+t)-i(x+t)\mu(x+t))e^{-\int_x^{x+t}\mu(a)da}I_0(x)dx.
\end{aligned}
$$

This yields the following system of integro-differential equations to determine $S(t)$, $I(t)$, and $J(t)$.

$$
\begin{aligned}
\dot{S}(t) &= -\sigma\frac{J(t)}{S(t)+I(t)}S(t)+\lambda(S,I)S(t)+\epsilon\eta(S,I)I(t),\\
\dot{I}(t) &= \sigma\frac{J(t)}{S(t)+I(t)}S(t)+(1-\epsilon)\eta(S,I)I(t)-\\
&\quad \int_0^t \mu(t-x)e^{-\int_0^{t-x}\mu(a)da}\left(\sigma\frac{J(x)}{S(x)+I(x)}S(x)+(1-\epsilon)\eta(S,I)I(x)\right)dx-\\
&\quad \int_0^\infty \mu(x+t)e^{-\int_x^{x+t}\mu(a)da}I_0(x)dx,\\
\dot{J}(t) &= i(0)\left(\sigma\frac{J(t)}{S(t)+I(t)}S(t)+(1-\epsilon)\eta(S,I)I(t)\right)+\\
&\quad \int_0^t (i'(t-x)-i(t-x)\mu(t-x))e^{-\int_0^{t-x}\mu(a)da}\left(\sigma\frac{J(x)}{S(x)+I(x)}S(x)+(1-\epsilon)\eta(S,I)I(x)\right)dx+\\
&\quad \int_0^\infty (i'(x+t)-i(x+t)\mu(x+t))e^{-\int_x^{x+t}\mu(a)da}I_0(x)dx.
\end{aligned}
$$

2.2 Comparison between models

We now want to explore the connection between the system we just derived and the original one a little bit closer. For this we assume, that μ and i are constants, independent of α. In that case $J(t)=iI(t)$. Since the constant i can be incorporated into σ, we assume without loss of generality, that $i=1$. The resulting systems looks like this

$$
\begin{aligned}
\dot{S}(t) &= -\sigma\frac{I(t)}{S(t)+I(t)}S(t)+\lambda(S,I)S(t)+\epsilon\eta(S,I)I(t),\\
\dot{I}(t) &= \sigma\frac{I(t)}{S(t)+I(t)}S(t)+(1-\epsilon)\eta(S,I)I(t)-\\
&\quad \int_0^t \mu e^{-(t-x)\mu}\left(\sigma\frac{I(x)}{S(x)+I(x)}S(x)+(1-\epsilon)\eta(S,I)I(x)\right)dx-\\
&\quad \int_0^\infty \mu e^{-t\mu}I_0(x)dx,
\end{aligned}
$$

which can be written as

$$
\begin{aligned}
\dot{S}(t) &= -\sigma\frac{I(t)}{S(t)+I(t)}S(t)+\lambda(S,I)S(t)+\epsilon\eta(S,I)I(t),\\
\dot{I}(t) &= \sigma\frac{I(t)}{S(t)+I(t)}S(t)+(1-\epsilon)\eta(S,I)I(t)-\\
&\quad \mu e^{-t\mu}\left(\int_0^t e^{x\mu}\left(\sigma\frac{I(x)}{S(x)+I(x)}S(x)+(1-\epsilon)\eta(S,I)I(x)\right)dx+I(0)\right).
\end{aligned}
$$

We can get rid of the integral in this equations by introducing an auxiliary variable H to get

$$\begin{aligned}\dot{S}(t) &= -\sigma\frac{I(t)}{S(t)+I(t)}S(t)+\lambda(S,I)S(t)+\epsilon\eta(S,I)I(t),\\ \dot{I}(t) &= \sigma\frac{I(t)}{S(t)+I(t)}S(t)+(1-\epsilon)\eta(S,I)I(t)-\mu e^{-t\mu}H(t),\\ \dot{H}(t) &= e^{t\mu}\left(\sigma\frac{I(t)}{S(t)+I(t)}S(t)+(1-\epsilon)\eta(S,I)I(t)\right),\end{aligned}$$

with $H(0)=I(0)$.
If we consider $f(t)=e^{t\mu}I(t)-H(t)$ we get

$$f'(t)=(e^{t\mu}I(t)-H(t))'=\mu e^{t\mu}I(t)+e^{t\mu}I'(t)-H'(t)=\mu e^{t\mu}I(t)-\mu H(t)=\mu f(t),$$

so

$$f(t)=ce^{t\mu}.$$

Since

$$f(0) = e^{0\mu}I(0)-H(0)=I(0)-H(0)=0,$$

we get $c=0$, i.e.

$$e^{t\mu}I(t)-H(t) = f(t)=0e^{t\mu}=0,$$

and therefore

$$H(t) = e^{t\mu}I(t).$$

Putting this in our system yields

$$\begin{aligned}\dot{S}(t) &= -\sigma\frac{I(t)}{S(t)+I(t)}S(t)+\lambda(S,I)S(t)+\epsilon\eta(S,I)I(t),\\ \dot{I}(t) &= \sigma\frac{I(t)}{S(t)+I(t)}S(t)+(1-\epsilon)\eta(S,I)I(t)-\mu I(t),\end{aligned}$$

which is for our choice of $\delta(S,I)$ exactly the homogeneous model we took as our starting point.

2.3 Eliminating the initial data

Turning back to the system dependent on α, our main problem remains that in order to calculate a solution, we need to know the boundary condition $I_0(\alpha)$. In order to deal with this, we introduce a function $g(t)$, yet to be defined, and replace the term $\int_0^\infty \mu(x+t)e^{\int_x^{x+t}\mu(a)da}I_0(x)dx$ with $g(t)I(0)$. The resulting equation

$$\begin{aligned}\dot{I}(t) &= \sigma\frac{J(t)}{S(t)+I(t)}S(t)+(1-\epsilon)\eta(S,I)I(t)-g(t)I(0)\\ &\int_0^t \mu(t-x)e^{-\int_0^{t-x}\mu(a)da}\left(\sigma\frac{J(x)}{S(x)+I(x)}S(x)+(1-\epsilon)\eta(S,I)I(x)\right)dx\end{aligned}$$

would yield the same result if $g(t)I(0) = \int_0^\infty \mu(x+t)e^{\int_x^{x+t}\mu(a)da} I_0(x)dx$. We rewrite the difference between these two terms as

$$\begin{aligned} g(t)I(0) - \int_0^\infty \mu(x+t)e^{\int_x^{x+t}\mu(a)da} I_0(x)dx &= g(t)\int_0^\infty I_0(x)dx - \int_0^\infty \mu(x+t)e^{\int_x^{x+t}\mu(a)da} I_0(x)dx = \\ &\int_0^\infty \left(g(t) - \mu(x+t)e^{\int_x^{x+t}\mu(a)da}\right) I_0(x)dx = \\ &\left\langle g(t) - \mu(\cdot+t)e^{-\int_\cdot^{\cdot+t}\mu(a)da}, I_0(\cdot)\right\rangle_{L^2[0,\infty]}. \end{aligned}$$

This suggests that a reasonable approximation to the correct solution might be found by choosing $g(t)$ as a minimizer of $\left\|g(t) - \mu(\cdot+t)e^{-\int_\cdot^{\cdot+t}\mu(a)da}\right\|_{L^2[0,\infty]}$. The obvious advantage of this approach is that it is independent of the boundary condition $I_0(\alpha)$ and thus can be calculated without its knowledge.

We will however define $g(t)$ as the minimizer of weighted L^2 norm. One technical reason for this is to ensure that the norm stays finite. But another one is also to allow for the possibility to incorporate partial knowledge about $I_0(\alpha)$ into the calculation.

For a non-negative function $w(x)$ we define the weighed L^2 norm of a function $f(x)$ as

$$\|f(\cdot)\|_{L^2([0,\infty],w(.))} = \sqrt{\int_0^\infty f(x)^2 w(x)dx} = \left\|f(\cdot)\sqrt{w(\cdot)}\right\|_{L^2[0,\infty]}.$$

Since $\left\|\left(g(t) - \mu(\cdot+t)e^{-\int_\cdot^{\cdot+t}\mu(a)da}\right)\sqrt{w(\cdot)}\right\|_{L^2[0,\infty]}$ depends smoothly on $g(t)$ we can identify $g(t)$ by setting

$$\begin{aligned} 0 &= \frac{d}{dg(t)}\left\|\left(g(t) - \mu(\cdot+t)e^{-\int_\cdot^{\cdot+t}\mu(a)da}\right)\sqrt{w(\cdot)}\right\|^2_{L^2[0,\infty]} = \\ &\frac{d}{dg(t)}\int_0^\infty \left(\left(g(t) - \mu(x+t)e^{-\int_x^{x+t}\mu(a)da}\right)\sqrt{w(x)}\right)^2 dx = \\ &\int_0^\infty 2\left(g(t) - \mu(x+t)e^{-\int_x^{x+t}\mu(a)da}\right) w(x)dx = \\ &2g(t)\int_0^\infty w(x)dx - 2\int_0^\infty \mu(x+t)e^{-\int_x^{x+t}\mu(a)da} w(x)dx = \\ &2g(t)\left\|\sqrt{w(\cdot)}\right\|^2_{L^2[0,\infty]} - 2\left\langle \mu(\cdot+t)e^{-\int_\cdot^{\cdot+t}\mu(a)da}, w(\cdot)\right\rangle_{L^2[0,\infty]}. \end{aligned}$$

Thus

$$g(t) = \frac{\left\langle \mu(\cdot + t) e^{-\int_x^{x+t} \mu(a)da}, w(\cdot) \right\rangle_{L^2[0,\infty]}}{\left\| \sqrt{w(\cdot)} \right\|^2_{L^2[0,\infty]}} = \frac{\int\limits_0^\infty \mu(x+t) e^{-\int_x^{x+t} \mu(a)da} w(x) dx}{\int\limits_0^\infty w(x) dx}.$$

This allows to incorporate information about $I_0(x)$ into the calculation for $g(t)$. If we know for example the decay rate of $I_0(x)$ or, more generally, know that we can decompose $I_0(x) = w(x)l(x)$ with known $w(x)$ but unknown $l(x)$, the weight can be chosen accordingly. In particular, if we do know $I_0(x)$, choosing $w(x) = I_0(x)$ yields

$$g(t)I(0) = I(0) \frac{\int\limits_0^\infty \mu(x+t) e^{-\int_x^{x+t} \mu(a)da} I_0(x) dx}{\int\limits_0^\infty I_0(x) dx} = \int\limits_0^\infty \mu(x+t) e^{-\int_x^{x+t} \mu(a)da} I_0(x) dx$$

and will therefore produce the exact result.

To deal with the appearance of $I_0(\alpha)$ in the equation for $\dot{J}(t)$, we employ exactly the same line of reasoning to introduce a function $h(t)$ by

$$h(t) = \frac{\left\langle \left(i'(\cdot + t) - i(\cdot + t)\mu(\cdot + t)\right) e^{-\int_{\cdot}^{\cdot+t} \mu(a)da}, w(\cdot) \right\rangle_{L^2[0,\infty]}}{\left\| \sqrt{w(\cdot)} \right\|^2_{L^2[0,\infty]}} =$$

$$\frac{\int\limits_0^\infty \left(i'(x+t) - i(x+t)\mu(x+t)\right) e^{-\int_x^{x+t} \mu(a)da} w(x)}{\int\limits_0^\infty w(x) dx}.$$

The resulting system is

$$
\begin{aligned}
\dot{S}(t) &= -\sigma\frac{J(t)}{S(t)+I(t)}S(t)+\lambda(S,I)S(t)+\epsilon\eta(S,I)I(t),\\
\dot{I}(t) &= \sigma\frac{J(t)}{S(t)+I(t)}S(t)+(1-\epsilon)\eta(S,I)I(t)-\\
&\quad \int_0^t \mu(t-x)e^{-\int_0^{t-x}\mu(a)da}\left(\sigma\frac{J(x)}{S(x)+I(x)}S(x)+(1-\epsilon)\eta(S,I)I(x)\right)dx-\\
&\quad \frac{I(0)}{\int_0^\infty w(x)dx}\int_0^\infty \mu(x+t)e^{-\int_x^{x+t}\mu(a)da}w(x)dx,\\
\dot{J}(t) &= i(0)\left(\sigma\frac{J(t)}{S(t)+I(t)}S(t)+(1-\epsilon)\eta(S,I)I(t)\right)+\\
&\quad \int_0^t (i'(t-x)-i(t-x)\mu(t-x))e^{-\int_0^{t-x}\mu(a)da}\left(\sigma\frac{J(x)}{S(x)+I(x)}S(x)+(1-\epsilon)\eta(S,I)I(x)\right)dx+\\
&\quad \frac{I(0)}{\int_0^\infty w(x)dx}\int_0^\infty (i'(x+t)-i(x+t)\mu(x+t))e^{-\int_x^{x+t}\mu(a)da}w(x)dx.
\end{aligned}
$$

If we scale $w(x)$ such that $\int_0^\infty w(x)dx = I(0)$ this reduces to simply replacing $I_0(x)$ with $w(x)$. The above considerations show that this obvious step is in a certain sense also the best possible action to take.

A seemingly different way of defining $g(t)$ can also be derived from the above considerations. It is reasonable to assume that $I_0(x)$ has bounded support, i.e. $I_0(x) = 0$ for $x \geq T$. If we know T (or treat is as a parameter to be found), the term we want to minimize is $\left\| g(t) - \mu(\cdot+t)e^{-\int_\cdot^{\cdot+t}\mu(a)da}\right\|_{L^2[0,T]}$. As the above equations show, this is achieved by defining $g(t)$ as the root of $f(s) = \int_0^T s - \mu(x+t)e^{-\int_x^{x+t}\mu(a)da}dx$. This gives

$$g(t) = \frac{1}{T}\int_0^T \mu(x+t)e^{-\int_x^{x+t}\mu(a)da}dx,$$

which yields the system

$$
\begin{aligned}
\dot{S}(t) &= -\sigma \frac{J(t)}{S(t)+I(t)} S(t) + \lambda(S,I)S(t) + \epsilon\eta(S,I)I(t), \\
\dot{I}(t) &= \sigma \frac{J(t)}{S(t)+I(t)} S(t) + (1-\epsilon)\eta(S,I)I(t) - \\
&\quad \int_0^t \mu(t-x)e^{-\int_0^{t-x}\mu(a)da}\left(\sigma \frac{J(x)}{S(x)+I(x)} S(x) + (1-\epsilon)\eta(S,I)I(x)\right) dx - \\
&\quad \frac{I(0)}{T}\int_0^T \mu(x+t)e^{-\int_x^{x+t}\mu(a)da} dx, \\
\dot{J}(t) &= i(0)\left(\sigma \frac{J(t)}{S(t)+I(t)} S(t) + (1-\epsilon)\eta(S,I)I(t)\right) + \\
&\quad \int_0^t (i'(t-x) - i(t-x)\mu(t-x))e^{-\int_0^{t-x}\mu(a)da}\left(\sigma \frac{J(x)}{S(x)+I(x)} S(x) + (1-\epsilon)\eta(S,I)I(x)\right) dx + \\
&\quad \frac{I(0)}{T}\int_0^T (i'(x+t) - i(x+t)\mu(x+t))e^{-\int_x^{x+t}\mu(a)da} dx.
\end{aligned}
$$

This coincides with the previous system and the choice of $w(x) = \chi_{[0,T]}(x)$, where $\chi_{[0,T]}(x)$ denotes the characteristic function of the set $[0,T]$.

3 A static heterogeneity

A different way of introducing heterogeneity into the original system is to divide the population according to some traits like genetic markers, natural resistance towards a disease, or social behaviour that influences the spreading of disease.

We assume that every individual has a trait $\omega \in \Omega$ that influences the risk of an individual by a factor $p(\omega)$ or $q(\omega)$ for susceptible or infected individuals respectively. This turns the original model into (see again [10])

$$
\begin{aligned}
\dot{\bar{S}}(t,\omega) &= -\sigma p(\omega)\frac{J(t)}{R(t)+J(t)}\bar{S}(t,\omega) + \lambda(S,I)\bar{S}(t,\omega) + \gamma(S,I)\frac{I(t)}{S(t)}\bar{S}(t,\omega), \quad \bar{S}(0,\omega) = S_0(\omega), \\
\dot{\bar{I}}(t,\omega) &= \sigma p(\omega)\frac{J(t)}{R(t)+J(t)}\bar{S}(t,\omega) - \delta(S,I)\bar{I}(t,\omega), \quad \bar{I}(0,\omega) = I_0(\omega),
\end{aligned}
$$

where

$$\begin{aligned}
S(t) &= \int_{\Omega} \bar{S}(t,\omega)d\omega, \\
I(t) &= \int_{\Omega} \bar{I}(t,\omega)d\omega, \\
R(t) &= \int_{\Omega} p(\omega)\bar{S}(t,\omega)d\omega, \\
J(t) &= \int_{\Omega} q(\omega)\bar{I}(t,\omega)d\omega.
\end{aligned}$$

Again our lack of knowledge about the initial conditions $S_0(\omega)$ and $I_0(\omega)$ and the inability to measure $S(t,\omega)$ or $I(t,\omega)$ at any subsequent point in time forces us again to reduce this infinite dimensional system to one containing only the quantities $S(t)$, $I(t)$, $R(t)$, and $J(t)$. In order to do so we first consider a more general problem.

3.1 A general solution

The theorem we prove in this section is a generalization of a theorem presented in [5].
We consider a system of the Form

$$\begin{aligned}
\frac{d}{dt}n_1(t,a) &= n_1(t,a)F_1(t,a), \\
\frac{d}{dt}n_2(t,a) &= n_2(t,a)F_2(t,a) + n_1(t,a)F_3(t,a).
\end{aligned} \tag{1}$$

The functions F_1, F_2, F_3 on the right hand side have the form

$$\begin{aligned}
F_1(t,a) &= \sum_{i=1}^{n} u_i(t, G^1_{\tau^1_1}(t), \ldots, G^1_{\tau^1_{a_1}}(t), G^2_{\kappa^1_1}(t), \ldots, G^2_{\kappa^1_{b_1}}(t))\phi_i(a), \\
F_2(t,a) &= \sum_{j=1}^{m} v_j(t, G^1_{\tau^2_1}(t), \ldots, G^1_{\tau^2_{a_2}}(t), G^2_{\kappa^2_1}(t), \ldots, G^2_{\kappa^2_{b_2}}(t))\phi_j(a), \\
F_3(t,a) &= \sum_{k=1}^{o} w_k(t, G^1_{\tau^3_1}(t), \ldots, G^1_{\tau^3_{a_3}}(t), G^2_{\kappa^3_1}(t), \ldots, G^2_{\kappa^3_{b_3}}(t))\phi_k(a).
\end{aligned}$$

Here, all functions $u_i, v_j, w_k, \phi_i, \phi_j, \phi_k$ are given, while a function $G^j_i(t)$ is defined by

$$G^j_i(t) = \int_A g_i(a)n_j(t,a)da,$$

where g_i is a given function.
For $d = 1, 2$ define

$$N_d(t) = \int_A n_d(t,a)da,$$

and

$$P_d(t,a) = \frac{n_d(t,a)}{N_d(t)}.$$

Further, define the generating functionals

$$\Phi_1(r,\lambda) = \int_A r(a) \exp(\sum_{i=1}^{n} \lambda_i \phi_i(a)) P_1(0,a) da$$

and

$$\Phi_2(r,\lambda) = \int_A r(a) \exp(\sum_{j=1}^{m} \lambda_j \phi_j(a)) P_2(0,a) da,$$

where $r(a)$ is measurable function on A and λ is vector of appropriate length.

Define auxiliary variables as solutions to the system of differential equations

$$\begin{aligned}
&\frac{d}{dt} q_{1,i}(t) = u_i(t, G^{1^*}_{\tau^1_1}(t), \ldots, G^{1^*}_{\tau^1_{a_1}}(t), G^{2^*}_{\kappa^1_1}(t), \ldots, G^{2^*}_{\kappa^1_{b_1}}(t)), \quad q_{1,i}(0) = 0,\ i = 1, \ldots, n, \\
&\frac{d}{dt} q_{2,j}(t) = v_j(t, G^{1^*}_{\tau^2_1}(t), \ldots, G^{1^*}_{\tau^2_{a_2}}(t), G^{2^*}_{\kappa^2_1}(t), \ldots, G^{2^*}_{\kappa^2_{b_2}}(t)), \quad q_{2,j}(0) = 0,\ j = 1, \ldots, m, \\
&\frac{d}{dt} q_{3,k}(t) = w_k(t, G^{1^*}_{\tau^3_1}(t), \ldots, G^{1^*}_{\tau^3_{a_3}}(t), G^{2^*}_{\kappa^3_1}(t), \ldots, G^{2^*}_{\kappa^3_{b_3}}(t)), \quad q_{3,k}(0) = 0,\ k = 1, \ldots, o, \\
&\frac{d}{dt} M(t,a) = \frac{F_3^*(t,a)}{K_3(t,a)} - M(t,a)\left(F_1^*(t,a) + F_3^*(t,a) - F_2^*(t,a)\right), \quad M(0,a) = 0.
\end{aligned} \tag{2}$$

Here, $G^{i^*}_j$ is defined by

$$\begin{aligned}
G^{1^*}_i(t) &= N_1(0)\Phi_1(g_i, q_1(t)), \\
G^{2^*}_i(t) &= N_2(0)\Phi_2(g_i, q_2(t)) + \int_A g_i(a) K_1(t,a) K_3(t,a) M(t,a) n_1(0,a) da,
\end{aligned}$$

the $K_j(t,a)$ are defined by

$$\begin{aligned}
K_1(t,a) &= \exp\left(\sum_{i=1}^{n} q_{1,i}(t)\phi_i(a)\right), \\
K_2(t,a) &= \exp\left(\sum_{j=1}^{m} q_{2,j}(t)\phi_j(a)\right), \\
K_3(t,a) &= \exp\left(\sum_{k=1}^{o} q_{3,k}(t)\phi_k(a)\right),
\end{aligned}$$

and the $F_j^*(t,a)$ denote the functions

$$
\begin{aligned}
F_1^*(t,a) &= \sum_{i=1}^{n} u_i(t, G_{\tau_1^1}^{1^*}(t), \ldots, G_{\tau_{a_1}^1}^{1^*}(t), G_{\kappa_1^1}^{2^*}(t), \ldots, G_{\kappa_{b_1}^1}^{2^*}(t))\phi_i(a), \\
F_2^*(t,a) &= \sum_{j=1}^{m} v_j(t, G_{\tau_1^2}^{1^*}(t), \ldots, G_{\tau_{a_2}^2}^{1^*}(t), G_{\kappa_1^2}^{2^*}(t), \ldots, G_{\kappa_{b_2}^2}^{2^*}(t))\phi_j(a), \\
F_3^*(t,a) &= \sum_{k=1}^{o} w_k(t, G_{\tau_1^3}^{1^*}(t), \ldots, G_{\tau_{a_3}^3}^{1^*}(t), G_{\kappa_1^3}^{2^*}(t), \ldots, G_{\kappa_{b_3}^3}^{2^*}(t))\phi_k(a).
\end{aligned}
$$

Theorem 1 *For $0 < T < \infty$, let $\{q_1(t), q_2(t), q_3(t), M(t,a)\}$ be a unique solution to (2) at $t \in [0,T)$. Then the functions*

$$
\begin{aligned}
n_1(t,a) &= n_1(0,a)K_1(t,a), \\
n_2(t,a) &= n_2(0,a)K_2(t,a) + n_1(0,a)K_1(t,a)K_3(t,a)M(t,a), \\
G_i^j(t) &= G_i^{j^*}(t),
\end{aligned}
$$

solve (1) at t. Conversely, if $\{n_1(t,a), n_2(t,a), G_i^j(t)\}$ is a solution of (1) at $t \in [0,T)$, then (2) has a solution at t and n_1, n_2, and G_i^j can be written as above.

Proof: First, we see that both

$$
G_i^1(t) = \int_A g_i(a)n_1(t,a)da = \int_A g_i(a)n_1(0,a)K_1(t,a)da = N_1(0)\Phi_1(g_i, q_1(t)) = G_i^{1^*}(t)
$$

and

$$
\begin{aligned}
G_i^2(t) &= \int_A g_i(a)n_2(t,a)da = \\
&\int_A g_i(a)n_2(0,a)K_2(t,a)da + \int_A g_i(a)n_1(0,a)K_1(t,a)K_3(t,a)M(t,a)da = G_i^{2^*}(t)
\end{aligned}
$$

hold true, so the definition of the $G_i^j(t)$ is consistent.
Consequently, we get

$$
\frac{d}{dt}n_1(t,a) = n_1(0,a)\frac{d}{dt}K_1(t,a) = n_1(0,a)K_1(t,a)\sum_{i=1}^{n}\frac{d}{dt}q_{1,i}(t)\phi_i(a) = n_1(t,a)F_1(t,a)
$$

and

$$\begin{aligned}
\frac{d}{dt}n_2(t,a) &= n_2(0,a)\frac{d}{dt}K_2(t,a) + n_1(0,a)\frac{d}{dt}\left(K_1(t,a)K_3(t,a)M(t,a)\right) = \\
&n_2(0,a)K_2(t,a)F_2(t,a) + n_1(0,a) * \\
&\left(\frac{d}{dt}K_1(t,a)K_3(t,a)M(t,a) + K_1(t,a)\frac{d}{dt}K_3(t,a)M(t,a) + K_1(t,a)K_3(t,a)\frac{d}{dt}M(t,a)\right) = \\
&n_2(0,a)K_2(t,a)F_2(t,a) + n_1(0,a)K_1(t,a) * \\
&\Big(F_1(t,a)K_3(t,a)M(t,a) + K_3(t,a)F_3(t,a)M(t,a) + \\
&K_3(t,a)\left(\frac{F_3(t,a)}{K_3(t,a)} - M(t,a)(F_1(t,a) + F_3(t,a) - F_2(t,a))\right)\Big) = \\
&n_2(0,a)K_2(t,a)F_2(t,a) + n_1(0,a)K_1(t,a)\left(F_3(t,a) + K_3(t,a)F_2(t,a)M(t,a)\right) = \\
&(n_2(0,a)K_2(t,a) + n_1(0,a)K_1(t,a)K_3(t,a)M(t,a))F_2(t,a) + n_1(0,a)K_1(t,a)F_3(t,a) = \\
&n_2(t,a)F_2(t,a) + n_1(t,a)F_3(t,a).
\end{aligned}$$

Conversely, suppose $n_1(t,a)$ satisfies (1). Define

$$q^*_{1,i}(t) = \int_0^t u_i(\theta, G^1_{\tau^1_1}(\theta), \ldots, G^1_{\tau^1_{a_1}}(\theta), G^2_{\kappa^1_1}(\theta), \ldots, G^2_{\kappa^1_{b_1}}(\theta))d\theta$$

and

$$K_1(t,a) = \exp\left(\sum_{i=1}^n q^*_{1,i}(t)\phi_i(a)\right).$$

Now consider

$$\begin{aligned}
\frac{d}{dt}\left(n_1(t,a) - n(0,a)K_1(t,a)\right) &= n_1(t,a)F_1(t,a) - n_1(0,a)K_1(t,a)F_1(t,a) = \\
&\left(n_1(t,a) - n(0,a)K_1(t,a)\right)F_1(t,a).
\end{aligned}$$

This differential equation has the solution

$$n_1(t,a) - n(0,a)K_1(t,a) = c\exp\left(\int_0^t F_1(\theta,a)d\theta\right).$$

Evaluating this equation at $t = 0$ yields $c = 0$, i.e.

$$n_1(t,a) = n_1(0,a)K_1(t,a).$$

Furthermore, we have

$$G^1_i(t) = \int_A g_i(a)n_1(t,a)da = \int_A g_i(a)n_1(0,a)K_1(t,a)da = N_1(0)\Phi_1(g_i, q_1(t)) = G^{1^*}_i(t)$$

Similarly, define

$$
\begin{aligned}
q_{2,j}^* &= \int_0^t v_j(\theta, G^1_{\tau_1^2}(\theta), \ldots, G^1_{\tau_{a_2}^2}(\theta), G^2_{\kappa_1^2}(\theta), \ldots, G^2_{\kappa_{b_2}^2}(\theta))d\theta, \\
q_{3,k}^* &= \int_0^t w_k(\theta, G^1_{\tau_1^3}(\theta), \ldots, G^1_{\tau_{a_3}^3}(\theta), G^2_{\kappa_1^3}(\theta), \ldots, G^2_{\kappa_{b_3}^3}(\theta))d\theta, \\
K_2(t,a) &= \exp\left(\sum_{j=1}^{m} q_{2,j}^*(t)\phi_j(a)\right), \\
K_3(t,a) &= \exp\left(\sum_{k=1}^{o} q_{3,k}^*(t)\phi_k(a)\right),
\end{aligned}
$$

and $M(t,a)$ with

$$
\frac{d}{dt}M(t,a) = \frac{F_3(t,a)}{K_3(t,a)} - M(t,a)(F_1(t,a) + F_3(t,a) - F_2(t,a)), \quad M(0,a) = 0.
$$

Then for $n_2(t,a)$ satisfying (1) we get

$$
\begin{aligned}
&\frac{d}{dt}(n_2(t,a) - n_2(0,a)K_2(t,a) - n_1(0,a)K_1(t,a)K_3(t,a)M(t,a)) = \\
&n_2(t,a)F_2(t,a) + n_1(t,a)F_3(t,a) - n_2(0,a)K_2(t,a)F_2(t,a) - \\
&\qquad n_1(0,a)K_1(t,a)F_3(t,a) - n_1(0,a)K_1(t,a)K_3(t,a)F_2(t,a)M(t,a) = \\
&(n_2(t,a) - n_2(0,a)K_2(t,a) - n_1(0,a)K_1(t,a)K_3(t,a)M(t,a))F_2(t,a),
\end{aligned}
$$

since we already know, that $n_1(t,a) = n_1(0,a)K_1(t,a)$. As above this yields

$$
n_2(t,a) = n_2(0,a)K_2(t,a) + n_1(0,a)K_1(t,a)K_3(t,a)M(t,a),
$$

and also $G_i^2(t) = G_i^{2^*}(t)$.

$\square$

3.2 Reducing the system

We return to the model

$$
\begin{aligned}
\dot{\bar{S}}(t,\omega) &= -\sigma p(\omega)\frac{J(t)}{R(t)+J(t)}\bar{S}(t,\omega) + \lambda(S,I)\bar{S}(t,\omega) + \gamma(S,I)\frac{I(t)}{S(t)}\bar{S}(t,\omega), \\
\dot{\bar{I}}(t,\omega) &= \sigma p(\omega)\frac{J(t)}{R(t)+J(t)}\bar{S}(t,\omega) - \delta(S,I)\bar{I}(t,\omega),
\end{aligned}
$$

where

$$\begin{aligned}
S(t) &= \int_\Omega \bar{S}(t,\omega)d\omega, \\
I(t) &= \int_\Omega \bar{I}(t,\omega)d\omega, \\
R(t) &= \int_\Omega p(\omega)\bar{S}(t,\omega)d\omega, \\
J(t) &= \int_\Omega q(\omega)\bar{I}(t,\omega)d\omega.
\end{aligned}$$

We set

$$\begin{aligned}
u_1(S,I,R,J) &= -\sigma\frac{J(t)}{R(t)+J(t)}, \\
u_2(S,I,R,J) &= \lambda(S,I)+\gamma(S,I)\frac{I(t)}{S(t)}, \\
v(S,I,R,J) &= -\delta(S,I), \\
w(S,I,R,J) &= \sigma\frac{J(t)}{R(t)+J(t)},
\end{aligned}$$

then

$$\begin{aligned}
\dot{\bar{S}}(t,\omega) &= \bar{S}(t,\omega)\left(u_1(S,I,R,J)p(\omega)+u_2(S,I,R,J)\right), \\
\dot{\bar{I}}(t,\omega) &= \bar{I}(t,\omega)v(S,I,R,J)+\bar{S}(t,\omega)w(S,I,R,J)p(\omega).
\end{aligned}$$

Define

$$\begin{aligned}
\frac{d}{dt}q_{1,1}(t) &= u_1(S^*,I^*,R^*,J^*), \quad q_{1,1}(0)=0, \\
\frac{d}{dt}q_{1,2}(t) &= u_2(S^*,I^*,R^*,J^*), \quad q_{1,2}(0)=0, \\
\frac{d}{dt}q_2(t) &= v(S^*,I^*,R^*,J^*), \quad q_2(0)=0, \\
\frac{d}{dt}q_3(t) &= w(S^*,I^*,R^*,J^*), \quad q_3(0)=0, \\
\frac{d}{dt}M(t,\omega) &= \frac{w(S^*,I^*,R^*,J^*)p(\omega)}{\exp\left(q_3(t)p(\omega)\right)} - M(t,\omega)\left(u_2(S^*,I^*,R^*,J^*)-v(S^*,I^*,R^*,J^*)\right), \quad M(0,\omega)=0,
\end{aligned}$$

with

$$\begin{aligned}
S^*(t) &= \int_\Omega \exp\left(q_{1,1}(t)p(\omega) + q_{1,2}(t)\right) \bar{S}(0,\omega)d\omega, \\
I^*(t) &= \int_\Omega \exp\left(q_2(t)\right) \bar{I}(0,\omega)d\omega + \int_\Omega \exp(q_{1,1}(t)p(\omega) + q_{1,2}(t) + q_3(t)p(\omega))M(t,\omega)\bar{S}(0,\omega)d\omega, \\
R^*(t) &= \int_\Omega p(\omega)\exp\left(q_{1,1}(t)p(\omega) + q_{1,2}(t)\right) \bar{S}(0,\omega)d\omega, \\
J^*(t) &= \int_\Omega q(\omega)\exp\left(q_2(t)\right) \bar{I}(0,\omega)d\omega + \\
&\qquad \int_\Omega q(\omega)\exp(q_{1,1}(t)p(\omega) + q_{1,2}(t) + q_3(t)p(\omega))M(t,\omega)\bar{S}(0,\omega)d\omega.
\end{aligned}$$

From Theorem 1 we know that

$$\begin{aligned}
\bar{S}(t,\omega) &= \bar{S}(0,\omega)\exp(q_{1,1}(t)p(\omega) + q_{1,2}(t)), \\
\bar{I}(t,\omega) &= \bar{I}(0,\omega)\exp(q_2(t)) + \bar{S}(0,\omega)\exp(q_{1,1}(t)p(\omega) + q_{1,2}(t) + q_3(t)p(\omega))M(t,\omega), \\
S(t) &= S^*(t), \\
I(t) &= I^*(t), \\
R(t) &= R^*(t), \\
J(t) &= J^*(t),
\end{aligned}$$

is a solution of the system. Differentiating $S(t)$ and $I(t)$ to get differential equations for them yields

$$\begin{aligned}
\dot{S}(t) &= u_1(S,I,R,J)\int_\Omega p(\omega)\exp\left(\int_0^t u_1(S,I,R,J)d\tau p(\omega) + \int_0^t u_2(S,I,R,J)d\tau\right)\bar{S}(0,\omega)d\omega + \\
&\qquad u_2(S,I,R,J)S(t), \\
\dot{I}(t) &= v(S,I,R,J)I(t) - \\
&\qquad u_1(S,I,R,J)\int_\Omega p(\omega)\exp\left(\int_0^t u_1(S,I,R,J)d\tau p(\omega) + \int_0^t u_2(S,I,R,J)d\tau\right)\bar{S}(0,\omega)d\omega.
\end{aligned}$$

Seeing that

$$\begin{aligned}
R(t) &= \int_\Omega p(\omega)\bar{S}(t,\omega)d\omega = \int_\Omega p(\omega)\bar{S}(0,\omega)\exp(q_{1,1}(t)p(\omega) + q_{1,2}(t))d\omega = \\
&\int_\Omega p(\omega)\exp\left(\int_0^t u_1(S,I,R,J)d\tau p(\omega) + \int_0^t u_2(S,I,R,J)d\tau\right)\bar{S}(0,\omega)d\omega,
\end{aligned}$$

we get

$$\begin{aligned}
\dot{S}(t) &= u_1(S,I,R,J)R(t) + u_2(S,I,R,J)S(t), \\
\dot{I}(t) &= v(S,I,R,J)I(t) - u_1(S,I,R,J)R(t).
\end{aligned}$$

Doing the same for $R(t)$ and $J(t)$ gives the equations

$$\begin{aligned}
\frac{d}{dt}R(t) &= \frac{d}{dt}\int_\Omega p(\omega)\bar{S}(t,\omega)d\omega = \frac{d}{dt}\int_\Omega p(\omega)\bar{S}(0,\omega)\exp(q_{1,1}(t)p(\omega)+q_{1,2}(t))d\omega = \\
&\int_\Omega p(\omega)\exp(q_{1,1}(t)p(\omega)+q_{1,2}(t))\left(\frac{d}{dt}q_{1,1}(t)p(\omega)+\frac{d}{dt}q_{1,2}(t)\right)\bar{S}(0,\omega)d\omega = \\
&u_1(S,I,R,J)\int_\Omega (p(\omega))^2\exp\left(\int_0^t u_1(S,I,R,J)d\tau p(\omega)+\int_0^t u_2(S,I,R,J)d\tau\right)\bar{S}(0,\omega)d\omega + \\
&\quad u_2(S,I,R,J)\int_\Omega p(\omega)\exp\left(\int_0^t u_1(S,I,R,J)d\tau p(\omega)+\int_0^t u_2(S,I,R,J)d\tau\right)\bar{S}(0,\omega)d\omega = \\
&u_1(S,I,R,J)\int_\Omega (p(\omega))^2\exp\left(\int_0^t u_1(S,I,R,J)d\tau p(\omega)+\int_0^t u_2(S,I,R,J)d\tau\right)\bar{S}(0,\omega)d\omega + \\
&\qquad u_2(S,I,R,J)R(t)
\end{aligned}$$

and

$$\begin{aligned}
\frac{d}{dt}J(t) &= \frac{d}{dt}\int_\Omega q(\omega)\bar{I}(t,\omega)d\omega = \\
&\frac{d}{dt}\int_\Omega q(\omega)\left(\bar{I}(0,\omega)\exp(q_2(t))+\bar{S}(0,\omega)\exp(q_{1,1}(t)p(\omega)+q_{1,2}(t)+q_3(t)p(\omega))M(t,\omega)\right)d\omega = \\
&\int_\Omega q(\omega)\exp\left(\int_0^t v(S,I,R,J)\tau\right)\bar{I}(0,\omega)v(S,I,R,J)d\omega + \\
&\quad\int_\Omega q(\omega)\exp\left(\int_0^t u_1(S,I,R,J)d\tau p(\omega)+\int_0^t u_2(S,I,R,J)d\tau\right)w(S,I,R,J)p(\omega)\bar{S}(0,\omega)d\omega + \\
&\quad\int_\Omega q(\omega)\exp\left(\int_0^t u_1(S,I,R,J)d\tau p(\omega)+\int_0^t u_2(S,I,R,J)d\tau+\int_0^t w(S,I,R,J)d\tau p(\omega)\right) * \\
&\qquad v(S,I,R,J)M(t,a)\bar{S}(0,\omega)d\omega = \\
&w(S,I,R,J)\int_\Omega q(\omega)p(\omega)\exp\left(\int_0^t u_1(S,I,R,J)d\tau p(\omega)+\int_0^t u_2(S,I,R,J)d\tau\right)\bar{S}(0,\omega)d\omega + \\
&\qquad v(S,I,R,J)J(t),
\end{aligned}$$

since

$$\begin{aligned}
J(t) &= \int_\Omega q(\omega)\exp\left(\int_0^t v(S,I,R,J)\tau\right)\bar{I}(0,\omega)d\omega + \\
&\int_\Omega q(\omega)\exp\left(\int_0^t u_1(S,I,R,J)d\tau p(\omega)+\int_0^t u_2(S,I,R,J)d\tau+\int_0^t w(S,I,R,J)d\tau p(\omega)\right) * \\
&\quad M(t,a)\bar{S}(0,\omega)d\omega.
\end{aligned}$$

Thus we get the closed system

$$\begin{aligned}
\dot{S}(t) &= u_1(S,I,R,J)R(t) + u_2(S,I,R,J)S(t),\\
\dot{I}(t) &= v(S,I,R,J)I(t) - u_1(S,I,R,J)R(t),\\
\dot{R}(t) &= u_2(S,I,R,J)R(t) +\\
&\quad u_1(S,I,R,J)\int_\Omega (p(\omega))^2 \exp\left(\int_0^t u_1(S,I,R,J)d\tau p(\omega) + \int_0^t u_2(S,I,R,J)d\tau\right)\bar{S}(0,\omega)d\omega,\\
\dot{J}(t) &= v(S,I,R,J)J(t) +\\
&\quad w(S,I,R,J)\int_\Omega q(\omega)p(\omega) \exp\left(\int_0^t u_1(S,I,R,J)d\tau p(\omega) + \int_0^t u_2(S,I,R,J)d\tau\right)\bar{S}(0,\omega)d\omega,
\end{aligned}$$

where $S(0)$, $I(0)$, $R(0)$, $J(0)$, $S(0,\omega)$, $p(\omega)$, and $q(\omega)$ need to be given.
Substituting the terms u_1, u_2, v, and w to apply to our specific model we get

$$\begin{aligned}
\dot{S}(t) &= -\sigma\frac{J(t)}{R(t)+J(t)}R(t) + \left(\lambda(S,I) + \gamma(S,I)\frac{I(t)}{S(t)}\right)S(t),\\
\dot{I}(t) &= -\delta(S,I)I(t) + \sigma\frac{J(t)}{R(t)+J(t)}R(t),\\
\dot{R}(t) &= \left(\lambda(S,I) + \gamma(S,I)\frac{I(t)}{S(t)}\right)R(t) - \sigma\frac{J(t)}{R(t)+J(t)}e^{\int_0^t \lambda(S,I)+\gamma(S,I)\frac{I(\tau)}{S(\tau)}d\tau} *\\
&\qquad \int_\Omega (p(\omega))^2 e^{-\int_0^t \sigma\frac{J(\tau)}{R(\tau)+J(\tau)}d\tau p(\omega)} S_0(\omega)d\omega,\\
\dot{J}(t) &= -\delta(S,I)J(t) + \sigma\frac{J(t)}{R(t)+J(t)}e^{\int_0^t \lambda(S,I)+\gamma(S,I)\frac{I(\tau)}{S(\tau)}d\tau}\int_\Omega q(\omega)p(\omega)e^{-\int_0^t \sigma\frac{J(\tau)}{R(\tau)+J(\tau)}d\tau p(\omega)} S_0(\omega)d\omega.
\end{aligned}$$

3.3 Comparison between models

We again want to show how this model reduces to the original model if we get rid of the heterogeneity. So we will assume that $p(\omega) = p$ and $q(\omega) = q$ are constant.
In this case the equation for $R(t)$ can be written as

$$\dot{R}(t) = \left(\lambda(S,I) + \gamma(S,I)\frac{I(t)}{S(t)}\right)R(t) - \sigma\frac{J(t)}{R(t)+J(t)}e^{\int_0^t -\sigma\frac{J(\tau)}{R(\tau)+J(\tau)}p + \lambda(S,I)+\gamma(S,I)\frac{I(\tau)}{S(\tau)}d\tau}p^2\int_\Omega S_0(\omega)d\omega.$$

Noting that we can write

$$p\int_\Omega S_0(\omega)d\omega = \int_\Omega pS_0(\omega)d\omega = R(0),$$

and also know that

$$R(t) = R(0)e^{\int_0^t -\sigma\frac{J(\tau)}{R(\tau)+J(\tau)}p + \lambda(S,I)+\gamma(S,I)\frac{I(\tau)}{S(\tau)}d\tau},$$

this can be written as

$$\dot{R}(t) = \left(\lambda(S,I) + \gamma(S,I)\frac{I(t)}{S(t)}\right)R(t) - \sigma\frac{J(t)}{R(t)+J(t)}pR(t).$$

Define $f(t) = pS(t) - R(t)$. Obviously we have $f(0) = 0$. For the derivative we get

$$\frac{d}{dt}f(t) = p\dot{S}(t) - \dot{R}(t) = \left(\lambda(S,I) + \gamma(S,I)\frac{I(t)}{S(t)}\right)(pS(t) - R(t)) = \left(\lambda(S,I) + \gamma(S,I)\frac{I(t)}{S(t)}\right)f(t),$$

which shows that

$$f(t) = ce^{\int_0^t \lambda(S,I)+\gamma(S,I)\frac{I(\tau)}{S(\tau)}d\tau}.$$

Since $f(0) = 0$, we have $c = 0$, i.e. $R(t) = pS(t)$.
Completely analogous reasoning shows that $J(t) = qI(t)$. This leads to the system

$$\begin{aligned}
\dot{S}(t) &= -\sigma\frac{qI(t)}{pS(t)+qI(t)}pS(t) + \left(\lambda(S,I) + \gamma(S,I)\frac{I(t)}{S(t)}\right)S(t),\\
\dot{I}(t) &= -\delta(S,I)I(t) + \sigma\frac{qI(t)}{pS(t)+qI(t)}pS(t).
\end{aligned}$$

In particular, if $p = q = 1$ the resulting system is exactly the original one. Also, if $p = q$ the resulting system is

$$\begin{aligned}
\dot{S}(t) &= -\sigma p\frac{I(t)}{S(t)+I(t)}S(t) + \left(\lambda(S,I) + \gamma(S,I)\frac{I(t)}{S(t)}\right)S(t),\\
\dot{I}(t) &= -\delta(S,I)I(t) + \sigma p\frac{I(t)}{S(t)+I(t)}S(t),
\end{aligned}$$

which is again exactly the original model if we incorporate the constant p into the constant σ.

3.4 Eliminating the initial data

One way to deal with the unknown function $S_0(\omega)$ is to repeat everything we did in section 2.3 to reach the same conclusions as before.
Under two additional assumptions however, we are able to simplify the model even further. We will therefore assume

1. $p(\omega)$ and $q(\omega)$ are linear functions of ω,
2. $f(\omega) = \frac{S_0(\omega)}{S(0)}$ is the probability density function of a generalized inverse Gaussian distribution.

ad 1.) We will restrict ourselves to the case $p(\omega) = \omega$ and $q(\omega) = \kappa\omega$ for some $\kappa \in \mathbb{R}$. Letting $p(\omega)$ and $q(\omega)$ take a more general form would only complicate notation. Furthermore, every important aspect of the calculation is already included when considering this easy functional form.
ad 2.) Since the integral over $\frac{S_0(\omega)}{S(0)}$ is 1 we can treat it as a probability density function $f(\omega)$. This can be interpreted as the distribution of the trait ω amongst the initial susceptible population

$S(0)$. The generalized inverse Gaussian distribution is a distribution with three parameters $a > 0$, $b > 0$, and $p \in \mathbb{R}$. Its probability density function is

$$f(\omega) = \frac{\left(\frac{a}{b}\right)^{\frac{p}{2}}}{2K_p(\sqrt{ab})}\omega^{p-1}e^{-\frac{a\omega}{2}-\frac{b}{2\omega}}$$

with parameters a, b, and p, where K_p is the modified Bessel function of second kind, i.e.

$$\begin{aligned} I_\alpha(x) &= \sum_{m=0}^{\infty}\frac{1}{m!\Gamma(m+\alpha+1)}\left(\frac{x}{2}\right)^{2m+\alpha}, \\ K_\alpha(x) &= \frac{\pi}{2}\frac{I_{-\alpha}(x)-I_\alpha(x)}{\sin(\alpha\pi)}. \end{aligned}$$

The moments of a generalized inverse Gaussian with parameters a, b, and p are given by

$$\mathbb{E}[\omega^n] = \left(\frac{b}{a}\right)^{\frac{n}{2}}\frac{K_{p+n}(\sqrt{ab})}{K_p(\sqrt{ab})}.$$

The generalized inverse Gaussian is a very general distribution and includes for example the Wald and Gamma distributions as special or limit cases.

Using these two assumptions turns our system into

$$\begin{aligned} \dot{S}(t) &= -\sigma\frac{J(t)}{R(t)+J(t)}R(t) + \left(\lambda(S,I)+\gamma(S,I)\frac{I(t)}{S(t)}\right)S(t), \\ \dot{I}(t) &= -\delta(S,I)I(t) + \sigma\frac{J(t)}{R(t)+J(t)}R(t), \\ \dot{R}(t) &= \left(\lambda(S,I)+\gamma(S,I)\frac{I(t)}{S(t)}\right)R(t) - \sigma\frac{J(t)}{R(t)+J(t)}e^{\int_0^t \lambda(S,I)+\gamma(S,I)\frac{I(\tau)}{S(\tau)}d\tau}S(0)\int_\Omega \omega^2 e^{-\int_0^t \sigma\frac{J(\tau)}{R(\tau)+J(\tau)}d\tau\omega}f(\omega)d\omega, \\ \dot{J}(t) &= -\delta(S,I)J(t) + \sigma\frac{J(t)}{R(t)+J(t)}e^{\int_0^t \lambda(S,I)+\gamma(S,I)\frac{I(\tau)}{S(\tau)}d\tau}\kappa S(0)\int_\Omega \omega^2 e^{-\int_0^t \sigma\frac{J(\tau)}{R(\tau)+J(\tau)}d\tau\omega}f(\omega)d\omega. \end{aligned}$$

We will look more closely at the term

$$\int_\Omega \omega^2 e^{-\int_0^t \sigma\frac{J(\tau)}{R(\tau)+J(\tau)}d\tau\omega}f(\omega)d\omega.$$

We will abbreviate $c(t) = -\int_0^t \sigma \frac{J(\tau)}{R(\tau)+J(\tau)} d\tau$. It is now possible to rewrite

$$
\begin{aligned}
\int_\Omega \omega^2 e^{c(t)\omega} f(\omega) d\omega &= \int_\Omega \omega^2 e^{c(t)\omega} \frac{\left(\frac{a}{b}\right)^{\frac{p}{2}}}{2K_p(\sqrt{ab})} \omega^{p-1} e^{-\frac{a\omega}{2} - \frac{b}{2\omega}} d\omega = \\
& \int_\Omega \omega^2 \frac{\left(\frac{a}{b}\right)^{\frac{p}{2}}}{2K_p(\sqrt{ab})} \omega^{p-1} e^{\left(c(t) - \frac{a}{2}\right)\omega - \frac{b}{2\omega}} d\omega = \\
& \int_\Omega \omega^2 \frac{\left(\frac{a}{b}\right)^{\frac{p}{2}}}{2K_p(\sqrt{ab})} \omega^{p-1} e^{\frac{(2c(t)-a)\omega}{2} - \frac{b}{2\omega}} d\omega = \\
& \frac{a^{\frac{p}{2}} 2K_p(\sqrt{(a-2c(t))b})}{(a-2c(t))^{\frac{p}{2}} 2K_p(\sqrt{ab})} \int_\Omega \omega^2 \frac{\left(\frac{a-2c(t)}{b}\right)^{\frac{p}{2}}}{2K_p(\sqrt{(a-2c(t))b})} \omega^{p-1} e^{-\frac{(a-2c(t))\omega}{2} - \frac{b}{2\omega}} d\omega.
\end{aligned}
$$

We now see that the integral in the last term can be interpreted as the second moment of generalized inverse Gaussian distribution with the parameters $a - 2c(t)$, b, and p. We therefore get

$$
\begin{aligned}
\int_\Omega \omega^2 e^{c(t)\omega} f(\omega) d\omega &= \frac{a^{\frac{p}{2}} 2K_p(\sqrt{(a-2c(t))b})}{(a-2c(t))^{\frac{p}{2}} 2K_p(\sqrt{ab})} \frac{b}{a-2c(t)} \frac{K_{p+2}(\sqrt{(a-2c(t))b})}{K_p(\sqrt{(a-2c(t))b})} = \\
& \frac{a^{\frac{p}{2}} b}{(a-2c(t))^{\frac{p}{2}+1}} \frac{K_{p+2}(\sqrt{(a-2c(t))b})}{K_p(\sqrt{ab})}.
\end{aligned}
$$

Putting this in our model yields the following system

$$
\begin{aligned}
\dot{S}(t) &= -\sigma \frac{J(t)}{R(t)+J(t)} R(t) + \left(\lambda(S,I) + \gamma(S,I)\frac{I(t)}{S(t)}\right) S(t), \\
\dot{I}(t) &= -\delta(S,I) I(t) + \sigma \frac{J(t)}{R(t)+J(t)} R(t), \\
\dot{R}(t) &= \left(\lambda(S,I) + \gamma(S,I)\frac{I(t)}{S(t)}\right) R(t) - \sigma \frac{J(t)}{R(t)+J(t)} e^{\int_0^t \lambda(S,I)+\gamma(S,I)\frac{I(\tau)}{S(\tau)} d\tau} * \\
& \qquad S(0) \frac{a^{\frac{p}{2}} b}{\left(a + 2\int_0^t \sigma \frac{J(\tau)}{R(\tau)+J(\tau)} d\tau\right)^{\frac{p}{2}+1}} \frac{K_{p+2}\left(\sqrt{(a + 2\int_0^t \sigma \frac{J(\tau)}{R(\tau)+J(\tau)} d\tau) b}\right)}{K_p\left(\sqrt{ab}\right)}, \\
\dot{J}(t) &= -\delta(S,I) J(t) + \sigma \frac{J(t)}{R(t)+J(t)} e^{\int_0^t \lambda(S,I)+\gamma(S,I)\frac{I(\tau)}{S(\tau)} d\tau} * \\
& \qquad \kappa S(0) \frac{a^{\frac{p}{2}} b}{\left(a + 2\int_0^t \sigma \frac{J(\tau)}{R(\tau)+J(\tau)} d\tau\right)^{\frac{p}{2}+1}} \frac{K_{p+2}\left(\sqrt{(a + 2\int_0^t \sigma \frac{J(\tau)}{R(\tau)+J(\tau)} d\tau) b}\right)}{K_p\left(\sqrt{ab}\right)}.
\end{aligned}
$$

With the initial conditions $S(0)$ and $I(0)$ known, this model now only depends on the parameters a, b, and p as well as the initial condition for J (The value $R(0)$ can be calculated with the knowledge of a, b, and p).

References

[1] F.A.B.Coutinho, E.Massad, L.F.Lopez, M.N.Burattini: Modelling Heterogeneities in Individual Frailties in Epidemic Models, *Math. Comput. Model. 30 (1999)*, 97-115.

[2] J.Dushoff: Host heterogeneity and disease endemicity: A moment-based approach, *Theor. Popul. Biol. 56 (1999)*, 325-335.

[3] G.Feichtinger, T.Tsachev, V.Veliov: Maximum principle for age and duration structured systems: a tool for optimal prevention and treatment of HIV, *Math. Popul. Stud. 11(1) (2004)*, 3 - 28

[4] H.Inaba: Endemic threshold results in an age-duration-structured population model for HIV infection. *Math. Biosci. 201(1) (2006)*, 15-47.

[5] G.P.Karev: On mathematical theory of selection: continuous time population dynamics, *J. Math. Biol. 60 (2010)*, 107-129.

[6] G.P.Karev: Dynamics of Heterogeneous Populations and Communities and Evolution of Distributions, *Discrete Contin. Dyn. Sys. (2005)*, 487-496.

[7] G.P.Karev: Dynamics of inhomogeneous populations and global demography models, *J. Biol. Syst. 13(1) (2005)*, 83-104.

[8] M.Kretzschmar: Comparison of an infinite dimensional model for parasitic diseases with a related 2-dimensional system. *J. Math. Anal. Appl. 176.1 (1993)*, 235-260.

[9] A.S.Novozhilov: On the spread of epidemics in a closed heterogeneous population, *Math. Biosci. 215(2) (2008)*, 177-185.

[10] V.Veliov: On the effect of population heterogeneity on dynamics of epidemic diseases, *J. Math. Biol. 51 (2005)*, 123-143.