A MODEL OF INDIRECT EFFECT OF VACCINATION

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This paper presents a mathematical model to explain the rise in congenital rubella syndrome (CRS) cases following partial vaccination. Starting from the classical SIR model, we extend it by incorporating age structure using the McKendrick model and renewal theory. We derive an age-structured epidemic model with vaccination and define a reproduction number suited for this framework. Our analysis shows that insufficient vaccination shifts the average age of infection, increasing the risk to women of childbearing age.

MODEL POSREDNEGA UČINKA CEPLJENJA

V članku predstavimo matematični model, ki pojasni porast primerov kongenitalnega sindroma rdečk (CSR) po delnem cepljenju. Izhajamo iz klasičnega SIR-modela, ki ga razširimo z vpeljavo starostne strukture s pomočjo McKendrickovega modela in teorije obnove. Dobimo starostno strukturiran epidemiološki model s cepljenjem ter opredelimo reprodukcijsko število, prilagojeno temu okviru. Analiza pokaže, da nezadostna precepljenost pomakne povprečno starost okužbe navzgor in s tem poveča tveganje za ženske v rodni dobi.

1. Motivation

Rubella is a contagious viral infection that is typically mild in children and adults, but can have severe consequences for unborn children if a woman contracts the disease during pregnancy. In such cases, the virus can cause congenital rubella syndrome (CRS), which is associated with serious birth defects or miscarriage. For this reason, vaccination against rubella is a key public health strategy aimed at protecting not only individuals but also future generations.

However, vaccination efforts can sometimes lead to counterintuitive effects. A notable example occurred in Greece, where a mass vaccination campaign against rubella unexpectedly resulted in a higher number of CRS cases than before the campaign. Initially puzzling, this phenomenon was later linked to low vaccination coverage and a shift in the age of infection. Since children are often vaccinated for convenience – such as through school programs – the average age of infection can rise, increasing the risk for women of childbearing age.

The aim of this paper is to provide a mathematical explanation for this observed phenomenon. We begin by presenting the classical SIR (Susceptible-Infectious-Recovered) model, which forms the foundation of many epidemiological models. Since the risk of CRS is closely tied to maternal age at the time of infection, it is essential to account for the age structure of the population. We therefore introduce the theory of age-structured population models, which allows us to track how individuals of different ages move through the stages of infection and recovery.

We then integrate the SIR framework with age-structured dynamics to develop an age-structured epidemic model. This enriched model captures both the temporal spread of the disease and the demographic factors that influence infection risk. Finally, we apply this model to the case of rubella in Greece, offering a rigorous mathematical account of why partial vaccination can, under certain conditions, increase the number of CRS cases rather than reduce them.

2. Simple SIR model

Epidemic modeling often begins with the Susceptible-Infected-Recovered (SIR) model, a foundational compartment model that simplifies the dynamics of infectious diseases within a homogeneous population. The population is divided into three compartments:

- **Susceptible ($S(t)$):** Individuals who are not yet infected but are capable of becoming infected.
- **Infected ($I(t)$):** Individuals who are currently infected and can transmit the disease.
- **Recovered ($R(t)$):** Individuals who have recovered from the infection, are immune, and can no longer transmit the disease.

The dynamics of the SIR model are typically described by a system of ordinary differential equations, assuming a constant total population $N = S(t) + I(t) + R(t)$:

$$\frac{dS}{dt} = -\beta S(t)I(t)$$

$$\frac{dI}{dt} = \beta S(t)I(t) - \alpha I(t)$$

$$\frac{dR}{dt} = \alpha I(t)$$

Here, β represents the effective contact rate (the rate at which susceptible individuals become infected upon contact with an infected individual), and α is the recovery rate (the rate at which infected individuals recover).

2.1 The Basic Reproduction Number (R_0)

A crucial concept derived from epidemic models is the *basic reproduction number*, denoted as R_0. It represents the average number of secondary infections produced by a single infected individual in a completely susceptible population during their entire infectious period.

For the basic SIR model, R_0 can be derived by considering the initial growth of infections. When an infected individual is introduced into a fully susceptible population ($S(0) \approx N$), the rate of new infections is $\beta N I(t)$. The average duration an individual remains infectious is $1/\alpha$. Therefore, R_0 is given by:

$$R_0 = \frac{\beta N}{\alpha}$$

A more detailed derivation of R_0 is given in Chapter 4.1.1 of Ref. [1].

The value of R_0 is critical for understanding and predicting the trajectory of an epidemic:

- If $R_0 > 1$: Each infected individual, on average, infects more than one other person. This indicates that the disease will spread within the population, leading to an epidemic. The larger R_0 is, the faster and more extensively the disease is likely to spread.
- If $R_0 < 1$: Each infected individual, on average, infects less than one other person. This implies that the disease will eventually die out in the population.
- If $R_0 = 1$: The disease is endemic, meaning it will persist in the population without growing or declining.

In essence, R_0 serves as a threshold parameter that determines whether a disease can establish itself and cause an epidemic. It is a fundamental metric for public health interventions, as strategies often aim to reduce R_0 below 1 to control or eradicate an outbreak.

3. Age structured models

Since our goal is to write an age structured epidemic model, we first have to build the theory of continuous age structured models, that is a *continuous McKendrick model*. This section follows the Chapter 7.2 in Ref. [2].

In this model we consider only the female population or equivalently consider pairs of a male and a female. We denote with $p(a,t)$ the density of individuals of age a at time t. Therefore, $p(a,t)\Delta a$ is aproximatley the number of individuals aged between a and $a+\Delta a$ at time t. Sending $\Delta a \to 0$ we get the total population size at time t, $P(t) = \int_0^\infty p(a,t)da$.

We make the following assumptions. First, the individuals age continuously, that is over time interval Δt an individual of age a will become of age $a+\Delta t$. And second, we assume an age-dependent death rate $\mu(a)$, that is a fraction of deaths for individuals of age a.

In a time interval $[t, t+\Delta t]$ the number of deaths from age cohort $[a, a+\Delta a]$ is equal to

$$p(a,t)\Delta a \cdot \mu(a)\Delta t.$$

Those who survive this interval of time, will at time $t+\Delta t$ have age in the following interval $[a+\Delta t, a+\Delta t+\Delta a]$. Therefore the number of individuals from this age interval at time $t+\Delta t$ is aproximatley equal to number of individuals of age a at time t minus the number the number of deaths that we defined above. This is described in the following equation

$$p(a+\Delta t, t+\Delta t)\Delta a \approx p(a,t)\Delta a - p(a,t)\mu(a)\Delta a\Delta t. \tag{1}$$

Dividing the whole equation by $\Delta a\Delta t$ and sending $\Delta t \to 0$ we get the following partial differential equation

$$p_a(a,t) + p_t(a,t) + \mu(a)p(a,t) = 0, \tag{2}$$

called the *McKendrick equation*.

Further we assume an age-dependent birth rate $\beta(a)$, called the *birth modulus*. Now, we can define the boundary condition, also called the *renewal condition*, as

$$p(0,t) = \int_0^\infty \beta(a)p(a,t)da =: B(t),$$

which represents the number of newborns at time t. To have a complete PDE system we also need the *initial condition* which we define as

$$p(a,0) = \Phi(a),$$

where $\Phi(a)$ is the initial age distribution.

3.1 The method of characteristics

We solve this PDE system by using the method of characteristics. We introduce a parameter τ to parametrize the characteristic curves. We transform the PDE into a system of ODEs along characteristic curves and obtain the following *characteristic system*

$$\begin{aligned} \dot{a} &= 1 \\ \dot{t} &= 1 \\ \dot{p} &= -\mu(a)p. \end{aligned} \tag{3}$$

Integrating the first two equations we obtain the general form of the characteristic curves

$$\begin{aligned} a(\tau) &= \tau + a_0 \\ t(\tau) &= \tau + t_0. \end{aligned} \tag{4}$$

From these, it follows that $a - t = \text{const}$. This shows that the characteristic curves are straight lines with a slope of 1 in the (a, t) plane. Along these curves, the PDE reduces to an ODE for p.

Due to the constant positive slope of the characteristic curves, points in the solution domain (a, t) are influenced by either an initial condition at $t = 0$ or a boundary condition at $a = 0$, as illustrated in Figure 1.

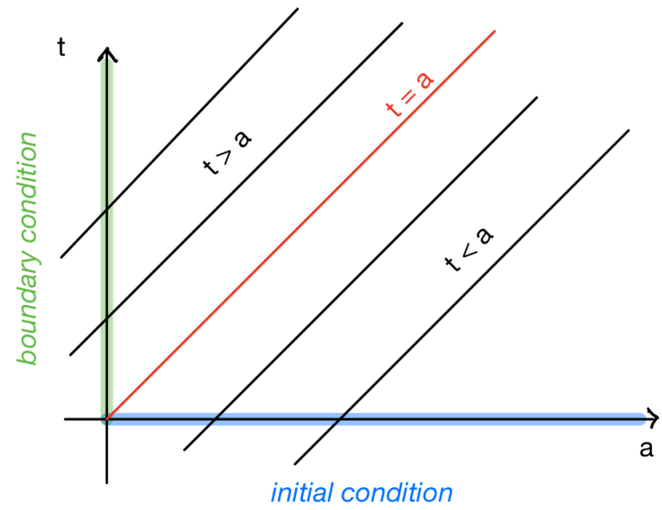

Figure 1. Characteristic curves and initial/boundary condition.

Therefore we differentiate two cases. For $t < a$ we will solve the characteristic system using the initial condition and for $t \geq a$ we use the boundary condition.

Case 1 ($t < a$)*:* Using the initial condition $p(a, 0) = \Phi(a)$, we parametrize the initial curve at $\tau = 0$ using a parameter s

$$\gamma(s) = (a_0(s), t_0(s), p_0(s)) = (s, 0, \Phi(s)).$$

We check the implicit function theorem condition. The determinant

$$\det \begin{pmatrix} \frac{da}{ds} & \frac{dt}{ds} \\ \frac{da_0}{ds} & \frac{dt_0}{ds} \end{pmatrix} = \det \begin{pmatrix} 1 & 1 \\ 1 & 0 \end{pmatrix} = -1,$$

is not equal to zero, therefore the initial condition is well-posed with respect to the characteristics in this region. We now plug the initial condition in the system Eq. (4) and get $t = \tau$, $a = \tau + s$. Therefore we can consider t as our parameter and get the solution for a as

$$a(t) = t + s.$$

By plugging the solution for a in the Eq. (3) for p and integrating it we get

$$\frac{dp}{dt} = -\mu(t + s)p(t),$$
$$p(s, t) = C(s)e^{-\int_0^t \mu(x+s)dx}.$$

Now using the initial condition ($t = 0$), we get that $C(s) = \Phi(s)$. Further, we replace s with $s = a - t$. Together with the shift of variable $\alpha = x + a - t$ we get the final solution

$$p(a, t) = \Phi(a - t)e^{-\int_{a-t}^{a} \mu(\alpha)d\alpha}, \; t < a. \tag{5}$$

Case 2 ($t \geq a$)*:* For points (a, t) where $t \geq a$, the solution is determined by the boundary condition $p(0, t) = B(t)$. We parametrize the boundary curve at $\tau = 0$ using a parameter s:

$$\gamma(s) = (a_0(s), t_0(s), p_0(s)) = (0, s, B(s)).$$

Simmilarly to the initial condition, it can be easily shown that the implicit function theorem requirement is satisifed. By plugging the boundary curve parametrization in the system Eq. (4), we get

$$\begin{aligned} a = \tau + a_0(s) &\implies a = \tau + 0 \implies a = \tau \\ t = \tau + t_0(s) &\implies t = \tau + s. \end{aligned}$$

From $a = \tau$, we can directly substitute a for τ in the characteristic ODEs. Also, we can express s in terms of a and t: $s = t - a$. We proceed to solve the ODE for p along the characteristics. Plugging $\tau = a$ in the Eq. (3) for p and integrating, we get:

$$\begin{aligned} \frac{dp}{d\tau} &= -\mu(\tau)p(\tau), \\ p(a, s) &= C(s)e^{\int_0^a \mu(\alpha)d\alpha}. \end{aligned}$$

Using the boundary condition at $\tau = a = 0$, we get $C(s) = B(s)$. Further plugging $s = t - \tau = t - a$, we get the final solution of p as

$$p(a, t) = B(t - a)e^{-\int_0^a \mu(\alpha)d\alpha},\ t \geq a. \tag{6}$$

3.2 The Renewal Equation

Further, we want to rewrite the *renewal condition* $p(0, t) = B(t) = \int_0^\infty \beta(a)p(a, t)da$ with the solution for p that we got using the method of characteristic. To do that we have to split the integral into two sections, $t \geq a$ and $t < a$:

$$\begin{aligned} B(t) &= \int_0^t \beta(a)p(a, t)da + \int_t^\infty \beta(a)p(a, t)da \\ &= \int_0^t \beta(a)B(t - a)\pi(a)da + \int_t^\infty \beta(a)\Phi(a - t)e^{-\int_{a-t}^a \mu(\alpha)d\alpha}da, \end{aligned}$$

where we defined $\pi(a) = e^{-\int_0^a \mu(\alpha)d\alpha}$, which is the probability of survival from birth to age a. The first integral represents the rate of births from members born after $t = 0$ and the second the rate of births from individuals already born at $t = 0$. We denote the second integral as $\Psi(t)$.

The renewal condition then reads as

$$B(t) = \int_0^t \beta(a)\pi(a)B(t - a)da + \Psi(t), \tag{7}$$

and it is called the *renewal equation.* This is a *linear Volterra integral equation of the convolution type*, with the kernel $K(a) = \beta(a)\pi(a)$. The solution $B(t)$ describes the future trajectory of the birth rate within the population.

3.3 Equilibrium Age Distribution and Asymptotic Behavior

To understand the long-term behavior of the population, we analyze the asymptotic properties of the solutions to the renewal equation. This analysis provides insights into whether the population will grow, decline, or stabilize over time. We make the following assumptions:

- the influence of the initial population distribution $\Phi(t)$ fades over time, specifically, $\Phi(t) \to 0$ as $t \to \infty$,
- the initial population is integrable, meaning $\int_0^\infty \Phi(a)da < \infty$, which implies a finite total initial population size,
- the net *reproduction rate* R is finite, defined as $R = \int_0^\infty \beta(a)\pi(a)da < \infty$.

Here R represents the expected number of offspring for an individual over its entire lifetime, since it is an integral over all ages a of probability of survival to age a multiplied by the number of offspring at age a. It is analogous to the basic reproduction number R_0 in epidemiology:

- if $R > 1$ the population is expected to grow,
- if $R = 1$ the population is expected to be stable,
- if $R < 1$ the population will decline over time.

In order to analyze the asyptotic behaviour we first have to solve the renewal equation. We do that using the *Laplace transform*. Recall the definition of the Laplace transform:

Definition 1. Let $f : [0, \infty) \to \mathbb{R}$ be a function, and let $z \in \mathbb{C}$. The *Laplace transform* of f is defined by

$$\mathcal{L}\{f(t)\}(z) = \hat{f}(z) := \int_0^\infty f(t)e^{-tz}\,dt,$$

whenever the integral converges. If f is bounded and continuous, then the Laplace transform $\hat{f}$ is holomorphic in the half-plane $\{z \in \mathbb{C} : \mathrm{Re}(z) > 0\}$.

Let us also recall the properties of the Laplace transform that we are going to need:

1. linearity: $\mathcal{L}(af(t) + bg(t))(z) = a\hat{f}(z) + b\hat{g}(z)$,
2. convolution: for a convolution $(f * g)(t) = \int_0^t f(a)g(t-a)da$, its Laplace Transform is the product of the individual transforms: $\mathcal{L}\{(f * g)(t)\}(z) = \hat{f}(z)\hat{g}(z)$.

Knowing these properties, we use the Laplace transform on the renewal equation Eq. (7) and get

$$\hat{B}(z) = \hat{\Psi}(z) + \hat{F}(z)\hat{B}(z),$$

where we defined $F(a) = \beta(a)\pi(a)$, and therefore $\hat{F}(z) = \mathcal{L}\{\beta(a)\pi(a)\}(z) = \int_0^\infty \beta(a)\pi(a)e^{-za}da$. We can express $\hat{B}$ and get

$$\hat{B}(z) = \frac{\hat{\Psi}(z)}{1 - \hat{F}(z)} \tag{8}$$

Here $\hat{F}$ and $\hat{\Psi}$ are holomorphic in the right half-plane $\mathrm{Re}(z) > 0$, because they are Laplace transforms of bounded and continuous functions: the birth rate function β and the survival probability π are both bounded and continuous, as well as Ψ which is the rate of births from individuals already born at $t = 0$. So the only singularities that can arrise in the Eq. (8) are those z for which $\hat{F}(z) = 1$.

Let's analyze the properties of $\hat{F}(x)$ for $x \in \mathbb{R}$:

- At $x = 0$: $\hat{F}(0) = \int_0^\infty \beta(a)\pi(a)e^{-0a}da = \int_0^\infty \beta(a)\pi(a)da = R$.
- As $x \to \infty$: $\lim_{x\to\infty} \hat{F}(x) = \lim_{x\to\infty} \int_0^\infty \beta(a)\pi(a)e^{-xa}da = 0$.

- Since $\beta(a) \geq 0$ (birth rate) and $\pi(a) \geq 0$ (probability of survival), and e^{-xa} is a strictly decreasing function of x for $a > 0$, it follows that $\hat{F}(x)$ is a strictly monotonically decreasing function for real $x \geq 0$.

Thus there is a unique real root x_0 of function $1 - \hat{F}(x)$. Moreover, since $\hat{F}$ is strictly decreasing on the real line, the root is simple. From the Fig. 2 we can observe that the value of x_0 depends on R: if $R > 1$, then $x_0 > 0$, if $R = 1$, then $x_0 = 0$ and if $R < 1$ then $x_0 < 0$.

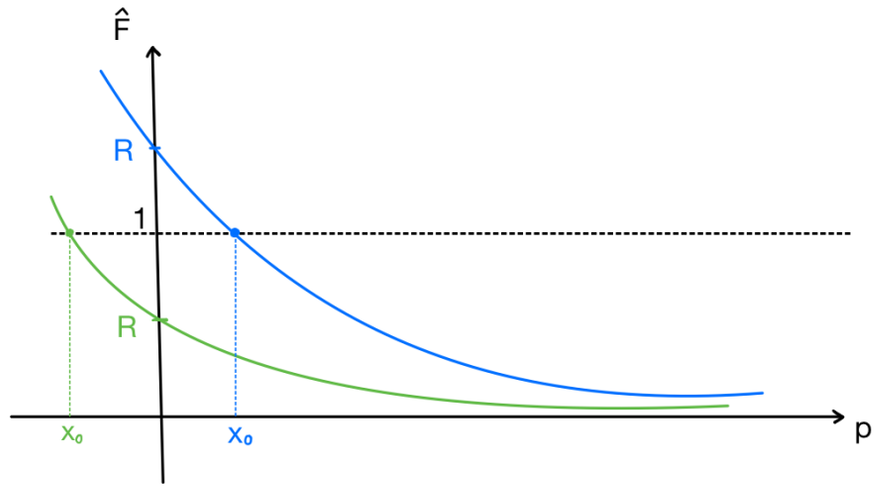

Figure 2. Sketch of function $\hat{F}(z)$.

Now, consider complex values of $z = x + iy$, $y \neq 0$:

$$\hat{F}(z) = \hat{F}(x+iy) = \int_0^\infty \beta(a)\pi(a)e^{-(x+iy)a}da = \int_0^\infty \beta(a)\pi(a)e^{-xa}(\cos(ya) - i\sin(ya))da$$

The real part is $\mathrm{Re}(\hat{F}(x+iy)) = \int_0^\infty \beta(a)\pi(a)e^{-xa}\cos(ya)da$. If we suppose $x \geq x_0$ and $y \neq 0$:

$$\begin{aligned} |\mathrm{Re}(\hat{F}(x+iy))| &\leq \int_0^\infty \beta(a)\pi(a)e^{-xa}|\cos(ya)|da < \int_0^\infty \beta(a)\pi(a)e^{-xa}da \\ &\leq \int_0^\infty \beta(a)\pi(a)e^{-x_0 a} = 1, \end{aligned}$$

where, in the second inequality, we take into account that $|\cos(ya)| < 1$ for some values of a and $\beta(a) \neq 0$ on a big enough interval of a, therefore we get the strict inequality. In the third inequality we took into account the assumption $x \geq p$.

We just showed that x_0 is a *dominant root* of characteristic equation $\hat{F}(z) = 1$, that is the solution with highest real value. Since $\hat{F}$ is analytic on a neighbourhood of x_0 we can use the idenitiy theorem to see that the solutions of $\hat{F}(z) = 1$ are isolated. Furthermore, we showed before that x_0 is a simple zero of $1 - \hat{F}(x)$, therefore x_0 is a simple pole of function $\frac{1}{1-\hat{F}(z)}$. Since $\hat{\Psi}(z)$ is holomorphic at x_0, multiplying does not change the order of the pole. Thus, $\hat{B}(z)$ has a simple pole at x_0. In the follwing we denote $z_0 = x_0$. We can then write $\hat{B}$ as a Laurent series around z_0:

$$\hat{B}(z) = \frac{c_{-1}}{z - z_0} + h(z),$$

where $c_{-1} = \text{Res}(\hat{B}, z_0)$ and $h(z)$ is an analytic function in some neighbourhood of z_0. More precisely, since we showed that all other singularities have strictly smaller real part than z_0, h is analytic on $z > \text{Re}(z_0)$. For a simple pole, the residue is given by:

$$c_{-1} = \text{Res}(\hat{B}, z_0) = \lim_{z \to z_0} [(z - z_0)\hat{B}(z)] = \lim_{z \to z_0} \left[(z - z_0) \frac{\hat{\Psi}(z)}{1 - \hat{F}(z)} \right].$$

We can easily show that $\hat{\Psi}(z) \neq 0$ and since both terms $z - z_0$ and $1 - \hat{F}(z)$ tend to 0 as $z \to z_0$, we use the L'Hospital rule and get $c_{-1} = -\frac{\hat{\Psi}(z_0)}{\hat{F}'(z_0)} =: B$. Therefore,

$$\hat{B}(z) = \frac{B}{z - z_0} + h(z).$$

We want to get back the solution for $B(t)$, so we apply the inverse Laplace transform. For an elementary function $\frac{1}{z-a}$, the inverse Laplace transform is $\frac{1}{z-a}$ is $\mathcal{L}^{-1}(\frac{1}{z-a})(t) = e^{at}$. So, in our example

$$B(t) = Be^{z_0 t} + E(t),$$

where $E(t) = \mathcal{L}^{-1}\{\mathcal{R}(z)\}(t)$. In order to get an estimate for $E(t)$, we use the following theorem.

Theorem 2 (Mellin's Inverse Formula for Laplace Transforms)**.** Let $\hat{f}(z)$ be the Laplace transform of a function $f(t)$ defined for $t \in [0, \infty)$. If $\hat{f}(z)$ converges for $\text{Re}(z) > \gamma_0$ for some real γ_0, and $\hat{f}(z)$ is analytic in this region, then the inverse Laplace transform $f(t)$ is given by the contour integral:

$$f(t) = \mathcal{L}^{-1}\{\hat{f}(z)\}(t) = \frac{1}{2\pi i} \lim_{T \to \infty} \int_{\gamma - iT}^{\gamma + iT} \hat{f}(z) e^{zt} dz$$

where γ is a real constant chosen such that $\gamma > \gamma_0$, meaning the vertical integration path $\text{Re}(z) = \gamma$ lies in the region of convergence of $\hat{f}(z)$ and to the right of all singularities of $\hat{f}(z)$.

The singularities of the function $h(z)$ are the solutions of equation $\hat{F}(z) = 1$ without z_0. We can order these solutions as $\text{Re}(z_1) > \text{Re}(z_2) > ....$ Choose an $\epsilon > 0$ such that $\gamma := \text{Re}(z_0) - \epsilon = z_0 - \epsilon > \text{Re}(z_1)$. Hence, using the Mellin's Inverse Formula,

$$\begin{aligned} E(t) = \mathcal{L}^{-1}\{h(z)\}(t) &= \frac{1}{2\pi i} \int_{\gamma - i\infty}^{\gamma + i\infty} e^{zt} h(z) dz \\ &= \frac{1}{2\pi i} \int_{-\infty}^{\infty} h(\gamma + i\omega) e^{(\gamma + i\omega)t} i d\omega \\ &= \frac{1}{2\pi} \int_{-\infty}^{\infty} h(\gamma + i\omega) e^{(\gamma + i\omega)t} d\omega, \end{aligned}$$

where we defined $z = \gamma + i\omega$. Further,

$$\begin{aligned} |E(t)| &\leq \frac{1}{2\pi} \int_{-\infty}^{\infty} |h(\gamma + i\omega) e^{(\gamma + i\omega)t}| d\omega \\ &\leq \frac{1}{2\pi} e^{\gamma t} \int_{-\infty}^{\infty} |h(\gamma + i\omega)| d\omega \\ &\leq C e^{(z_0 - \epsilon)t}, \end{aligned} \tag{9}$$

where we assume that the integral $\frac{1}{2\pi} \int_{-\infty}^{\infty} |h(\gamma + i\omega)| d\omega$ exists and we define it as C.

Since we are interested in the asymptotic behaviour we consider large t, particulary $a < t$. So from the solution that we got using the method of characteristics, the population density is given by $p(a, t) = B(t - a)\pi(a)$. Plugging in the solution for $B(t)$ we have just derived, we get:

$$p(a, t) = Be^{z_0(t-a)}\pi(a) + E(t - a)\pi(a).$$

Using this in the definition of the total population at time t, we get

$$\begin{aligned} P(t) &= B\int_0^\infty e^{z_0(t-a)}e^{-\int_0^a \mu(\alpha)d\alpha}da + \int_0^\infty E(t-a)\pi(a)da \\ &= B\int_0^\infty e^{-z_0 a}e^{-\int_0^a \mu(\alpha)d\alpha}da\ e^{z_0 t} + F(t) \\ \Rightarrow P(t) &= Pe^{z_0 t} + F(t), \end{aligned}$$

where we defined $P = B\int_0^\infty e^{-z_0 a}e^{-\int_0^a \mu(\alpha)d\alpha}da$ and $F(t) = \int_0^\infty E(t-a)\pi(a)da$. We can estimate $F(t)$ as

$$|F(t)| \leq \int_0^\infty |E(t-a)|\pi(a)da \leq Ce^{(z_0-\epsilon)t}\int_0^\infty \pi(a)da = Ce^{(z_0-\epsilon)t} \tag{10}$$

where we used the estimate (9) for E and took into account that $\pi(a)$ is a probability so it integrates into 1.

Taking a look at the term $\frac{p}{P}$ as $t \to \infty$:

$$\begin{aligned} \lim_{t\to\infty}\frac{p(a,t)}{P(t)} &= \lim_{t\to\infty}\frac{Be^{z_0(t-a)}\pi(a) + E(t-a)\pi(a)}{Pe^{z_0 t} + F(t)} \\ &= \frac{Be^{-z_0 a}\pi(a) + E(t-a)e^{-z_0 t}\pi(a)}{P + F(t)e^{-z_0 t}} \\ &= \frac{B}{P}e^{-z_0 a}\pi(a) =: \rho_0(a), \end{aligned} \tag{11}$$

where we took into account that by (9) and (10) both $E(t-a)e^{-z_0 t} \to 0$ and $F(t)e^{-z_0 t} \to 0$ as $t \to \infty$.

The function $\rho_0(a)$ is the *equilibrium age distribution*. It depends only on age a and the demographic parameters. It represents the proportion of the population that is of age a in the stable state. This stable age distribution emerges regardless of the initial population structure, which eventually fades out.

4. Age structured epidemic models

To investigate the dynamics of infectious diseases within populations that exhibit age-dependent vital rates, we extend the classical SIR epidemiological model to include an age structure and explicit population dynamics. Many diseases, especially childhood diseases, require a refinement of the model structure where different age classes do not mix randomly; instead, it is more likely that persons of similar age mix than randomly selected individuals. This age-structured approach allows for a more realistic representation of disease transmission, as contact patterns and vulnerability to infection or disease progression often vary with age. This section follows the Chapter 4.3.1 in Ref. [1] and Chapter 9 in Ref. [3].

The population is, similarly as in section 1, divided into three compartments based on their epidemiological status, with an explicit dependence on time t and age a: $S(t,a)$ – density of susceptible individuals, $I(t,a)$ – density of infected individuals and $R(t,a)$ – density of recovered individuals. The total population density at age a and time t is given by $p(t,a) = S(t,a) + I(t,a) + R(t,a)$. The total population size at time t is then $P(t) = \int_0^\infty p(t,a)da$.

The model incorporates age-dependent vital rates and disease-specific dynamics:

- $\mu(a)$: Age-specific death rate.
- $\beta(a)$: Age-specific birth rate (implicitly included in the birth term).

- $\alpha(a)$: Age-specific recovery rate for infected individuals.
- $\psi(a)$: Age-specific vaccination rate for susceptible individuals.
- $k(a,c)$: Contact rate between an individual of age a and an individual of age c. A common simplification for $k(a,c)$ is separable mixing, $k(a,c) = k_1(a)k_2(c)$.

The force of infection, which represents the rate at which susceptible individuals acquire infection at time t, is determined by the contact rate and the density of infected individuals across all ages. It is defined as:

$$\frac{1}{P(t)} \int_0^\infty k(a,c) I(c,t) dc$$

From the age structured population model we get the equation for total population density: $p_a(a,t) + p_t(a,t) + \mu(a)p(a,t) = 0$. Simmilarly we adapt this to the epidemic model with vaccination:

$$\begin{aligned}
(\partial_t + \partial_a) S(a,t) &= -\mu(a) S(a,t) - \frac{S(a,t)}{P(t)} \int_0^\infty k(a,c) I(c,t) dc - \psi(a) S(a,t) \\
S(0,t) &= \int_0^\infty \beta(c)(S(c,t) + I(c,t) + R(c,t)) dc \\
(\partial_t + \partial_a) I(a,t) &= -\mu(a) I(a,t) + \frac{S(a,t)}{P(t)} \int_0^\infty k(a,b) I(c,t) dc - \alpha I(a,t) \\
I(0,t) &= 0 \\
(\partial_t + \partial_a) R(a,t) &= -\mu(a) R(a,t) + \alpha I(a,t) + \psi(a) S(a,t) \\
R(0,t) &= 0
\end{aligned}$$

To simplify the analysis, particularly the interaction with the total population $N(t)$, we transform the system into proportions of the total population density at each age. We define:

- $s(a,t) = \frac{S(a,t)}{p(a,t)}$: proportion of susceptibles at age a and time t.
- $i(a,t) = \frac{I(a,t)}{p(a,t)}$: proportion of infected individuals at age a and time t.
- $r(a,t) = \frac{R(a,t)}{p(a,t)}$: proportion of recovered individuals at age a and time t.
- $\rho(a,t) = \frac{p(a,t)}{P(t)}$: proportion of the total population at age a and time t (normalized distribution).

The system then translates to

$$\begin{aligned}
(\partial_t + \partial_a) s(a,t) &= (\partial_t + \partial_a) \left(\frac{S(a,t)}{p(a,t)} \right) \\
&= \frac{(\partial_t + \partial_a) S(a,t)}{p(a,t)} - \frac{S(a,t)}{p(a,t)} \frac{(\partial_t + \partial_a) p(a,t)}{p(a,t)} \\
&= \frac{-\mu(a) S(a,t) - \frac{S(a,t)}{P(t)} \int_0^\infty k(a,c) I(c,t) dc - \Psi(a) S(a,t)}{p(a,t)} - \frac{S(a,t)}{p(a,t)} \frac{-\mu(a) p(a,t)}{p(a,t)} \\
&= -\mu(a) s(a,t) - s(a,t) \int_0^\infty k(a,c) \frac{p(c,t)}{P(t)} \frac{I(c,t)}{p(c,t)} dc - \Psi(a) s(a,t) + \mu(a) s(a,t) \\
&= -s(a,t) \int_0^\infty k(a,c) \rho(c,t) i(c,t) dc - \psi(a) s(a,t) \\
s(0,t) &= \frac{S(0,t)}{p(0,t)} = \frac{S(0,t)}{S(0,t) + I(0,t) + R(0,t)} = \frac{1}{1+0+0} = 1,
\end{aligned}$$

and similarly,

$$\begin{aligned}(\partial_t + \partial_a)i(a,t) &= s(a,t)\int_0^\infty k(a,c)\rho(c,t)i(c,t)dc - \alpha i\\ i(0,t) &= 0,\\ (\partial_t + \partial_a)r(a,t) &= \alpha i(a,t) + \psi(a)s(a,t)\\ r(0,t) &= 0.\end{aligned}$$

Following the result from Eq. (11), we can, for large t, replace $\rho(a,t)$ with its equilibrium distribution $\rho_0(a)$:

$$\begin{aligned}(\partial_t + \partial_a)s(a,t) &= -s(a,t)\int_0^\infty k(a,c)\rho_0(c)i(c,t)dc - \psi(a)s(a,t)\\ s(0,t) &= 1\\ (\partial_t + \partial_a)i(a,t) &= s(a,t)\int_0^\infty k(a,c)\rho_0(c)i(c,t)dc - \alpha i\\ i(0,t) &= 0\\ (\partial_t + \partial_a)r(a,t) &= \alpha i(a,t) + \psi(a)s(a,t)\\ r(0,t) &= 0\end{aligned} \tag{12}$$

4.1 The Reproduction Number

We defined the reproduction number as the average number of secondary cases produced by one primary case. The problem in the age structured epidemologic models is that we do not know what age to pick for the first infected individual. We approach this by linearisation around the uninfected stationary state.

Let us first determine the uninfected state, that is $i = 0$. With that assumption we get the following system:

$$\begin{aligned}\left(\frac{\partial}{\partial t} + \frac{\partial}{\partial a}\right)s(a,t) &= -\psi(a)s(a,t)\\ s(0,t) &= 1\\ \left(\frac{\partial}{\partial t} + \frac{\partial}{\partial a}\right)r(a,t) &= \psi(a)s(a,t)\\ r(0,t) &= 0\end{aligned}$$

We consider the stationary state of this system, that is $\frac{\partial s}{\partial t} = \frac{\partial r}{\partial t} = 0$, and get the following ODEs:

$$\begin{aligned}\frac{\partial}{\partial a}s(a,t) &= -\Psi(a)s(a,t)\\ \frac{\partial}{\partial a}r(a,t) &= \Psi(a)s(a,t).\end{aligned}$$

Solving this system gives us the stationary solutions

$$s_0(a) = e^{-\int_0^a \Psi(\tau)d\tau},\ r_0(a) = 1 - s_0(a).$$

We proceed by linearizing the original system at the uninfected stationary solution:

$$\begin{aligned}s(t,a) &= s_0(a) + \tilde{s}(t,a)\\ i(t,a) &= 0 + \tilde{i}(t,a)\\ r(t,a) &= r_0(a) + \tilde{r}(t,a),\end{aligned}$$

where $\tilde{s}, \tilde{i}, \tilde{r}$ are small pertubations. Plugging this term in the PDEs from Eq. (12), we get:

$$\begin{aligned}(\partial_t + \partial_a)(s_0(a) + \tilde{s}(t,a)) &= (\partial_t + \partial_a)s(t,a) \\ &= -(s_0(a) + \tilde{s}(t,a)) \int_0^\infty k(a,c)\rho_0(c)i(c,t)dc - \psi(a)(s_0(a) + \tilde{s}(a,t)) \\ &= -s_0(a) \int_0^\infty k(a,c)\rho_0(c)\tilde{i}(c,t)dc - \tilde{s}(t,a) \int_0^\infty k(a,c)\rho_0(c)\tilde{i}(c,t)dc \\ &- \psi(a)s_0(a) - \psi(a)\tilde{s}(a,t).\end{aligned}$$

The left-hand side is equal to $-\Psi(a)s_0(a)+(\partial_t+\partial_a)\tilde{s}(t,a)$, so after cancelling the terms and ignoring the quadratic terms, we get

$$\begin{aligned}(\partial_t + \partial_a)\tilde{s} &= -s_0(a) \int_0^\infty k(a,c)\rho_0(c)\tilde{i}(c,t)dc - \psi(a)\tilde{s}(a,t) \\ \tilde{s}(0,t) &= s(0,t) - s_0(0) = 1 - 1 = 0,\end{aligned}$$

and similarly

$$\begin{aligned}(\partial_t + \partial_a)\tilde{i}(a,t) &= s_0(a) \int_0^\infty k(a,c)\rho_0(c)\tilde{i}(c,t)dc - \alpha\tilde{i} \\ \tilde{i}(0,t) &= 0.\end{aligned}$$

To analyze the exponential behavior of the infection, we employ the method of separation of variables. We assume solutions for $\tilde{i}(a,t)$ are of the form $\tilde{i}(a,t) = T(t)A(a)$. Plugging this into the PDE for $\tilde{i}$ and dividing by $T(t)$, we get:

$$\begin{aligned}A(a) \cdot \frac{T'(t)}{T(t)} + A'(a) &= s_0(a) \int_0^\infty k(a,c)\rho_0(c)A(c)dc - \alpha A(a) \\ \frac{T'(t)}{T(t)} &= -\frac{A'(a)}{A(a)} + s_0(a)\frac{1}{A(a)} \int_0^\infty k(a,c)\rho_0(c)A(c)dc - \alpha\end{aligned} \tag{13}$$

We observe that in the equation (13), all terms except $\frac{T'(t)}{T(t)}$ depend only on the age variable a. Since the equality must hold for all a and t, the time-dependent ratio $\frac{T'(t)}{T(t)}$ must in fact be constant. Denoting this constant by λ, we obtain

$$\frac{T'(t)}{T(t)} = \lambda \quad \Rightarrow \quad T(t) = Ce^{\lambda t}.$$

Plugging this back to Eq. (13) we get an ODE for function A:

$$A'(a) = s_0(a) \int_0^\infty k(a,c)\rho_0(c)A(c)dc - \alpha A(a) - \lambda A(a),$$

with initial condition $A(0) = 0$, since $\tilde{i}(0,t) = 0 = Ce^{\lambda t}A(a)$.

This is an inhomogeneous ODE, which we are going to solve using the *method of integrating factors*, which is an equivalent to the method of variation of constant.

Proposition 3 (Solving Differential Equations with Integrating Factors)**.** Consider a first-order linear differential equation of the form $\frac{dy}{dx} + P(x)y = Q(x)$ where $P(x)$ and $Q(x)$ are functions of x. The general solution can be found using an integrating factor $I(x)$ defined as $I(x) = e^{\int P(x)dx}$ Multiplying the differential equation by $I(x)$ and integrating both sides with respect to x yields the solution: $I(x)y = \int I(x)Q(x)dx$. Thus, the general solution for y is:

$$y = \frac{1}{I(x)} \int I(x)Q(x)dx$$

So, in our case the integrating factor is $I = e^{\int(\alpha+\lambda)da} = e^{(\alpha+\lambda)a}$, which using the method of integrating factor yields the solution:

$$A(a) = \int_0^a e^{-(\alpha+\lambda)(a-\sigma)} s_0(\sigma) \left(\int_0^\infty k(\sigma, c)\rho_0(c)A(c)dc \right) d\sigma. \tag{14}$$

This is an integral equation for A.

Let's remember how $\tilde{i}$ is defined with the assumption of separating variables:

$$\tilde{i}(a, t) = e^{\lambda t} A(a),$$

here $A(a)$ is the age profile for infected population, which has a fixed shape. So the term $e^{\lambda t}$ will describe the growth/decay of our perturbation $\tilde{i}$ over time:

- $\mathrm{Re}(\lambda) > 0$, $e^{\lambda t}$ grows exponentially, the uninfected state is unstable and epidemic occurs.
- $\mathrm{Re}(\lambda) < 0$, $e^{\lambda t}$ shrinks exponentially. The uninfected state is stable, the infection dies out.
- $\mathrm{Re}(\lambda) = 0$ is the critical threshold where the infection neither grows nor shrinks but can persist.

Therefore, to understand the behaviour we have to get λ. We do that by solving the integral equation for A.

We define a linear integral operator $\mathcal{T}_\lambda$ acting on a function $f(a)$ as:

$$\mathcal{T}_\lambda[f](a) = \int_0^a e^{-(\alpha+\lambda)(a-\sigma)} s_0(\sigma) \left(\int_0^\infty k(\sigma, c)\rho_0(c)f(c)dc \right) d\sigma$$

Our goal now is to find a non-trivial function $A(a) > 0$ that satisfies the fixed-point equation:

$$\mathcal{T}_\lambda[A](a) = A(a).$$

This is precisely an eigenvalue problem, where we are searching for an eigenfunction $A(a)$ corresponding to an eigenvalue of 1. To solve this problem we first have to develop some theory, that we take from Chapter 19.5 of Ref. [4].

Definition 4. Let X be a Banach space. A *cone* $K \subset X$ is a closed convex set such that $\lambda K \subset K$ for all $\lambda \geq 0$ and $K \cap (-K) = \{0\}$. Given a cone K we define a *partial ordering* $\leq$ *with respect to* K by $x \leq y$ if and only if $y - x \in K$.

Definition 5. Let X be a Banach space, $K \subset X$ a cone and $T \in L(X)$ a linear operator on X. We say that operator T is *strongly positive* if $\mathring{K} \neq \emptyset$ and $T(K \setminus \{0\}) \subset \mathring{K}$.

Theorem 6 (The Krein-Rutman Theorem)**.** Let X be a Banach space and $K \subset X$ a cone such that $K - K$ is dense in X, that is $\overline{\{u - v;\ u, v \in K\}} = X$, and $\mathring{K} \neq \emptyset$. Let $T : X \to X$ be a linear, compact and strongly positive operator. Let $\rho(T)$ be the spectral radius of operator T. Then $\rho(T) > 0$, $\rho(T)$ is a simple eigenvalue with an eigenvector $v \in \mathring{K}$ (therefore v is positive) and there is no other eigenvalue with a positive eigenvector.

We want to show that we can use the Krein-Rutman Theorem to solve the eigenvalue problem. For the Banach space we choose

$$X = \{f \in \mathcal{C}([0, A_{\max}]), f(0) = 0\},$$

with supremum norm, which is a natural choice in our setting. Biologically, the age of humans is finite, so it is sufficient to consider functions defined on the compact interval $[0, A_{\max}]$. Continuity reflects the assumption that population profiles vary smoothly with age. Next we take a set

$$K = \{f \in X, f(a) \geq 0 \; \forall a \in [0, A_{\max}]\},$$

which is again appropriate because negative population densities are not meaningful. In the next lemma we prove that K is indeed a cone.

Lemma 7. The set $K = \{f \in X, f(a) \geq 0 \; \forall a \in [0, A_{\max}]\}$ is a cone in X with $\mathring{K} \neq \emptyset$ and $K - K$ is dense in X.

Proof. We now prove that K satisfies the usual properties of a cone in X: closedness, convexity, positive homogeneity, pointedness, nonempty interior, and density of $K - K$.

(i) *Closedness:* If a sequence $(f_n) \subset K$ converges uniformly to f, then $f(0) = \lim f_n(0) = 0$. If for some a_0 we had $f(a_0) < 0$, uniform convergence would force $f_n(a_0) < 0$ for $n \to \infty$, contradicting $f_n \in K$. Hence $f(a) \geq 0$ for all a, so $f \in K$. Thus K is closed.

(ii) *Convexity:* If $f, g \in K$ and $\theta \in [0, 1]$, then the convex combination $\theta f + (1 - \theta)g$ still satisfies nonnegativity everywhere and vanishes at 0, hence belongs to K. Thus K is convex.

(iii) *Positive homogeneity:* For any $\lambda \geq 0$ and $f \in K$, the function λf also belongs to K. Hence $\lambda K \subset K$.

(iv) *Pointedness;* If $f \in K \cap (-K)$, then $f(a) \geq 0$ and $-f(a) \geq 0$ for all a, which forces $f \equiv 0$. Thus $K \cap (-K) = \{0\}$.

(v) *Nonempty interior:* Interior $K^\circ = \{f \in X : f(a) > 0 \text{ for all } a \in (0, A_{\max}], \; f(0) = 0\}$ is nonempty (for instance, $f(a) = a$ lies in K°).

(vi) *Density of $K - K$ in X:* Take any $f \in X = C([0, A_{\max}])$. Define the continuous nonnegative functions

$$f^+(a) = \max\{f(a), 0\}, \qquad f^-(a) = \max\{-f(a), 0\}.$$

Clearly $f^+, f^- \in K$ and $f = f^+ - f^-$. Thus every $f \in X$ can be expressed as a difference of two functions in K, which means $K - K = X$. In particular, $K - K$ is dense in X. ∎

Next we prove that the operator $\mathcal{T}_\lambda$ satisfies the assumptions of Krein-Rutman theorem. For that we use the next theorem whose proof can be read in Section 8.7 in [5].

Theorem 8 (Compact integral operator)**.** Let $J = [a, b]$ be a compact interval and let $X = C(J)$ be equipped with the supremum norm. Suppose $k\colon J \times J \to \mathbb{R}$ is continuous. Define $T : X \to X$ by

$$(Tx)(s) = \int_a^b k(s, t)\, x(t)\, dt, \qquad s \in J.$$

Then T is a linear and compact operator on X.

Lemma 9. $\mathcal{T}_\lambda : X \to X$ is a linear, compact and strongly positive operator.

Proof. We now establish that $\mathcal{T}_\lambda$ is linear, compact, and strongly positive by verifying these properties one by one.

(i) *Linearity and compactness:* Fix $A > 0$ and let $J = [0, A]$. Recall

$$(T_\lambda f)(a) = \int_0^a e^{-(\alpha+\lambda)(a-\sigma)}\, s_0(\sigma) \left(\int_0^A k(\sigma, c)\, \rho_0(c)\, f(c)\, dc \right) d\sigma, \qquad a \in J.$$

Note that $s_0 \in C(J),\ s_0 > 0; \quad k \in C(J \times J),\ k \geq 0; \quad \rho_0 \in C(J),\ \rho_0 \geq 0,\ \rho_0 \not\equiv 0$. Since the integrand is continuous and hence integrable on the compact set $\{(\sigma, c) : 0 \leq \sigma \leq a,\ 0 \leq c \leq A\}$, we may interchange integrals:

$$(\mathcal{T}_\lambda f)(a) = \int_0^A \left[\rho_0(c) \int_0^a e^{-(\alpha+\lambda)(a-\sigma)} s_0(\sigma) k(\sigma, c)\, d\sigma \right] f(c)\, dc = \int_0^A K_\lambda(a, c) f(c)\, dc,$$

where

$$K_\lambda(a, c) := \rho_0(c) \int_0^a e^{-(\alpha+\lambda)(a-\sigma)} s_0(\sigma) k(\sigma, c)\, d\sigma.$$

The map $(a, \sigma, c) \mapsto e^{-(\alpha+\lambda)(a-\sigma)} s_0(\sigma) k(\sigma, c) \rho_0(c)$ is continuous on the compact set $\{(a, \sigma, c) : 0 \leq \sigma \leq a \leq A,\ 0 \leq c \leq A\}$. The integral in σ with variable upper limit preserves continuity; hence $K_\lambda \in C(J \times J)$. Therefore, by Theorem 8 the operator $\mathcal{T}_\lambda : C(J) \to C(J)$ is linear and compact. Since $X = \{f \in C(J) : f(0) = 0\}$ is a closed subspace of X and $T_\lambda(X) \subset X$, the restriction $T_\lambda : X \to X$ is compact as well.

(ii) *Strong positivity:* Suppose $s_0(a) > 0$ on J, $\rho_0(c) > 0$ on $(0, A]$ and $k(\sigma, c) > 0$ on $(0, A] \times (0, A]$. Fix $f \in K \setminus \{0\}$. Then there exists $c_* \in (0, A]$ with $f(c_*) > 0$. By continuity of f there are $\delta > 0$ and $\eta > 0$ such that $f(c) \geq \eta \quad$ for all $c \in I := \big([c_* - \delta, c_* + \delta] \cap (0, A]\big)$. Since ρ_0 is continuous and strictly positive on $(0, A]$, we have

$$m := \min_{c \in I} \rho_0(c) > 0.$$

Fix $a \in (0, A]$. By continuity and strict positivity of k on $[0, a] \times I$ (a compact set), the minimum

$$\kappa_a := \min\{\, k(\sigma, c) :\ 0 \leq \sigma \leq a,\ c \in I \,\}$$

exists and satisfies $\kappa_a > 0$.

For any $\sigma \in [0, a]$ we bound the inner integral from below:

$$\int_0^A k(\sigma, c)\, \rho_0(c)\, f(c)\, dc \ \geq\ \int_I k(\sigma, c)\, \rho_0(c)\, f(c)\, dc \ \geq\ \kappa_a\, m\, \eta\, |I| \ =:\ \beta_a \ >\ 0,$$

where $|I|$ denotes the length of the interval I. Therefore,

$$\begin{aligned}(\mathcal{T}_\lambda f)(a) &= \int_0^a e^{-(\alpha+\lambda)(a-\sigma)}\, s_0(\sigma) \Big(\int_0^A k(\sigma, c)\, \rho_0(c)\, f(c)\, dc \Big)\, d\sigma \\ &\geq\ \beta_a \int_0^a e^{-(\alpha+\lambda)(a-\sigma)}\, s_0(\sigma)\, d\sigma.\end{aligned}$$

The last integral is strictly positive because $a > 0$, $s_0(\sigma) > 0$ and the exponential is positive. Hence $(\mathcal{T}_\lambda f)(a) > 0$ for every $a \in (0, A]$. Moreover, $(\mathcal{T}_\lambda f)(0) = 0$ by definition. Thus $\mathcal{T}_\lambda f \in K^\circ$. ∎

We can now use the Krein-Rutman theorem for our case. It tells us that a positive eigenfunction (which we want to have in our case) must correspond to eigenvalue $\rho(\mathcal{T}_\lambda)$. Since we are interested in an eigenfunction for eigenvalue 1, our problem reduces to finding λ such that

$$\rho(\mathcal{T}_\lambda) = 1$$

For simplicity, let's proceed to the specific case of seperable mixing,

$$k(a,b) := k_1(a) \cdot k_2(b).$$

Then the operator reads

$$\mathcal{T}_\lambda[f](a) = \left(\int_0^\infty k_2(c)\rho_0(c)f(c)dc\right)\left(\int_0^a e^{-(\alpha+\lambda)(a-\sigma)}k_1(\sigma)s_0(\sigma)d\sigma\right).$$

We denote the first integral as $\Phi(f)$ and the second one as $\hat{A}_\lambda(a)$. So we have $\mathcal{T}_\lambda f = \Phi(f)\hat{A}_\lambda$. We can observe that $\hat{A}_\lambda$ is an eigenfunction of $\mathcal{T}_\lambda$ for the eigenvalue $\Phi(\hat{A}_\lambda)$:

$$\mathcal{T}_\lambda \hat{A}_\lambda = \Phi(\hat{A}_\lambda)\hat{A}_\lambda.$$

If we prove that $\hat{A}_\lambda(a) > 0$, then this is, according to the Krein-Rutman Theorem, the only positive eigenfunction. The exponent is always positive, susceptibility s_0 is non-negative as well as k_1. An integral of non-negative functions over a non-negative range is positive. The only thing left to show is that the eigenvalue $\Phi(\hat{A}_\lambda)$ equals 1. So we obtain an equation for λ:

$$\begin{aligned}
1 &= \Phi(\hat{A}_\lambda) \\
&= \int_0^\infty k_2(c)\rho_0(c)\hat{A}(c)dc \\
&= \int_0^\infty k_2(c)\rho_0(c)\int_0^c e^{-(\alpha+\lambda)(c-\sigma)}s_0(\sigma)d\sigma\,dc =: g(\lambda).
\end{aligned}$$

Note that $g(\lambda)$ is a monotonically decreasing function of λ, therefore the equation $g(\lambda) = 1$ has only one solution. Following a simmilar idea as in Sec. 3.3 (also see Fig. 2), we get that

- if $g(0) > 1$, then $\lambda_0 > 0$
- if $g(0) = 1$, then $\lambda_0 = 0$
- if $g(0) < 1$, then $\lambda_0 < 0$.

Define

$$\Theta := g(0) = \int_0^\infty k_2(c)\rho_0(c)\int_0^c e^{-\alpha(c-\sigma)}k_1(\sigma)s_0(\sigma)d\sigma\,dc. \tag{15}$$

So if $\Theta < 1$ we have stable system, if $\Theta > 1$ we have unstable system. We take Θ to be our reproduction number. This is fully analogous to the classical SIR model, where the basic reproduction number R_0 plays the role of the threshold parameter that determines whether the infection dies out or spreads.

We can interpret that Θ is the reproduction number, it is the average number of secondary cases produced by one primary case, also biologically:

- The term $k_1(\sigma)s_0(\sigma)$ represents the effective rate at which a primary infected individual of age σ makes contacts that lead to transmission, weighted by the proportion of susceptible individuals at that age in the uninfected state.
- The exponential term $e^{-\int_\sigma^c \alpha(\tau)d\tau}$ captures the probability that an individual infected at age σ remains alive and infectious until age c. This accounts for the duration of their infectious period.
- The inner integral $\int_0^c(\dots)d\sigma$ accumulates the total infectious potential of a primary case over its entire infectious lifespan up to age c.

- The factor $k_2(c)\rho_0(c)$ incorporates the age distribution of the susceptible population ($\rho_0(c)$) and their propensity for contact ($k_2(c)$), ensuring that secondary cases are weighted by the demographic structure and mixing patterns of the population.
- Finally, the outer integral $\int_0^\infty(\dots)dc$ averages all these potential secondary infections across all relevant ages in the population, providing a comprehensive measure of transmissibility.

Note: this reproduction number differs from the basic reproduction number R_0 in the classical SIR model, as it accounts for age structure. Instead of a single typical infected individual, it reflects the average number of secondary cases produced by an infected individual drawn from the stationary age distribution.

5. Indirect effect of vaccination

In this section we give a mathematical model for the indirect effect of vaccination. Following the vaccination method, we suppose that the vaccination happens between newborns, so at age 0. Then, $s(0,t) = c$, where c is the fraction of newborns not vaccinated at birth.

We consider a simplified age structured vaccination model, where we assume:

- all rates are age-independent
- total population is constant up to maximal lifetime $L < 0$, so $\rho_0(a) = \rho_0$ and zero afterwards.

The epidemic system is then:

$$\begin{aligned}(\partial_t + \partial_a)s(a,t) &= -s(a,t)\int_0^L k_0\rho_0 i(x,t)dx\\ s(0,t) &= c\\ (\partial_t + \partial_a)i(a,t) &= s(a,t)\int_0^L k_0\rho_0 i(x,t)dx - \alpha i\\ i(0,t) &= 0\end{aligned}$$

Note that there is no term ψ_s comparing to model Eq. (12), since vaccination is already assumed with the initial condition.

Consider the stationary state, that is $\frac{\partial s}{\partial t} = \frac{\partial i}{\partial t} = 0$ and denote $i^* = \int_0^L i(x,t)dx$. Then the differential equation for s is:

$$\frac{\partial s}{\partial a} = -sk\rho_0 i^* \Rightarrow s(a) = ce^{-k\rho_0 i^* a}. \tag{16}$$

Define $K = k\rho_0 i^*$. By plugging the solution for s into the stationary equation for i, we get:

$$\begin{aligned}\frac{\partial i}{\partial a} &= sK - \alpha i\\ &= ce^{-Ka}K - \alpha i.\end{aligned}$$

This is an inhomogeneus differential equation, which we solve using the integating factor $I = e^{\int \alpha da} = e^{\alpha a}$, which yields:

$$\begin{aligned}i(a) &= Kce^{-\alpha a}\int_0^a e^{(\alpha-K)\sigma}d\sigma\\ &= \frac{Kc}{\alpha-K}e^{-\alpha a}\left[e^{\alpha a - Ka} - 1\right]\\ &= \frac{Kc}{\alpha-K}\left[e^{-Ka} - e^{-\alpha a}\right].\end{aligned} \tag{17}$$

Remember: we defined $i^* = \int_0^L i(c,t)dc$. Integrating Eq. (17) from 0 to L, we get

$$\begin{aligned} i^* &= \frac{Kc}{K-\alpha}\int_0^L e^{-\alpha a} - e^{-Ka}da \\ &= \frac{Kc}{K-\alpha}\left[-\frac{1}{\alpha}e^{-\alpha a} + \frac{1}{K}e^{-Ka}\right]_0^L. \end{aligned}$$

We assume that L is large, so $e^{(\dots)L} \approx 0$. Thus, the equation simplifies

$$i^* \approx \frac{Kc}{K-\alpha}\left[\frac{1}{\alpha} - \frac{1}{K}\right] = \frac{c}{\alpha}. \tag{18}$$

We now want to mathematically describe the rate at which new individuals are becoming infected at the age of a. Understanding the meaning of parameters k (transmition rate per individual), ρ_0 (total population density), i^* (density of infected individuals in stationary state), we get that $k\rho_0 i^*$ is the rate at which a single susceptible individual becomes infected. Therefore $s(a)k\rho_0 i^*$ is then the *density of newely infected individual at age a*. Plugging in the Eq. (16) and (18), this term reads as:

$$k\rho_0 \frac{c^2}{\alpha}e^{-k\rho_0 ca/\alpha}.$$

The *average age of newely infected person*, which we denote with A, then reads:

$$\begin{aligned} A &= \frac{\int_0^L ak\rho_0\frac{c^2}{\alpha}e^{-k\rho_0 ca/\alpha}da}{\int_0^L k\rho_0\frac{c^2}{\alpha}e^{-k\rho_0 c\tau/\alpha}d\tau} \\ &= \frac{\int_0^L ae^{-k\rho_0 ca/\alpha}da}{\int_0^L e^{-k\rho_0 c\tau/\alpha}d\tau} \\ &= \frac{\int_0^L ae^{-k\rho_0 ca/\alpha}da}{-\frac{\alpha}{k\rho_0 c}(e^{-k\rho_0 cL/\alpha}-1)} \\ &\approx \frac{k\rho_0 c}{\alpha}\left[0 + \frac{\alpha}{k\rho_0}\int_0^L e^{-k\rho_0 ca/\alpha}da\right] \\ &\approx \frac{\alpha}{2\rho_0 c}, \end{aligned}$$

where we used the fact that $e^{(\dots)L} \approx 0$ and the per partes method.

Now, recall the definition of reproduction number Θ (Eq. (15)) and use our assumptions ($k = k_1k_2$, $\rho_0(a) = \rho_0$, we have a finite maximum age L):

$$\Theta = k\rho_0\int_0^L\int_0^c e^{-\alpha(c-\sigma)}s_0(\sigma)d\sigma dc.$$

To calculate the *basic reproduction number* R_0, we must set $s_0(a) = 1$. Then we get

$$\begin{aligned} R &= k\rho_0\int_0^L\int_0^c e^{-\alpha(c-\sigma)}d\sigma dc \\ &= k\rho_0\int_0^L \frac{1}{\alpha}\left[1-e^{-\alpha c}\right]dc \\ &= \frac{k\rho_0 L}{\alpha} + \frac{k\rho_0}{\alpha^2}(e^{-\alpha L}-1) \\ &\approx \frac{k\rho_0}{\alpha}\left(L - \frac{1}{\alpha}\right) \end{aligned}$$

Since α is the recovery rate, it can be shown that the term $\frac{1}{\alpha}$ is the average period of infection. Morover L is the lifespan, so we can approximate $L - \frac{1}{\alpha} \approx L$. Therefore, $R_0 \approx \frac{k\rho_0 L}{\alpha}$ and,

$$A \approx \frac{L}{cR_0}.$$

This equation explains the observed phenomenon where the risk of congenital rubella syndrome (CRS) may initially rise following the introduction of partial vaccination. It shows that the mean age of infection, $A \approx \frac{L}{cR_0}$, increases as vaccination coverage rises. Since CRS primarily affects infants born to mothers infected during pregnancy, shifting infections to older age groups—particularly to women of childbearing age — can unintentionally raise the number of risk cases if not enough individuals are vaccinated. Therefore, when only a small proportion of the population is immunized (i.e., $1 - c$ is large), the average age at which infections occur increases, potentially elevating the number of susceptible pregnant women. To reduce CRS cases effectively, it is essential that vaccination coverage is sufficiently high to not only lower overall rubella incidence but also prevent this upward shift in the age of infection.

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