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A SIMPLE MATRIX MODEL OF EPIDEMIC OUTBREAK INVOLVING VACCINATION OF TWO AGE GROUPS

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ABSTRACT. In the work, we focus on designing and analyzing a simple mathematical model of epidemic outbreaks involving vaccination in a heterogeneous population composed of two age groups. The model is based on the framework of matrix population models. It is designed to include the fundamental phenomena of interest while also making it as explicit as possible for examination using methods of real function analysis. Our aim is to examine differences between separable and non-separable mixing and answer the question, how many vaccines are needed to achieve herd immunity. Additionally, we aim to gain a better understanding of some controversies in vaccination prioritization where a superficial view could lead to misconceptions and subsequent poor decisions.

1. Motivation

During the COVID-19 crisis, we found ourselves in a situation where several types of vaccines became available in rapid succession during the ongoing pandemic [28]. Their quantity was limited, and at the national levels, it was necessary to determine the priority of vaccination across the population [30], [17], [3]. Based on the observation of more severe cases among the older population (over 60 years old) compared to the rest of the population, the prioritization of vaccination often shifted from critical infrastructure workers to age groups [9], [30], [22], [3].

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The effectiveness and safety of vaccines were tested in standard double-blind trial studies. However, due to the acute epidemiological situation, long-term observation of the vaccine's impact was not possible [26], [29], leading to various doubts about the correctness of their deployment. Many vaccine properties, protective effects, as well as some very rare adverse effects, were gradually discovered.

The scale of the epidemic at the national level often led to such high numbers of forced hospitalizations that there was a risk of exceeding the capacities of an already long-strained and exhausted health-care system. Therefore, authorities often resorted to various non-medical measures that often severely damaged the economy. With the arrival of inexpensive antigen tests, testing campaigns were launched, but the advent of vaccines and later the arrival of less deadly rapidly spreading variants marked a significant improvement in the situation.

In the vaccination campaign, there was often a media advocacy for age prioritization [30], [22].The argument put forward was that, "Vaccines protect against severe disease and hospitalization, and older people have the highest risk of hospitalization." From this, and the fact that hospitals indeed had a higher proportion of older age groups, it was deduced that older age groups should be the main recipients of the vaccine. This argument was even questionably turned into a claim that, "younger age groups should not actually get vaccinated. That the vaccine reliably helps only against severe disease and hardly prevents disease transmission, thereby accelerating the already well-documented asymptomatic spread, which is known in the case of COVID-19." Possibility that the vaccines against COVID-19 reduce symptoms but the infectivity is suppressed only leakily is presented in [26].

Claims about the negative effect of the vaccination campaign may seem reasonable at first glance, but a deeper analysis of these phenomena reveals that even incomplete protection can significantly help mitigate the epidemic.

Currently, several extensive scientific studies have confirmed the effectiveness and safety of COVID-19 vaccination [28]. It has been shown that vaccines not only provide protection against severe outcomes (hospitalization) and symptomatic cases but also have the ability to slow down the spread of the virus [25].

The effort to understand the SARS-CoV-2 pandemic is just one motivation. Another motivation for this study is the problem that lies ahead of us, which is the growing anti-vaccine movement that has been gaining strength for some time. Despite the unprecedented success of the development, production, and global distribution of COVID-19 vaccines in modern medicine, the COVID-19 crisis itself, pressure for vaccination campaigns, and the possible loss of trust in government and healthcare authorities due to chaotic crisis management could accelerate the further spread of anti-vaccine sentiment also for other disease [29].

Diseases that were nearly eradicated through vaccination may re-emerge, especially in local communities with low vaccination rates, leading to outbreaks. These diseases are often highly contagious, exhibit different courses in children and adults, and are frequently deadly. This once again emphasizes the need to understand populations as interconnected, differently vaccinated subpopulations and to study how the dynamics of subpopulations and various vaccine characteristics alter a community's local resistance to outbreaks [29].

In such a scenario, it can be assumed that whole population is fully susceptible before an outbreak, and the effectiveness of vaccines remains very stable, often lifelong.

It is evident that in epidemiology, intuition can lead to incorrect decisions. In such situations, it is not advisable to rely on intuition but to use a mathematical model to get insight in such phenomena.

Therefore, this work focuses on design and analyzing a simple discrete deterministic mathematical model capable of assessing the effects of vaccination strategy with regard to the rate of hospitalization growth. This model should be able to provide a rough answer to questions like: when should each subpopulation be vaccinated and when not, how to allocate a limited quantity of vaccines among subpopulations (what vaccination strategy to employ), and how many vaccines are needed to achieve a herd immunity of whole population?

2. Scope of work

The overall impact of the vaccine on the population (society) depends not only on its individual effectiveness but also on its distribution in space, time, and across subpopulations of varying quality (considering risk groups). We will assume that the vaccine's individual-level properties are specified (known), and we will consider a sufficiently large, spatially well-localized population with good mixing (e.g., a city). We will primarily focus on the impact of vaccine distribution among subpopulations. The model will be primarily designed to analyze the outbreak of an epidemic under current local conditions. We will pay particular attention to a short period far from the endemic state when we can neglect the decrease in the susceptible population, and the epidemic will exhibit exponential (geometric) growth. With this in mind, in the following text, by the term "vaccination strategy" we will mean precisely the distribution of vaccines among subpopulations at the moment and place of the epidemic outbreak.

For the model proposal, let us assume:

- A closed, well-mixed population (with over 10,000 individuals).
- Two age groups: people under 60 years old and people over 60 years old.

- Both groups will have defined rates of vaccination coverage, susceptibility to infection, infectivity rate, and probability of hospitalization.
- Both groups will have defined vaccine's effects: reduction in susceptibility, reduction in infectivity, reduction in the probability of hospitalization.
- Interactions of subpopulations will be determined by a 2-dim. contact matrix [8], [24].
- There is no immunity in the population due to prior infection.
- Only a limited quantity of vaccines is available.
- The vaccination campaign will take place before the outbreak of infection.
- The vaccine does not lose its effectiveness over time.

We will distinguish four subpopulations that will arise from initially dividing the entire population into two groups: individuals under 60 years old and individuals over 60 years old. Each of these groups will then be further divided into vaccinated and unvaccinated subpopulations.

The model will consist of two parts. The first part will be a model of transmission that depends on the proportional representation of these four subpopulations in the overall population, the course of the disease, the impact of the age and the vaccine on the transmission, as well as on the average contact between subpopulations. The second part will be a simple proportional hospitalization model that takes into account the severity of symptoms and the ability of the vaccine to mitigate the severity of the disease, thereby reducing the need for medical care.

To construct the model, we will use a matrix framework developed for the field of modeling of population dynamics [5], [4], [2], [23], [10]. First, we will prepare the theory of matrix models of disease transmission in a homogeneous population in the time domain and generation domain [5]. Furthermore, we will theoretically explore matrix models of disease transmission in a heterogeneous population (with separable and non-separable mixing [14], [13], [1], [12], [6]) and investigate the conditions under which results from the generation domain can be interpreted in the time domain ([19], [27]). Then, we will propose a simple parametrization of the disease course and the vaccine's impact for both age groups [16], [11]. At this point we will incorporate some specific features of COVID-19 [16], [11], [28]. As the final step of model derivation, the proposed parameters will be incorporated into the prepared theoretical framework, leading us to an explicit analytical formula for calculating the reproductive number and the stable composition of the generation.

3. Model of transmission in a homogeneous population

Let us first assume a homogeneous population without division into different subpopulations. Let the disease lasts for N days.

The course of the disease will be determined by a time-discrete reproduction function represented by the vector $f = (f_1,\ f_2,\ \ldots,\ f_n,\ \ldots,\ f_N)^T,\ f_n \in \mathbb{R}_0^+$, that specifies the average number of people infected on each day n of the disease, and a time-discrete transport function represented by the vector $t = (t_1,\ t_2,\ \ldots,\ t_n,\ \ldots,\ t_{N-1})^T,\ t_n \in (0,\ 1]$, which, for each day of the disease, determines the probability of transition of an infected individual to the next day of the disease. Furthermore, let us assume an vector of infected $v(x) = (v_1(x),\ v_2(x),\ \ldots,\ v_n(x),\ \ldots,\ v_N(x))^T$, representing the number of infected individuals for each day x of the epidemic. The temporal evolution of the model is represented by a linear transformation:

$$v(x+1) = Pv(x),$$

where P is a non-negative projection matrix. In the trivial case of an unstructured population, it will be a Leslie matrix.

$$\underbrace{\begin{pmatrix} f_1 & \ldots & f_{N-1} & f_N \\ t_1 & \ldots & 0 & 0 \\ \vdots & \ddots & \vdots & \vdots \\ 0 & \ldots & t_{N-1} & 0 \end{pmatrix}}_{P} = \underbrace{\begin{pmatrix} f_1 & \ldots & f_{N-1} & f_N \\ 0 & \ldots & 0 & 0 \\ \vdots & \ddots & \vdots & \vdots \\ 0 & \ldots & 0 & 0 \end{pmatrix}}_{F} + \underbrace{\begin{pmatrix} 0 & \ldots & 0 & 0 \\ t_1 & \ldots & 0 & 0 \\ \vdots & \ddots & \vdots & \vdots \\ 0 & \ldots & t_{N-1} & 0 \end{pmatrix}}_{T}.$$

This matrix can naturally be decomposed into the fertility matrix $F \geqslant 0$ and the transport matrix $T > 0$, where $\sum_{i=1}^{N} T_{i,j} \leqslant 1$. For a given initial vector $v(0)$, the value of the infected vector on a given day x will be determined by

$$v(x) = P^x v(0).$$

The early development of the epidemic can be characterized by the daily growth (sometimes mentioned as geometric growth rate or only simply as growth rate). For a general initial vector $v(0)$, the oscillations of $v(x)$ could occur. Due to $P \geqslant 0$ the spectrum of the matrix $P \geqslant 0$ the Perron-Frobenius theorem [15], [20] is satisfied. Let us, mark eigenvalues P, λ_n. If we will assume that greatest eigenvalue of P, $\lambda_{\max} = \max(|\lambda_n|)$ is strictly greater than the others, the oscillations will be damped. In such a case, only a transient phenomenon will occur, which will dissipate faster when the ratio of the absolute values of the largest and second largest eigenvalues is greater. As x grows, the dominant eigenvalue prevails in the limit. Therefore, the asymptotic growth rate r will be determined by the spectral radius of the matrix $\rho(P) = \lambda_{\max}$. Besides stabilizing growth,

the structure of the infected vector v_{stab} will approach to right eigenvector corresponding to this largest eigenvalue (Perron vector). In the case of $v(0) = v_{\text{stab}}$, the transition process is eliminated, and the limiting behavior is achieved immediately after the onset of the epidemic.

The value of r can be determined from the characteristic polynomial of the matrix, which can be rewritten into the form of the well-known discrete Euler--Lotka equation [5]:

$$1 = \sum_{n=1}^{N} r^{-n} f_n l_n, \tag{3.1}$$

where l_n are elements of vector $l \in (0,\ 1]^N$ what representing the survival function until the Nth day of the disease. This vector is uniquely linked to the vector of transport by the relationship:

$$l_1 = 1, \quad l_{n\,>\,1} = \prod_{j=1}^{n-1} (t_j). \tag{3.2}$$

In general, if $r \leqslant 1$, there will be no epidemic. In the opposite case, if $r > 1$, geometric growth will occur. This parameter is possible use also for comparing of severity of two different situations.

In the time domain, a new state of infected individuals for the next day is generated from the currently infected population distributed over individual days of the disease. Currently infected individuals are a mixture of new cases and cases that have aged by one day.

In addition to the time domain, it is possible to study the epidemic in the domain of successive generations (generation domain). The kth generation refers to the set formed by infected individuals who arose from a cascade of k infectious transmissions from patient zero (generation zero). Similar to the state of the epidemic in time being represented by the vector of infected individuals $v(x)$, in the generation domain, the state of the epidemic in the kth generation is represented by a vector determining the composition of generation $g(k)$. In general, this vector has the same dimension as $v(x)$.

For matrix models that are decomposable into fertility and transport matrices, it is possible to derive a relationship for calculating the so-called Next Generation Matrix (NGM) [5], [2].

$$G = F(I - T)^{-1}. \tag{3.3}$$

(I represent unitary matrix.)

Given the assumptions $F,\ T \ \geqslant\ 0$, will also hold $G \geqslant 0$. This matrix has a similar meaning in the generation domain as the projection matrix in the time domain. P can be decomposed in many ways, thus structure of G depends on matrices F and T, not P itself [7].

Analogously to evolution of the vector of infected in time domain, there is also an implicit formula for the evolution of the kth generation:

$$g(k+1) = Gg(k),$$

and similarly, there is an explicit formula for generational development:

$$g(k) = G^k g(0). \tag{3.4}$$

In the generation domain, the details of the ongoing disease are lost. This causes successive generations not to mix with each other. Thanks to this, the matrix G and also the vector $g(k)$ can be significantly reduced what simplifies some analyses.

Just as with the projection matrix in the time domain, it is also possible to introduce an assessment of the epidemic growth here with NGM in the generation domain through the average intergenerational growth rate $R = \rho(G)$ (reproduction rate). Similarly to time domain, oscillations can be expected also here, and assuming that the magnitude of largest real eigenvalue of NGM is strictly greater than the magnitude of the other eigenvalues, it will only be a transient phenomenon [20]. In such a case, the reproduction rate asymptotically stabilizes, along with the structure of the generation, which will be identical to the structure of the right eigenvector corresponding to the dominant eigenvalue of the matrix G. The transient phenomenon can be avoided by giving the zero generation a stable generation structure directly. However, if we manage to determine all eigenvalues, it will be possible to model the transient phenomenon in detail. This will prove to be significant only after introducing a heterogeneous population.

It is essential to note that if we assume a nonzero duration of the disease, despite the stabilization the next generation in time, each subsequent generation will always have a greater time variance than the one before it, which can slightly complicate the interpretation of growth between the two domains (see [19]).

If we apply the relation for NGM (3.3) to the Leslie matrix, we get:

$$G = \begin{pmatrix} \sum_{n=1}^{N} f_n \frac{l_n}{l_1} & \dots & \sum_{n=N-1}^{N} f_n \frac{l_n}{l_{N-1}} & \sum_{n=N}^{N} f_n \frac{l_n}{l_N} \\ 0 & \dots & 0 & 0 \\ \vdots & \ddots & \vdots & \vdots \\ 0 & \dots & 0 & 0 \end{pmatrix}.$$

The form of the matrix G allows us to start the generational development from the zero generation composed of infected individuals in various stages of the disease. However, typically, the zero generation consists of one patient zero or it can be an asymptotic stable distribution of generations, suppressing the transient phenomenon. Since all rows of G except the first are zero, after the first

evaluation of (3.4) from zero generation to the first, all components are zeroed out except the one representing the state in which newly infected individuals are generated. The NGM matrix G as well as the vector $g(k)$ can be reduced without losing information about the asymptotic growth. This reduction does not change the spectral radius of the matrix.

If the model contains multiple mutually generating populations of different types, the only relevant components of the vector $g(k)$ will correspond to the states in which newly infected individuals of those types are generated. Thus, every Nth row and Nth column of the matrix G will be selected, as well as every Nth component of vector $g(k)$.

If we apply these concepts to G for the Leslie matrix, we are left with a reduced matrix 1×1 whose spectral radius is directly the value of that one matrix element. Thus, the reproduction rate is determined by:

$$R = \rho(G) = \sum_{n=1}^{N} f_n l_n.$$

If we take the biological definition of the basic reproduction number as the "average number of secondary infections generated by a typical infected individual during the entire period of his infection in a fully susceptible population" [23], [7], then we can easily show that in Leslie's models, an infected individual infects, on average, $f_n l_n$ people on the nth day of the disease — this is the product of the probability that the infected person remains sick until the nth day and the average number of new infections generated on that day. Thus, over the course of the entire disease, an infected person will infect exactly $\sum_{n=1}^{N} f_n l_n$ individuals. This implies that in Leslie's model, the reproduction rate is directly interpretable as the basic reproduction number. Such interpretation is also preserved in [2], [23] and also in all extensions of the model presented in this work.

4. Model of transmission in a heterogeneous population

Let us assume a heterogeneous population divided into M subpopulations. Let the disease lasts N days, with the preliminary assumption that the course of the disease will be different for different subpopulations. The upper left indexes i, j indicates the subpopulation, and the lower right index n indicates the number of days since infection.

Let us assume the existence of fertility vectors ${}^{i,j}f \in \mathbb{R}_0^{+N}$, vectors of transports ${}^{j}t \in (0,\ 1]^{N-1}$ and vectors ${}^{j}l \in (0,\ 1]^{N}$, where $i, j \in \{1,\ \ldots, M\}$.

We construct the projection matrix of the model from simpler submatrices of the form

$$ {}^{i,j}F = \begin{pmatrix} {}^{i,j}f_1 & \dots & {}^{i,j}f_{N-1} & {}^{i,j}f_N \\ 0 & \dots & 0 & 0 \\ \vdots & \ddots & \vdots & \vdots \\ 0 & \dots & 0 & 0 \end{pmatrix}, \quad {}^{j}T = \begin{pmatrix} 0 & \dots & 0 & 0 \\ {}^{j}t_1 & \dots & 0 & 0 \\ \vdots & \ddots & \vdots & \vdots \\ 0 & \dots & {}^{j}t_{N-1} & 0 \end{pmatrix}, $$

and then

$$ \tilde{P} = \underbrace{\begin{pmatrix} {}^{1,1}F & \dots & {}^{1,M}F \\ \vdots & \ddots & \vdots \\ {}^{M,1}F & \dots & {}^{M,M}F \end{pmatrix}}_{\tilde{F}} + \underbrace{\begin{pmatrix} {}^{1}T & \dots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \dots & {}^{M}T \end{pmatrix}}_{\tilde{T}}. \tag{4.1} $$

The matrix $\tilde{P}$ is nonnegative with size $\tilde{N} = MN$. On block diagonal of $\tilde{P}$, there are submatrices with nonzero fertilities and transports (these submatrices model the persistence of populations and their self-generation). Submatrices outside the main diagonal have only nonzero fertilities (these matrices model the mutual generation of subpopulations).

If a more complex matrix model is composed of Leslie-type matrices, this model can also be naturally decomposed into a transport matrix and a fertility matrix and the approach resulting in (3.3) will be valid also here [5], [23].

$$ \tilde{G} = \tilde{F}\left(\tilde{I} - \tilde{T}\right)^{-1}. \tag{4.2} $$

After substituting (4.1) into this equation and making adjustments, we obtain

$$ \tilde{G} = \begin{pmatrix} {}^{1,1}F \cdot \left(I - {}^{1}T\right)^{-1} & \dots & {}^{1,M}F \cdot \left(I - {}^{M}T\right)^{-1} \\ \vdots & \ddots & \vdots \\ {}^{M,1}F \cdot \left(I - {}^{1}T\right)^{-1} & \dots & {}^{M,M}F \cdot \left(I - {}^{M}T\right)^{-1} \end{pmatrix}. $$

Thus $\tilde{G}$ can be understood as a matrix composed of submatrices in the form of NGMs corresponding to special Leslie matrices. Therefore, the findings from the previous chapter can be also applied to them.

$$ {}^{i,j}G = {}^{i,j}F \cdot \left(I - {}^{j}T\right)^{-1} = \begin{pmatrix} \sum_{n=1}^{N} {}^{i,j}f_n \frac{{}^{j}l_n}{{}^{j}l_1} & \dots & \sum_{n=N-1}^{N} {}^{i,j}f_n \frac{{}^{j}l_n}{{}^{j}l_{N-1}} & {}^{i,j}f_N \\ 0 & \dots & 0 & 0 \\ \vdots & \ddots & \vdots & \vdots \\ 0 & \dots & 0 & 0 \end{pmatrix}. $$

All matrices ${}^{i,j}G$ for a fixed i have all their rows zero except the first one, so all rows $(i-1)\,N+k$ (where $k \in \{2,\ \ldots\ , N\}$) of matrix $\tilde{G}$ will be zero, and for the analysis of the asymptotic reproduction rate, we will be able to remove them. Each matrix ${}^{i,j}G$ is thus reduced to a matrix 1×1 with the element

$$ {}^{i,j}G_{1,1} = \sum_{n=1}^{N} {}^{i,j}f_n \frac{{}^{j}l_n}{{}^{j}l_1} = \sum_{n=1}^{N} {}^{i,j}f_n {}^{j}l_n. $$

Therefore, the spectral radius of the NGM $\tilde{G}$ of the composite model can be obtained by calculating the spectral radius of the reduced matrix:

$$ \breve{G} = \begin{pmatrix} {}^{1,1}G_{1,1} & \ldots & {}^{1,M}G_{1,1} \\ \vdots & \ddots & \vdots \\ {}^{M,1}G_{1,1} & \ldots & {}^{M,M}G_{1,1} \end{pmatrix} = \begin{pmatrix} \sum\limits_{n=1}^{N} {}^{1,1}f_n {}^{1}l_n & \ldots & \sum\limits_{n=1}^{N} {}^{1,M}f_n {}^{M}l_n \\ \vdots & \ddots & \vdots \\ \sum\limits_{n=1}^{N} {}^{M,1}f_n {}^{1}l_n & \ldots & \sum\limits_{n=1}^{N} {}^{M,M}f_n {}^{M}l_n \end{pmatrix}, $$

$$ \rho(\tilde{G}) \;=\; \rho(\breve{G}). \tag{4.3} $$

The individual elements of the reduced matrix $\breve{G}$ can be interpreted as spectral radii of special Leslie matrices. Along with the reduction of the matrix, it is also necessary to reduce the composition vector $g(k)$. This reduced vector will be denoted $\breve{g}(k)$ in agreement with the notation of the reduced matrix.

At this stage of model derivation, further modifications and simplifications will require specifying (constraining) the shape of vectors ${}^{i,j}f$, ${}^{j}l$ or ${}^{j}t$.

From an epidemiological perspective, the current generation (vector $\breve{g}(k)$) consists of infected individuals of various types, and when the NGM is multiplied by this vector from the right, it results in scalar products of $\breve{g}(k)$ with the rows of the matrix $\breve{G}$. Thus, the characteristics of the healthy (susceptible) population affecting the generation of new infections, such as susceptibility to infection, vaccination coverage, or the protective effect of vaccines by reducing susceptibility, manifest themselves as scaling of the NGM rows. Conversely, the characteristics of the currently infected population related to the generation of new infections (such as infectivity and the protective effect by reducing infectivity) are reflected in the scaling of the NGM columns. (It corresponds to the well-known separable mixing, see [14], [12] and others.)

So there is an opportunity to separate the effects, which enable further adjustments.

For example, we can directly assume that the matrix $\breve{G}$ is separable $\breve{G}_{i,j} = a_i b_j$, i.e., it can be expressed as an outer product of vectors

$$a = (a_1, \ \dots, \ a_M)^T \quad \text{and} \qquad b = (b_1, \ \dots, \ b_M)^T.$$

$$\breve{G} = \begin{pmatrix} a_1 b_1 & \dots & a_1 b_M \\ \vdots & \ddots & \vdots \\ a_M b_1 & \dots & a_M b_M \end{pmatrix} = \begin{pmatrix} a_1 \\ \vdots \\ a_M \end{pmatrix} \cdot \begin{pmatrix} b_1 & \cdots & b_M \end{pmatrix} = ab^T. \tag{4.4}$$

By iterating the matrix, we get

$$\breve{G}^k = \breve{G} \cdot \breve{G} \ \cdots \ \breve{G} = a \underbrace{b^T a}_{R} b^T \cdots \ ab^T = aR^{k-1} b^T = R^{k-1} ab^T. \tag{4.5}$$

It means that the reproduction rate (spectral radius) R of separable $\breve{G}$ is determined by the scalar product of the vectors a and b, thus

$$R = \sum_{i=1}^{M} a_i b_i. \tag{4.6}$$

In the case of a separable model all rows are linearly dependent and the matrix $\breve{G}$ has precisely one eigenvalue different from zero, which is $\lambda = R$. Due to

$$\left(ab^T\right) a = a \left(b^T a\right) = aR,$$

the a has to be eigenvector corresponds to λ. In this case, the transient phenomenon is limited only to the first iteration, after which the vector of the composition of the generation acquires a stable structure $\breve{g}_{\text{stab}} = a/\|a\|$. Let us have the vector of the composition of subpopulations of the zeroth generation $\breve{g}(0)$. Then the explicit equation for $\breve{g}(k)$ will be

$$\begin{aligned} 2\breve{g}(1) &= \breve{G}\breve{g}(0), \\ \breve{g}(k) &= \breve{g}(1) R^{k-1}. \end{aligned} \tag{4.7}$$

In the case that $\breve{g}(0)$ is precisely one patient zero from the jth subpopulation, $\breve{g}(1)$ will be directly the jth column of matrix $\breve{G}$.

Let us now move on to the more complex non-separable case in which we consider the interaction of subpopulations based on the given contact matrix for two age groups:

$$\hat{C} = \begin{pmatrix} c_{11} & c_{12} \\ c_{21} & c_{22} \end{pmatrix}. \tag{4.8}$$

Such a matrix can result from direct sociological studies during epidemic or be modeled based on the analysis of contact patterns in various communities [8], [24].

Assume that the subpopulations are constructed by dividing the total population with a cascade of binary decisions. For example, the total population is first divided into people over 60 and under 60 years old, and then each of these groups is further divided into vaccinated and unvaccinated subgroups. Without loss of generality, the matrix $\breve{G}$ and the vector of compositions of generation $\breve{g}(k)$ can be rearranged so that, with respect to one selected characteristic (for example, age), blocks are formed in the matrix $\breve{G}$.

Subsequently, if we assume that the rate of interaction in the population is specified by just one characteristic, such as age, but is independent of vaccination, then the influence of the contact between infected and susceptible individuals from different subpopulations will manifest as scaling of the prepared blocks of this NGM matrix. So, let us introduce additional scaling parameters for contact modeling.

$$\kappa_{i,j} = \begin{cases} c_{11},\ i \in \{1,\ \dots,M/2\}, & j \in \{1,\ \dots,M/2\}, \\ c_{12},\ i \in \{1,\ \dots,M/2\}, & j \in \{M/2+1,\ \dots,M\}, \\ c_{21},\ i \in \{M/2+1,\ \dots,M\}, & j \in \{1,\ \dots,M/2\}, \\ c_{22},\ i \in \{M/2+1,\ \dots,M\}, & j \in \{M/2+1,\ \dots,M\}. \end{cases} \tag{4.9}$$

If we now apply all the ideas mentioned so far to $\breve{G}$, the elements will be

$$\breve{G}_{i,j} = a_i b_j \kappa_{i,j},$$

and the matrix will take the form

$$\breve{G} = \begin{pmatrix} a_1b_1c_{11} & \dots & a_1b_{\frac{M}{2}}c_{11} & a_1b_{\frac{M}{2}+1}c_{12} & \dots & a_1b_Mc_{12} \\ \vdots & \ddots & \vdots & \vdots & \ddots & \vdots \\ a_{\frac{M}{2}}b_1c_{11} & \dots & a_{\frac{M}{2}}b_{\frac{M}{2}}c_{11} & a_{\frac{M}{2}}b_{\frac{M}{2}+1}c_{12} & \dots & a_{\frac{M}{2}}b_Mc_{12} \\ a_{\frac{M}{2}+1}b_1c_{21} & \dots & a_{\frac{M}{2}+1}b_{\frac{M}{2}}c_{21} & a_{\frac{M}{2}+1}b_{\frac{M}{2}+1}c_{22} & \dots & a_{\frac{M}{2}+1}b_Mc_{22} \\ \vdots & \ddots & \vdots & \vdots & \ddots & \vdots \\ a_Mb_1c_{21} & \dots & a_Mb_{\frac{M}{2}}c_{21} & a_Mb_{\frac{M}{2}+1}c_{22} & \dots & a_Mb_Mc_{22} \end{pmatrix}. \tag{4.10}$$

This matrix can be decomposed into the product of three matrices

$$\breve{G} = \underbrace{\begin{pmatrix} a_1 & & 0 \\ & \ddots & \\ 0 & & a_M \end{pmatrix}}_{A} \underbrace{\begin{pmatrix} c_{11} & \dots & c_{11} & c_{12} & \dots & c_{12} \\ \vdots & \ddots & \vdots & \vdots & \ddots & \vdots \\ c_{11} & \dots & c_{11} & c_{12} & \dots & c_{12} \\ c_{21} & \dots & c_{21} & c_{22} & \dots & c_{22} \\ \vdots & \ddots & \vdots & \vdots & \ddots & \vdots \\ c_{21} & \dots & c_{21} & c_{22} & \dots & c_{22} \end{pmatrix}}_{C} \underbrace{\begin{pmatrix} b_1 & & 0 \\ & \ddots & \\ 0 & & b_M \end{pmatrix}}_{B}.$$

From theory [15], [18], we know that if we have the spectrum of the product of several matrices in a specified order, then after a cyclic permutation of these matrices in the product, we obtain a matrix that is similar, and its spectrum is the same as that of the original matrix. Therefore, as a consequence, we have $\rho(ACB) = \rho(CBA)$. If we multiply the matrices in a new order, we obtain

$$\breve{G}_{\text{rot}} = CBA = \begin{pmatrix} a_1b_1c_{11} & \dots & a_{\frac{M}{2}}b_{\frac{M}{2}}c_{11} & a_{\frac{M}{2}+1}b_{\frac{M}{2}+1}c_{12} & \dots & a_Mb_Mc_{12} \\ \vdots & \ddots & \vdots & \vdots & \ddots & \vdots \\ a_1b_1c_{11} & \dots & a_{\frac{M}{2}}b_{\frac{M}{2}}c_{11} & a_{\frac{M}{2}+1}b_{\frac{M}{2}+1}c_{12} & \dots & a_Mb_Mc_{12} \\ a_1b_1c_{21} & \dots & a_{\frac{M}{2}}b_{\frac{M}{2}}c_{21} & a_{\frac{M}{2}+1}b_{\frac{M}{2}+1}c_{22} & \dots & a_Mb_Mc_{22} \\ \vdots & \ddots & \vdots & \vdots & \ddots & \vdots \\ a_1b_1c_{21} & \dots & a_{\frac{M}{2}}b_{\frac{M}{2}}c_{21} & a_{\frac{M}{2}+1}b_{\frac{M}{2}+1}c_{22} & \dots & a_Mb_Mc_{22} \end{pmatrix}.$$

In this new matrix, it can be noticed that all rows within the width of a single block are the same. This means that $\breve{G}_{\text{rot}}$ has at least $M-2$ zero eigenvalues in its spectral decomposition.

If we start evolving $\breve{g}(k+1) = \breve{G}\breve{g}(k)$ by any nonzero vector $\breve{g}(0)$, after the first iteration, the elements corresponding to the same rows will be the same. After the following iterations and all subsequent ones, we will obtain vectors that will have the same values on elements corresponding to the same rows. This means that the same rows can be replaced with a single row. Since the matrix should be square to allow its iterated powering, it is necessary to replace the corresponding columns with one column in such a way that the total number of newly generated individuals in the replacement row remains the same as in the original ones. This can be achieved by replacing the corresponding columns with their sum.

In this way, the matrix $\breve{G}_{\mathrm{rot}}$ can be reduced to the matrix $\hat{G} \in \mathbb{R}^{2\times 2}$:

$$\hat{G}=\begin{pmatrix} a_1b_1c_{11}+\cdots+a_{M/2}b_{M/2}c_{11},\ a_{M/2+1}b_{M/2+1}c_{12}+\cdots+a_Mb_Mc_{12} \\ a_1b_1c_{21}+\cdots+a_{M/2}b_{M/2}c_{21},\ a_{M/2+1}b_{M/2+1}c_{22}+\cdots+a_Mb_Mc_{22} \end{pmatrix}, \tag{4.11}$$

whose two eigenvalues complete the spectral decomposition of the original matrix $\breve{G}_{\mathrm{rot}}$. Since all the other eigenvalues are zero, it follows that the spectral radius is $\rho(\breve{G}) = \rho(\hat{G})$.

By introducing the substitution

$$X = a_1b_1+\cdots+a_{M/2}b_{M/2} \quad \text{and} \quad Y = a_{M/2+1}b_{M/2+1}+\cdots+a_Mb_M, \tag{4.12}$$

we can simplify it to the trivial form

$$\hat{G} = \begin{pmatrix} c_{11}X & c_{12}Y \\ c_{21}X & c_{22}Y \end{pmatrix}, \tag{4.13}$$

whose eigenvalues can be obtained as roots of the characteristic polynomial.

$$\begin{aligned} \lambda_\pm &= \mathrm{root}\begin{vmatrix} c_{11}X-\lambda & c_{12}Y \\ c_{21}X & c_{22}Y-\lambda \end{vmatrix} \\ &= \frac{1}{2}\left(c_{11}X+c_{22}Y \pm \sqrt{(c_{11}X+c_{22}Y)^2-4XY\,(c_{11}c_{22}-c_{12}c_{21})}\right) \\ &= \frac{1}{2}\left(c_{11}X+c_{22}Y \pm \sqrt{(c_{11}X-c_{22}Y)^2+4XYc_{12}c_{21}}\right). \end{aligned} \tag{4.14}$$

Of course, the spectral radius will be the larger of these two values. Since all parameters are real and non-negative, $\rho(\breve{G}) = \lambda_+$. Furthermore, it can be noticed that if $c_{12} = 0$ or $c_{21} = 0$, then $\hat{G}$ is reducible and $\lambda_+ = \max(c_{11}X,\ c_{22}Y)$.

In irreducible case

$$c_{12} \neq 0 \wedge c_{21} \neq 0 \wedge X \neq 0 \wedge Y \neq 0,$$

the eigenvector $\hat{g}_\pm$ corresponding to eigenvalues $\lambda_\pm$ will be

$$\begin{aligned} \hat{g}_\pm &= (1,\ \Psi_\pm)^T, \\ \Psi_\pm &= \frac{\lambda_\pm - c_{11}X}{c_{12}Y}. \end{aligned} \tag{4.15}$$

If we know eigenvalues, we can determine the corresponding right eigenvectors of the original matrix $\breve{G}$ by solving the system of equations $\breve{G}\breve{g}_\pm = \lambda_\pm\breve{g}_\pm$. With some effort, it can be found that the vectors satisfying such system of equations have the form

$$\breve{g}_\pm = \left(a_1,\ \ldots,\ a_{M/2},\ \Psi_\pm a_{M/2+1},\ \ldots,\ \Psi_\pm a_M\right)^T. \tag{4.16}$$

The sought reproductive number will be $R = \rho(\breve{G}) = \lambda_+$ and the stable generation structure will be determined by $\breve{g}_{\text{stab}} = \breve{g}_+/\|\breve{g}_+\|$.

To study the transient behavior of the generation composition, knowledge of the spectrum of the matrix $\breve{G}$ can be utilized. Assuming that $\breve{G} > 0$ and $\lambda_+ > \lambda_-$, the matrix $\breve{G}$ will be diagonalizable.

Let us consider an arbitrary nonnegative column vector representing the composition of subpopulations of the zeroth generation $\breve{g}(0)$. If we multiply the matrix from the right by this vector, we obtain a vector in the form

$$\breve{g}(1) = \Lambda_1\big(a_1,\ \dots\ ,\ a_{M/2},\ \Psi_1 a_{M/2+1},\ \dots\ ,\ \Psi_1 a_M\big)^T, \quad \text{where} \quad \Lambda_1, \Psi_1 \in \mathbb{R}^+.$$

The structure of the vector will remain the same even for $\breve{g}(k)$, $k > 1$. Thus we will have

$$\breve{g}(k) = \Lambda_k\big(a_1,\ \dots\ ,\ a_{M/2},\ \Psi_k a_{M/2+1},\ \dots\ ,\ \Psi_k a_M\big)^T. \tag{4.17}$$

The transition phenomenon from the second generation will depend solely on the evolution of the parameters Λ_k, Ψ_k. From the shape of the vector $\breve{g}(1)$, we obtain

$$\Lambda_1 = \frac{\breve{g}_1(1)}{a_1} \quad \text{and} \quad \Psi_1 = \frac{\breve{g}_{M/2+1}(1)}{a_{M/2+1}\Lambda_1} = \frac{a_1}{a_{M/2+1}}\frac{\breve{g}_{M/2+1}(1)}{\breve{g}_1(1)}.$$

If we are able to find parameters $\Lambda_+,\ \Lambda_-$ such that

$$\breve{g}(1) = \Lambda_+\lambda_+\breve{g}_+ + \Lambda_-\lambda_-\breve{g}_-, \tag{4.18}$$

then for the kth generation

$$\breve{g}(k) = \breve{G}^{k-1}\breve{g}(1) = \Lambda_+{\lambda_+}^k\breve{g}_+ + \Lambda_-{\lambda_-}^k\breve{g}_-. \tag{4.19}$$

By substituting known values $\lambda_+,\ \lambda_-$ and expressing equation (4.18) for the first and $M/2+1$th element of $\breve{g}(1)$, $\breve{g}_+, \breve{g}_-$, we obtain two equations with two unknowns $\Lambda_+,\ \Lambda_-$:

$$\Lambda_1 a_1 = \Lambda_+\lambda_+ a_1 + \Lambda_-\lambda_- a_1,$$

$$\Lambda_1\Psi_1 a_{M/2+1} = \Lambda_+\lambda_+\Psi_+ a_{M/2+1} + \Lambda_-\lambda_-\Psi_- a_{M/2+1}.$$

Solving it, we get

$$\Lambda_+ = \frac{\Lambda_1\,(\Psi_1 - \Psi_-)}{\lambda_+\,(\Psi_+ - \Psi_-)}, \qquad \Lambda_- = \frac{\Lambda_1\,(\Psi_+ - \Psi_1)}{\lambda_-\,(\Psi_+ - \Psi_-)}.$$

Upon substituting the found values of $\Lambda_+,\ \Lambda_-$ into (4.19), we obtain the expression for the kth generation:

$$\breve{g}(k) = \Lambda_1\frac{\Psi_1 - \Psi_-}{\Psi_+ - \Psi_-}{\lambda_+}^{k-1}\breve{g}_+ + \ \Lambda_1\frac{\Psi_+ - \Psi_1}{\Psi_+ - \Psi_-}{\lambda_-}^{k-1}\breve{g}_-. \tag{4.20}$$

From this equation, through the first and $M/2+1$-th elements of the vectors $\breve{g}_+$ and $\breve{g}_-$, we can determine an explicit relationship for $\Lambda_k,\ \Psi_k$:

$$\Lambda_k = \frac{\breve{g}_1(k)}{a_1} = \Lambda_1 \frac{(\Psi_1 - \Psi_-)\,{\lambda_+}^{k-1} + (\Psi_+ - \Psi_1)\,{\lambda_-}^{k-1}}{\Psi_+ - \Psi_-},$$

$$\Psi_k = \frac{\breve{g}_{M/2+1}(k)}{\Lambda_k a_{M/2+1}} = \frac{\Psi_+ (\Psi_1 - \Psi_-)\,{\lambda_+}^{k-1} + \Psi_- (\Psi_+ - \Psi_1)\,{\lambda_-}^{k-1}}{(\Psi_1 - \Psi_-)\,{\lambda_+}^{k-1} + (\Psi_+ - \Psi_1)\,{\lambda_-}^{k-1}}.$$

Now, it is straightforward to deduce that under assumption $\lambda_+ > \lambda_-$, as k increases, Λ_{k+1}/Λ_k will approach λ_+, and Ψ_k will approach Ψ_+.

At this point, we are able to explicitly describe the transient process, the asymptotic reproduction rate, and the structure of the stable composition of the generation for separable and non-separable model. Now, let us take a closer look at the relations between the generation domain and the time domain.

5. Relationship between the generation domain and the time domain

We assume that in the time domain, the asymptotic behavior will be governed by the dominant eigenvalue of the nonnegative projection matrix (4.1), which represents the growth rate of newly infected individuals. In the generation domain, the asymptotic behavior will be governed by the dominant eigenvalue of NGM (4.3), which represents reproduction rate or the reproduction number.

Using the reproduction number R, it is possible to test whether an epidemic will occur or be suppressed. $R > 1$ indicates that an epidemic will occur, while $R \leqslant 1$ indicates the opposite, that there will be no epidemic outbreak. The threshold value $R = 1$ occurs at same moment as the growth rate $r = 1$. In general, when course of the disease is changing, it is not always the case that an increase in R necessarily leads to an increase in r. Therefore, if we can calculate R for two different scenarios in the generation domain, it is generally not possible to determine which situation is worse in terms of the epidemic's severity based solely on their comparison. For a broader discussion, we recommend [27], where the authors address this issue for continuous models, however their findings are applicable to discrete ones as well.

Due to this, we have decided to explore the conditions under which comparing R could replace the comparison of the growth rates of newly infected individuals. If we will assume that the development of number of newly infected proportionally affects the number of hospitalizations the comparison of the reproduction rates (in the generation domain) would resolve also comparison of growth rates of hospitalizations. This is one of the main objectives of the work.

Similar to previous chapters, we will first focus on the case of a simple Leslie model and then move on to a complex model for a heterogeneous population.

If we normalize the average daily increments of new infections caused by an infected person by the number of transmission that this infected person causes throughout the entire duration of the disease (which is the reproduction number $R = \sum_{n=1}^{N} f_n l_n$), we obtain the generation time distribution:

$$w_n = f_n l_n \Big/ \sum_{n=1}^{N} f_n l_n = f_n l_n / R. \tag{5.1}$$

Using Euler-Lotka equation (3.1) and the distribution w, we can determine the relationship between the growth rate and the reproduction number:

$$R = \left(\sum_{n=1}^{N} r^{-n} w_n \right)^{-1}. \tag{5.2}$$

From this equation it can be demonstrated that if w is conserved then this transformation is monotonic.

$$\begin{aligned} \frac{dR}{dr} &= \frac{d}{dr} \left(\sum_{n=1}^{N} r^{-n} w_n \right)^{-1} \\ &= -\left(\sum_{n=1}^{N} r^{-n} w_n \right)^{-2} \sum_{n=1}^{N} -n r^{-n-1} w_n = \left(\sum_{n=1}^{N} r^{-n} w_n \right)^{-2} \sum_{n=1}^{N} n r^{-n-1} w_n, \end{aligned} \tag{5.3}$$

$$r > 0,\ w_n > 0 \ \Rightarrow \ \sum_{n=1}^{N} n r^{-n-1} w_n > 0 \ \Rightarrow \ \frac{dR}{dr} > 0 \ \Rightarrow \ R \uparrow \Leftrightarrow r \uparrow .$$

Due to monotonicity it can be also easily shown that $r = 1 \Leftrightarrow R = 1$.

Now let us move on to a heterogeneous population. Assume a matrix of constants $E = M \times M$ with elements $e_{i,j} \geqslant 0$ and assume that

$$^{i,j} f_n = e_{i,j} f_n \quad \text{and} \quad ^{j} l_n = l_n.$$

Then, the elements of NGM (4.3) can be written in the form

$$\breve{G}_{i,j} = \sum_{n=1}^{N} {}^{i,j} f_n \, {}^{j} l_n = e_{i,j} \sum_{n=1}^{N} f_n l_n.$$

In this case, it will be possible to factor out $\sum_{n=1}^{N} f_n l_n$ from the matrix. Since it is a constant, the spectral radius of this matrix will be

$$\rho(\breve{G}) = \rho(E) \sum_{n=1}^{N} f_n l_n.$$

Therefore,

$$R = \rho\,(E) \sum_{n=1}^{N} f_n l_n. \tag{5.4}$$

Furthermore, $\breve{G}$ and E share the same normalized eigenvector corresponding to the largest eigenvalue, so $\breve{g}_{\text{stab}}$ can be obtained directly from E.

Now, let us apply the same assumptions to a model of a heterogeneous population in the time domain.

For a heterogeneous population, we assume a vector of infected individuals in the form $\tilde{v} = \left({}^{1}\tilde{v}_1,\ \ldots\ , {}^{1}\tilde{v}_N,\ \ldots\ , {}^{M}\tilde{v}_1,\ \ldots\ , {}^{M}\tilde{v}_N\right)^T$. The upper left index indicates the subpopulation, and the lower right index indicates the number of days since infection.

The eigenvalues of the projection matrix for a heterogeneous population (4.1) shall satisfy the equation $\tilde{P}\tilde{v}_{\text{stab}} = \lambda\tilde{v}_{\text{stab}}$. Expanding this matrix equation yields N algebraic equations for each $i \in \{1,\ \ldots\ ,\ M\}$.

$$\sum_{j=1}^{M}\sum_{n=1}^{N} {}^{j}\tilde{v}_n e_{i,j} f_n = {}^{i}\tilde{v}_1 \lambda\,,$$

$${}^{i}\tilde{v}_1 l_2 = {}^{i}\tilde{v}_2 \lambda\,, \qquad {}^{i}\tilde{v}_2 l_3 = {}^{i}\tilde{v}_3 \lambda\ \cdots\ {}^{i}\tilde{v}_{N-1} l_N = {}^{i}\tilde{v}_N \lambda\,.$$

Each ${}^{m}\tilde{v}_n$ can be expressed in terms of ${}^{m}\tilde{v}_1$ and substituted into the first equation. After this adjustment, we obtain one equation for each $i \in \{1,\ \cdots\ ,\ M\}$ in the form

$$\sum_{j=1}^{M}\sum_{n=1}^{N} {}^{j}\tilde{v}_1 e_{i,j} f_n l_n \lambda^{-n} = {}^{i}\tilde{v}_1.$$

It can be noticed that the terms in the composite sum depend either on one summation index or the other, allowing us to write the sum as a product of sums. In this way, we obtain M equations in the form:

$$\left(\sum_{j=1}^{M} {}^{j}\tilde{v}_1 e_{i,j}\right) \underbrace{\left(\sum_{n=1}^{N} f_n l_n \lambda^{-n}\right)}_{\breve{\lambda}^{-1}} = {}^{i}\tilde{v}_1.$$

This system of equations can be rewritten in matrix form $E\breve{v} = \breve{\lambda}\breve{v}$, where $\breve{v} = \left({}^{1}v_1,\ \ldots,\ {}^{M}v_1\right)^T$ can be interpreted as the eigenvector and $\breve{\lambda}$ as the eigenvalue of the matrix E. Since we assume that both P and E are non-negative matrices with a dominant eigenvalue strictly greater than the others, we can write

$$\lambda = \rho(P) = r \quad \text{and} \quad \breve{\lambda} = \rho(E).$$

Therefore, the spectral radius of the matrix E is:

$$\rho(E) = \left(\sum_{n=1}^{N} f_n l_n r^{-n} \right)^{-1}. \tag{5.5}$$

Substituting (5.5) into (5.4) and using the definition for the distribution of the generation time w_n (5.1), we obtain, after adjustments,

$$R = \left(\sum_{n=1}^{N} w_n r^{-n} \right)^{-1}.$$

This is equivalent to equation (5.2), and thus, the procedure (5.3) applies to it. This means that in the case of a heterogeneous population model, if the distribution of the generation time does not depend on the subpopulation type (can be factored out before the NGM matrix) and remains unchanged, will r monotonically increase with respect to R ($R \uparrow \Leftrightarrow r \uparrow$).

Considering that both $\breve{v}$ and $\breve{g}_{\text{stab}}$ are eigenvectors corresponding to the largest eigenvalue of the matrix E, the composition of both newly infected and currently infected subpopulations will approach the stable generation structure $\breve{g}_{\text{stab}}$ over time. If we use this structure as the probability distribution of subpopulation occurrence in the zeroth generation, the transient phenomenon will be eliminated, and both newly infected individuals and currently infected individuals will exhibit the predetermined stable composition of subpopulations immediately after the outbreak of the epidemic.

It's worth to mention that if the distribution of the generation time were different for different columns of the matrix $\breve{G}$, variability in the coefficients $e_{i,j}$ would affect the distribution of the generation time for the entire population, and the monotonicity of r with respect to R (and other results) could be violated. This should be taken into account when parameterizing the transmission model.

6. Model parametrization

We assume the entire population is divided by age into people over 60 and under 60 years old, and by vaccination status into unvaccinated and vaccinated individuals. This results in four subpopulations created by combining these two characteristics. We consider the subpopulation "unvaccinated over 60 years" as the reference and it will be represented by the first element of the vector $\breve{g}(k)$ (index 1). The second element of the vector (index 2) corresponds to the subpopulation "vaccinated over 60 years." The third element of the vector (index 3) will represent the subpopulation "unvaccinated under 60 years," and the last fourth element of the vector (index 4) will belong to "vaccinated under 60 years".

We assume a respiratory disease similar to COVID-19 [16], [11], [26]. We want the model to be easily interpretable and parameterizable. For COVID-19, we know that immediately after infection, the infected person is non-infectious and without clinical symptoms. This period is referred to as the exposure phase (E). This is followed by the preclinical phase ($\mathrm{I_{Pc}}$), during which the infected person is infectious but still without symptoms, and only after that does the infectious phase with symptoms ($\mathrm{I_C}$) occur. By its end, the infected person becomes non-infectious again. In the case of COVID-19, the infection primarily spreads through asymptomatic transmission. In addition to transmissions that occurred during the preclinical phase, it is appropriate to assume the existence of less infectious but fully asymptomatic cases which pass through a single subclinical phase ($\mathrm{I_{Sc}}$) instead of the preclinical and clinical phases.

We will evaluate the epidemiological situation based solely on the reproductive number R obtained as the spectral radius of NGM (4.3). The individual elements of this matrix $\breve{G}_{i,j} = \sum_{n=1}^{N} {}^{i,j}f_n {}^{j}l_n$ depend on reproduction (fertility) ${}^{i,j}f_n$ and the survival function ${}^{j}l_n$. Therefore, we will introduce a simple parametric model for these functions and demonstrate how the parameters of this model are related to age and vaccination status, of both the infected and susceptible populations, so this shows how such properties influence the individual elements of the matrix $\breve{G}$.

The model will depend on the following parameters:

t_{E} – The day of infectivity onset,

t_{S} – The day of symptoms onset,

t_{R} – The day of recovery,

p – Probability of transmission in contact of symptomatic and susceptible,

κ – The avg. num. of contacts per day for a person without symptoms,

d – The relative reduct. in infectiousness of asymptomatic to symptomatic,

q – The probability of asymptomatic case development,

s – The fraction of symptomatic who remain active after symptoms onset,

where,

$$t_{\mathrm{E}} \leq t_{\mathrm{S}} < t_{\mathrm{R}}, \qquad t_{\mathrm{Pc}} = t_{\mathrm{S}} - t_{\mathrm{E}} \quad \text{and} \quad t_{\mathrm{C}} = t_{\mathrm{R}} - t_{\mathrm{S}}.$$

In our simplified model, fertility $f(n)$ will have the shape of a discrete rectangular function that takes a value

$$f(n) = \begin{cases} \kappa p[(1-q) + dq], & n \in \{t_{\mathrm{E}}, \ldots, t_{\mathrm{R}} - 1\}, \\ 0, & \text{otherwise.} \end{cases} \tag{6.1}$$

The survival function $l(n)$ will have a stepwise shape, taking a value of 1 within the interval $n \in \{-\infty, \ldots, t_{\mathrm{S}} - 1\}$ and a value of $s(1-q)+q$ within the interval $n \in \{t_{\mathrm{S}}, \ldots, +\infty\}$. This value represents the probability of an infected individual remaining in the active population after a portion of symptomatic cases self-isolate. (The survival function should change to 0 at t_{R}, but given that reproduction also changes to 0 on that day, the result will be the same.)

By substituting $f(n)$ and $l(n)$ into the equation for $\breve{G}_{i,j}$ (see (4.3)), we obtain:

$$
\begin{aligned}
\breve{G}_{i,j} &= \sum_{n=1}^{N} {}^{i,j}f_n \, {}^{j}l_n = \sum_{n=t_{\mathrm{E}i,j}}^{t_{\mathrm{S}j}-1} \overbrace{\kappa_{i,j} p_{i,j} \left[(1-q_j) + d_{i,j} q_j\right]}^{{}^{i,j}f_n} \cdot \overbrace{1}^{{}^{j}l_n} \\
&\quad + \sum_{n=t_{\mathrm{S}j}}^{t_{\mathrm{R}i,j}-1} \overbrace{\kappa_{i,j} p_{i,j} \left[(1-q_j) + d_{i,j} q_j\right]}^{{}^{i,j}f_n} \cdot \overbrace{\left(s_j(1-q_j) + q_j\right)}^{{}^{j}l_n} \\
&= \kappa_{i,j} p_{i,j} \left[(1-q_j) + d_{i,j} q_j\right] \left(t_{\mathrm{S}j} - t_{\mathrm{E}i,j}\right) \\
&\quad + \kappa_{i,j} p_{i,j} \left[(1-q_j) + d_{i,j} q_j\right] \left(s_j(1-q_j) + q_j\right) \left(t_{\mathrm{R}i,j} - t_{\mathrm{S}j}\right) \\
&= \kappa_{i,j} p_{i,j} \underbrace{\left[(1-q_j) + d_{i,j} q_j\right] \left[\left(t_{\mathrm{S}j} - t_{\mathrm{E}i,j}\right) + \left(s_j(1-q_j) + q_j\right) \left(t_{\mathrm{R}i,j} - t_{\mathrm{S}j}\right)\right]}_{z_{i,j}} \\
&= \kappa_{i,j} p_{i,j} z_{i,j}. \qquad (6.2)
\end{aligned}
$$

(Parameters t_{S}, s, and q appear in the expression ${}^{j}l_n$ and are therefore dependent only on j. Other parameters, on which ${}^{j}l_n$ does not depend, can vary in i and also in j.)

As you can see, the model of element of the NGM matrix $\breve{G}$ can be expressed as the product of individual influences.

Now, it is necessary to map parameters to the structure of NGM $\breve{G}$ of the separable model (4.4), which uses a_i and b_j, or to the structure of the non-separable model (4.10), which uses a_i, b_j and the values of c_{11}, c_{12}, c_{21}, c_{22} (see (4.8)). Some influences can be extracted from the matrix. The product of these extracted constants will be denoted as R_{ref}.

In the matrix model, the properties of the non-infected (susceptible) population are reflected in the rows (in the parameters a_i), while the properties of the infected population are reflected in the columns (in the parameters b_j). First, we will propose the basic structure of a_i, b_j, and as we proceed with additional influences, we will gradually expand these parameters with additional corrections.

For the susceptible population, the essential factor is the resistance to infection. For the infected population, it is the level of infectivity. With vaccination,

the infectivity of the infected population should decrease, and the resistance of the susceptible population should increase.

$p_{i,j}$ is a direct parameter of the model $f(n)$, see (6.1), and can be divided into the product of a reference value p (which corresponds to the unvaccinated population over 60 years old) and corrections due to vaccination α and age γ for the susceptible population, and corrections due to vaccination β and age δ for the infected population. Assuming that the reference value will be the maximum, we have $\alpha, \beta, \gamma, \delta \in [0, 1]$. The value p will appear in all matrix elements and can be extracted.

In the case of b_j, the first index corresponds to the reference subpopulation, so $b_1 = 1$. The second subpopulation is only vaccinated compared to the reference, so $b_2 = \beta$. The third subpopulation is only younger than the reference, so $b_3 = \delta$, and the fourth subpopulation is both younger and vaccinated than the reference, so $b_4 = \beta\delta$. Like b_j, the coefficients in a_i will have the first index corresponding to the reference subpopulation, so $a_1 = 1$. The value $a_2 = \alpha$, $a_3 = \gamma$ and fourth subpopulation is both younger and vaccinated than the reference, so $a_4 = \alpha\gamma$. At this point, we have proposed the basic structure a_i, b_j.

In addition, in a_i, we can also consider the different effects of the vaccine on age groups by adding a coefficient σ for reducing susceptibility due to vaccination at an older age. In this case, $a_2 = \alpha\sigma$.

$z_{i,j}$ can be influenced by both the susceptible and infected populations. However, it is not a direct parameter of the model, see (6.2), so it cannot be trivially decomposed into a product of influences. To maintain the separable model scheme, it is necessary to keep this parameter variable only with respect to the matrix columns. The possibility of incorporating z_j into the coefficients b_j significantly enriches the behavior of the proposed model. On the other hand, all parameters influencing the shape of the generation time distribution (except scaling) are concentrated inside of z_j. If we want to further use the results obtained in the chapter 5 we need to prevent this variability. Therefore, we will assume that z_j will not change, i.e., $z_j = z$, and that it can be extracted from the matrix.

For the coefficient in front of the matrix, we will obtain the product of the reference transmission probability p and the coefficient z, i.e., the constant

$$R_{\text{ref}} = p\left[(1-q) + dq\right]\left[(t_{\text{S}} - t_{\text{E}}) + (s(1-q)+q)\,(t_{\text{R}} - t_{\text{S}})\right]. \tag{6.3}$$

Now let us take a closer look at parameterizing the vaccination strategy, which will influence the probability of contact between vaccinated and unvaccinated (susceptible) individuals within different age groups.

Assume that the number of infected individuals is negligible compared to the size of the entire population, and there won't be enough vaccines to vaccinate the entire population. This leads to the problem of how to distribute them among age groups.

The vaccination strategy will be fully determined by three parameters:

- the proportion of people over 60 years old in the total population

$$\zeta = N_{60+}/N_{\text{all}},$$

- the vaccination coverage of people aged 60 and over

$$\Omega_1 = V_{60+}/N_{60+} \in [0,\ 1],$$

- the vaccination coverage of people under 60 years old

$$\Omega_2 = V_{60-}/N_{60-} \in [0,\ 1].$$

For the purposes of this work, it will sometimes be convenient to use another triplet, namely

$$\zeta, \varphi = \Omega_1,$$

and the overall vaccination coverage

$$\omega = V_{\text{all}}/N_{\text{all}}.$$

If we express ω through the parameters ζ, $\varphi = \Omega_1$ and Ω_2, we obtain

$$\omega = \frac{V_{\text{all}}}{N_{\text{all}}} = \left(1 - \frac{N_{60+}}{N_{\text{all}}}\right)\frac{V_{60-}}{N_{60-}} + \frac{N_{60+}}{N_{\text{all}}}\frac{V_{60+}}{N_{60+}} = (1-\zeta)\,\Omega_2 + \zeta\Omega_1.$$

Now, assuming that no one is vaccinated from the younger population $\Omega_2 = 0$, we get the minimum value $\underline{\omega} = \zeta\varphi$, on the contrary, if whole younger population is vaccinated $\Omega_2 = 1$, we get the maximum value

$$\overline{\omega} = \zeta\varphi + 1 - \zeta.$$

Therefore,

$$\omega \in [\underline{\omega},\ \overline{\omega}] = [\varphi\zeta,\ \varphi\zeta + 1 - \zeta] \subseteq [0,\ 1]\,. \tag{6.4}$$

Based on the parameters ζ, ω, φ we can reversely express the conditional probabilities of occurrence of vaccinated in each age groups:

$$\begin{aligned} P\,(\text{vaccinated}|\text{age} \geqslant 60) &= \Omega_1 = V_{60+}/N_{60+} = \varphi, \\ P\,(\text{vaccinated}|\text{age} < 60) &= \Omega_2 = \frac{V_{60-}}{N_{60-}} = \frac{\frac{V_{\text{all}}}{N_{all}} - \frac{V_{60+}}{N_{60+}}\frac{N_{60+}}{N_{\text{all}}}}{-\frac{N_{60+}}{N_{\text{all}}}} = \frac{\omega - \varphi\zeta}{1-\zeta}. \end{aligned} \tag{6.5}$$

Using the complements Ω_1 and Ω_2, we can then determine the conditional probabilities of occurrence of unvaccinated: $P\,(\text{unvaccinated}|\text{age} \geq 60) = 1 - \Omega_1$, $P\,(\text{unvaccinated}|\text{age} < 60) = 1 - \Omega_2$. At this point, we have not yet determined the a priori probabilities of encounters between different age groups. The problem of how to determine them is closely related to modeling contacts between age groups.

Since we have two variants of the heterogeneous population model available: separable and non-separable, two approaches are possible: κ is a direct parameter of the model $f(n)$, see (6.1), which allows us to decompose it into the influence of the infectious and susceptible populations. This approach would lead to a separable model (4.4). Similarly, it is possible to map it by blocks and determine the average numbers of contacts for the elements $\breve{G}$ from an externally specified contact matrix $\hat{C}$ using (4.9). This procedure would lead us to a non-separable model (4.10). The structure of the non-separable model is designed precisely to allow the utilization of realistically available contact parameters from sociological studies [8], [24], while preserving the possibilities of a separable model for other phenomena.

As a first approach, the ratio of the number of young and old active people to the total number of active people during the pandemic can be used as a prior probability. However, as an initial estimate, it is also possible to use the ratio of people over and under 60 years to the total population.

$$\Theta_1 = P(\text{age} \geq 60) = \frac{N_{60+}}{N_{\text{all}}} = \zeta, \quad \Theta_2 = P(\text{age} < 60) = \frac{N_{60-}}{N_{\text{all}}} = 1 - \zeta.$$

As a consequence, the overall probabilities of occurrence for individual subpopulations are obtained as the product of these a priori and the conditional probabilities (6.5). Such overall probabilities determine the occurrence of the susceptible (healthy) population and thus will scale the individual rows of the matrix $\breve{G}$. For this reason, they can be considered as additional scaling coefficients in a_i.

Furthermore, it should be noted that each type of infected individual may encounter a different number of people on average during the day. The number of contacts of the older population is denoted as c_1 and that of the younger population as c_2. It is necessary to assume that these values, as well as Θ_1 and Θ_2, do not reflect the normal state of the community but rather the state during an ongoing epidemic. If the community responds to the outbreak by closing schools or restaurants or advises the population over 60 to minimize contact with others, these changes from usual behavior should be reflected in these parameters. In these parameters, it is also possible to incorporate the impact of psychological phenomena, such as a reduction in contact due to fear of infection or an increase in contact due to trust in the protective effect of the vaccine. In the case of vaccines with low efficacy, this allows for modeling the effect of false assurance. An analysis of these influences and their impact on the individual coefficients, however, is beyond the scope of this work. Regardless of that, the average number of contacts c_1 and c_2 are a property of the infected populations and they will therefore appear as additional scaling of the columns of the matrix $\breve{G}$. They can also be considered as additional scaling coefficients in b_j.

In such a case, the NGM matrix will take the form

$$\breve{G} = R_{\text{ref}} \begin{pmatrix} c_1\Theta_1(1-\Omega_1) & c_1\Theta_1(1-\Omega_1)\beta & c_2\Theta_1(1-\Omega_1)\delta & c_2\Theta_1(1-\Omega_1)\beta\delta \\ c_1\Theta_1\Omega_1\alpha\sigma & c_1\Theta_1\Omega_1\beta\alpha\sigma & c_2\Theta_1\Omega_1\delta\alpha\sigma & c_2\Theta_1\Omega_1\beta\delta\alpha\sigma \\ c_1\Theta_2(1-\Omega_2)\gamma & c_1\Theta_2(1-\Omega_2)\beta\gamma & c_2\Theta_2(1-\Omega_2)\delta\gamma & c_2\Theta_2(1-\Omega_2)\beta\delta\gamma \\ c_1\Theta_2\Omega_2\alpha\gamma & c_1\Theta_2\Omega_2\beta\alpha\gamma & c_2\Theta_2\Omega_2\delta\alpha\gamma & c_2\Theta_2\Omega_2\beta\delta\alpha\gamma \end{pmatrix}. \tag{6.6}$$

(The meaning of all basic parameters of model and their ranges is summarized in Table 1.)

The matrix $\breve{G}$ is separable $\breve{G} = ab^T$ (see (4.4)),

$$a = \left(\Theta_1(1-\Omega_1),\ \Theta_1\Omega_1\alpha\sigma,\ \Theta_2(1-\Omega_2)\gamma,\ \Theta_2\Omega_2\alpha\gamma\right)^T,$$
$$b = (c_1,\ c_1\beta,\ c_2\delta,\ c_2\beta\delta)^T,$$

thus (4.6) can be used, from which we obtain the formula for the reproductive number

$$\begin{aligned} R &= R_{\text{ref}}(a \cdot b) \\ &= R_{\text{ref}}\left[\Theta_1(1-\Omega_1)c_1 + \Theta_1\Omega_1\alpha\sigma c_1\beta + \Theta_2(1-\Omega_2)\gamma c_2\delta + \Theta_2\Omega_2\alpha\gamma c_2\beta\delta\right] \\ &= R_{\text{ref}}\left\{c_1\Theta_1[1-\Omega_1(1-\alpha\sigma\beta)] + c_2\Theta_2\gamma\delta[1-\Omega_2(1-\alpha\beta)]\right\}. \end{aligned} \tag{6.7}$$

The vector of stable structure of the generation will be $\breve{g}_{\text{stab}} = a/\|a\|$.

Another approach to the prior probability of meetings between different age groups is to directly specify the contact matrix between age groups $\hat{C}$ (4.8). Since we have divided the subpopulations by age, the 4×4 matrix $\breve{G}$ can be interpreted as a 2×2 block matrix (see (4.10)). The elements of the provided contact matrix will directly determine the scaling coefficients for the individual blocks of the matrix $\breve{G}$.

The contact matrix will replace the prior probability of contact between different age groups Θ_1, Θ_2 as well as the average number of contacts of age groups c_1, c_2. It is necessary to explicitly incorporate the influence of conditional probabilities Ω_1, Ω_2 into the coefficients a_i.

The shape of the matrix $\breve{G}$ in this case will be:

$$\breve{G} = R_{\text{ref}} \begin{pmatrix} c_{11}(1-\Omega_1) & c_{11}(1-\Omega_1)\beta & c_{12}(1-\Omega_1)\delta & c_{12}(1-\Omega_1)\beta\delta \\ c_{11}\Omega_1\alpha\sigma & c_{11}\Omega_1\beta\alpha\sigma & c_{12}\Omega_1\delta\alpha\sigma & c_{12}\Omega_1\beta\delta\alpha\sigma \\ c_{21}(1-\Omega_2)\gamma & c_{21}(1-\Omega_2)\beta\gamma & c_{22}(1-\Omega_2)\delta\gamma & c_{22}(1-\Omega_2)\beta\delta\gamma \\ c_{21}\Omega_2\alpha\gamma & c_{21}\Omega_2\beta\alpha\gamma & c_{22}\Omega_2\delta\alpha\gamma & c_{22}\Omega_2\beta\delta\alpha\gamma \end{pmatrix}. \tag{6.8}$$

In this approach, the matrix is non-separable, and (4.14) can be applied to it. The final structure of vector of parameters a and b will be

$$a = \left((1-\Omega_1)\,,\ \Omega_1\alpha\sigma,\ (1-\Omega_2)\,\gamma,\ \Omega_2\alpha\gamma\right)^T,$$

$$b = \left(1,\ \beta,\ \delta,\ \beta\delta\right)^T.$$

For the non-separable model, the following relationships hold: (4.12), (4.14), (4.15), (4.16) from which we obtain a sequence of explicit relationships:

$$X = \Omega_1\left(\alpha\sigma\beta - 1\right) + 1,\ Y = \gamma\delta\left[\Omega_2\left(\alpha\beta - 1\right) + 1\right], \tag{6.9}$$

$$\lambda = \frac{1}{2}\left(c_{11}X + c_{22}Y + \sqrt{\left(c_{11}X - c_{22}Y\right)^2 + 4XYc_{12}c_{21}}\right), \tag{6.10}$$

$$\Psi = \frac{\lambda - c_{11}X}{c_{12}Y}, \tag{6.11}$$

$$\breve{g}_+ = \left((1-\Omega_1)\,,\ \Omega_1\alpha\sigma,\ \Psi\,(1-\Omega_2)\,\gamma,\ \Psi\Omega_2\alpha\gamma\right)^T. \tag{6.12}$$

The sought reproduction number will then be:

$$R = R_{\text{ref}}\lambda\,, \tag{6.13}$$

and vector of stable structure of generation will be

$$\breve{g}_{\text{stab}} = \breve{g}_+ / \|\breve{g}_+\|.$$

For clarity and readability of the proposed models, we provide Table 1 of all basic parameters of both models, their interpretation, and their possible ranges.

- Considering the primary parameters of the model, $X,\ Y \in [0,\ 1]$.
- Both models have a reproduction number depending on the parameters α, β, γ, δ only through the products $\alpha\beta$ and $\gamma\delta$.
- In the separable model (6.6), $\breve{g}_{\text{stab}}$ does not depend on β, δ or the parameters of the contact model c_1, c_2.

We will address further properties of the models in the Chapter 8. Before that, we will first introduce a simple model of hospitalization.

Table 1.

List of Parameters	
	Description
$\alpha \in [0,1]$	Proportional reduction in susceptibility due to vaccination
$\beta \in [0,1]$	Proportional reduction in infectivity due to vaccination
$\gamma \in [0,1]$	Proportional reduction in susceptibility due to lower age
$\delta \in [0,1]$	Proportional reduction in infectivity due to lower age
$\sigma \in [0,1]$	Correction for susceptibility reduction due to vaccination for older
$\Omega_1 \in [0,1]$	Probability of vaccinated individuals in the population above 60
$\Omega_2 \in [0,1]$	Probability of vaccinated individuals in the population below 60
$\Theta_1 \in [0,1]$	Probability of people above 60 in the active population
$\Theta_2 \in [0,1]$	Probability of people below 60 in the active population
$c_1 \in \mathbb{R}_0^+$	Avg. num. of daily contacts for ind. above 60
$c_2 \in \mathbb{R}_0^+$	Avg. num. of daily contacts for ind. below 60
$c_{11} \in \mathbb{R}_0^+$	Avg. num. of daily contacts for ind. above 60 with others above 60
$c_{12} \in \mathbb{R}_0^+$	Avg. num. of daily contacts for ind. below 60 with others above 60
$c_{21} \in \mathbb{R}_0^+$	Avg. num. of daily contacts for ind. above 60 with others below 60
$c_{22} \in \mathbb{R}_0^+$	Avg. num. of daily contacts for ind. below 60 with others below 60
$R_{\text{ref}} \in \mathbb{R}_0^+$	$p\,[(1-q)+dq]\,[(t_{\text{S}}-t_{\text{E}})+(s(1-q)+q)\,(t_{\text{R}}-t_{\text{S}})]$, see (6.3)

7. Simple model of hospitalization

We assume that during the outbreak of the epidemic (and in its earlier stages), it is reasonable to neglect the reduction in susceptibility and assume a geometric growth in the number of infected cases with a growth rate coefficient r. During this phase, the growth rate of newly hospitalized will be the same as the growth rate of newly infected, whereas the probability and delay of hospitalization will be reflected only by the scaling of the development of the number of newly infected cases. If the current number of hospitalizations is modeled as the integral (sum) of the difference between the daily admissions to and discharges from the hospital, then the current number of hospitalizations will also be a scaled geometric progression of newly infected cases with a growth rate r.

Taking into account the results presented in the Chapter 5 we can conclude that by comparing the reproduction numbers, we can directly compare the growth coefficients r. If the proportions of subpopulations in the newly infected

population of the kth generation stabilize with the increase of k, then the composition of the subpopulations of newly infected individuals on each day of the epidemic will also approach these ratios. As a consequence of that, the composition of the newly hospitalized (and also currently hospitalized) will stabilize to a composition derived by scaling the newly infected from each subpopulation by the rate of hospitalization of that subpopulation.

Individual hospitalization rates can then be modeled using the reference hospitalization rate η, the vaccine-induced reduction coefficient μ, the age-induced reduction coefficient ν, and the additional reduction in hospitalization due to vaccination at older ages σ_{H}:

$$\eta_1 = \eta, \quad \eta_2 = \sigma_{\mathrm{H}}\mu\eta, \quad \eta_3 = \nu\eta, \quad \eta_4 = \mu\nu\eta, \quad \text{where} \quad \eta,\ \mu,\ \nu,\ \sigma_{\mathrm{H}} \in [0,\ 1]. \tag{7.1}$$

Therefore, the stable structure of subpopulations in the currently hospitalized population in both the separable and non-separable models will be:

$$\breve{h}_{\mathrm{stab},i} = \eta_i \breve{g}_{\mathrm{stab},i}, \quad i \in \{1,\ \ldots, M\}\,. \tag{7.2}$$

The described model is suitable for analyzing the effectiveness of the vaccine against hospitalization of the infected individuals. It illustrates the fundamental difference between the protective effect of the vaccine against transmission, which exhibits geometric growth during the outbreak of the epidemic, and protection against hospitalization of the infected, which manifests as additional scaling of the number of infected cases.

8. Analysis of the model

We designed the model to include the fundamental phenomena of interest while also making it as explicit as possible for examination using methods of real function analysis. Our goal was to achieve a better understanding of certain controversial phenomena where a superficial view might lead to misconceptions (and wrong decisions). First, we will demonstrate the relationship between the separable and non-separable models of transmission. After that, we will focus on the conditions for achieving herd immunity, and, finally, we will examine the impact of the contact patterns of the young population on the optimal vaccine distribution.

8.1. Relation between separable and non-separable models

If the course of the disease and the effects of the vaccine were independent of age, and age was not considered during vaccination, it would still not be possible to reduce the proposed models to a single age group due to the different model of contacts.

From (4.14), it follows that if the determinant of the contact matrix (4.8) is zero, the $\hat{C}$ can be written in the form of an outer product, and the eigenvalue λ_- will be 0. In such a case, this model becomes separable. The closer the non-separable model (4.10) is to the separable case, the smaller the ratio of the absolute values of the two largest eigenvalues λ_-/λ_+, and the faster the generation composition will converge to a stable generation structure.

Considering that different age groups tend to interact more with their peers [8], it is natural to assume separability violation $c_{11}c_{22} - c_{12}c_{21} > 0$. In such a case, from (4.14), we obtain that $\lambda_+,\ \lambda_- > 0$. Thus, the transition phenomenon caused by λ_- will not oscillate. It will only contribute a positive increment to the overall behavior driven by the dominant eigenvalue λ_+. Therefore, by neglecting the transition phenomenon $\lambda_- = 0$ in (4.20), we obtain a lower estimate of the growth or decline of newly infected cases per generation.

If $\hat{C}$ is separable, it is possible to make a unique mapping of the both contact models

$$c_{11} = \Theta_1 c_1, \quad c_{12} = \Theta_1 c_2, \quad c_{21} = \Theta_2 c_1, \quad c_{22} = \Theta_2 c_2. \tag{8.1}$$

Of course, in such case, the Θ_1, Θ_2 may no longer be interpretable as representation of age groups in the overall population.

In the case of a separable model with $\gamma = 1, \quad \sigma = 1, \quad \Omega_1 = \Omega_2 = \Omega$, age groups can be merged, and the model will contain only a subpopulation of vaccinated and unvaccinated individuals.

$$\breve{G} = R_{\text{ref}}\,(\Theta_1 + \Theta_2) \begin{pmatrix} (1-\Omega)\,(c_1 + c_2\delta) & (1-\Omega)\,\beta\,(c_1 + c_2\delta) \\ \Omega\alpha\,(c_1 + c_2\delta) & \Omega\alpha\delta\,(c_1 + c_2\delta) \end{pmatrix}.$$

In this case, if the ratio of older to younger individuals in the population is Θ_1/Θ_2, this ratio will also be preserved in the infected population.

If we wanted to merge age groups in case of the non-separable model, the necessary simplifications would lead to its transition into a separable model, where the mapping of contact models (8.1) can be utilized, and the subsequent steps and results will be the same as in the case of separable model.

8.2. Herd immunity in a heterogeneous population

In this subsection, we will demonstrate how to analytically solve the problem of finding the optimal strategy for achieving herd immunity in the non-separable model. For the following considerations, we assume that under normal conditions without intervention (vaccination), an epidemic would occur

$$R(\Omega_1 = 0, \quad \Omega_2 = 0) > 1.$$

All primary parameters of the model are known and the proportional representation of people over 60 years in the total population $\zeta = N_{60+}/N_{\text{all}}$ is also determined. We assume that all parameters will be chosen in such a way as to prevent division by zero during the calculation.

To verify whether a vaccination strategy that achieves herd immunity, i.e., $R \leq 1$ exists, we can construct a strategy based on the parametrization using ω, φ that leads to the greatest reduction in the overall reproductive number, and test whether at least under this strategy, the required condition $R \leq 1$ is met. If it turns out that even this strategy does not achieve the desired goal, then herd immunity cannot be achieved in such a heterogeneous community under the given vaccine properties. The most effective strategy corresponds to $\Omega_1 = 1$, $\Omega_2 = 1$ what is equivalent to parametrization $\varphi = 1$, $\omega = 1$, see page 211. By inserting this parametrization into the separable model (6.7) or into the non-separable model (6.9), (6.10), and (6.13), we obtain $R_{\min} = R$. If $R_{\min} > 1$, then there is no such ω, φ for which herd immunity can be achieved. (Of course, in the opposite case $R_{\min} \leqslant 1$, such a strategy will exist and additional analysis is required.)

In case that herd immunity is attainable, we can seek the optimal boundary for achieving them, i.e., seek a pair of ω_{opt}, φ_{opt}, for which the epidemic outbreak threshold $R = 1$ is achieved using the minimum number of vaccines for the entire population.

We will now formally describe the solution procedure. First, we express ω under the assumption $R = 1$ as a function of φ: $\omega_{R=1}(\varphi)$. The minimum of this function in the allowed domain defined by the bounds $\varphi \in [0,\ 1]$, $\omega \in [\varphi\zeta,\ \varphi\zeta + 1 - \zeta] \subseteq [0,\ 1]$ will either be an extreme of the function within this domain or be the value of this function at the boundary of the domain. Therefore, it is necessary to determine the intersection of the function $\omega_{\min} = \omega_{R=1}(\varphi_{\min})$ with the line $\omega_{\min} = \zeta\varphi_{\min}$ (solving a system of two equations), similarly, intersection of the function $\omega_{\max} = \omega_{R=1}(\varphi_{\max})$ with another line $\omega_{\max} = \varphi_{\max}\zeta + 1 - \zeta$, and test whether $\varphi_{\min},\ \varphi_{\max} \in [0,\ 1]$. Subsequently, we determine $\omega_0 = \omega_{R=1}(\varphi = 0)$ and test whether $\omega_0 \in [0,\ 1 - \zeta]$ and determine $\omega_1 = \omega_{R=1}(\varphi = 1)$ and test whether $\omega_1 \in [\zeta,\ 1]$. The positions of the local extremes $\varphi_+,\ \varphi_-$ are determined from the equation $\partial\omega_{R=1}/\partial\varphi = 0$. Then we determine the corresponding $\omega_\pm = \omega_{R=1}(\varphi_\pm)$, and test whether these local extremes are located within the allowed domain $\varphi_\pm \in [0,\ 1]$, $\omega_\pm \in [\varphi\zeta,\ \varphi\zeta + 1 - \zeta]$. In addition to its own constraints, it is also necessary to verify, for each pair of candidates, the conditions under which the analyzed function $\omega_{R=1}(\varphi)$ was derived. Then, the smallest of the values $\omega_{\min},\ \omega_{\max},\ \omega_0,\ \omega_1,\ \omega_+,\ \omega_-$ which satisfies all constraints will be the sought global minimum.

Before further derivation, let us first introduce substitutions that will simplify the notation and reduce the total number of operations required for the calculation (the notation for auxiliary variables will be valid only in this chapter).

$$U = \frac{\zeta}{\alpha\sigma\beta - 1}, \quad Q = \frac{1-\zeta}{\alpha\beta - 1},$$

$$B = R_{\text{ref}}^2 \gamma\delta \left(c_{11}c_{22} - c_{12}c_{21} \right),$$

$$C = c_{22}R_{\text{ref}}\gamma\delta, \quad D = c_{11}R_{\text{ref}}, \quad E = R_{\text{ref}}\sqrt{\frac{\gamma\delta Q c_{12}c_{21}}{U}}.$$

$$X = \frac{\zeta\varphi}{U} + 1 = \varphi\left(\alpha\sigma\beta - 1\right) + 1 \quad \text{(the notation is consistent with (6.9))}.$$

The calculation will depend on $\alpha,\ \beta,\ \sigma$ only through auxiliary variables $U,\ Q$, on $\gamma,\ \delta,\ c_{11},\ c_{12},\ c_{21},\ c_{22},\ R_{\text{ref}}$ only through auxiliary variables $B,\ C,\ D,\ E$, and on φ only through the auxiliary variable X. By substituting $\Omega_1 = \varphi$, $\Omega_2 = (\omega - \varphi\zeta)/(1-\zeta)$, and $R = 1$ into the non-separable model (consist of (6.5), (6.9), (6.10), (6.13)) and isolating ω, we obtain the relationship for $\omega_{R=1}(\varphi)$:

$$\omega = U\big(X(\varphi) - 1\big) + Q\left(\frac{DX(\varphi) - 1}{BX(\varphi) - C} - 1\right). \tag{8.2}$$

This formula was derived under the assumption $R = \lambda_+ = 1$ from which a nontrivial condition for its validity follows:

$$0 \le 2 - D\left(\frac{\varphi\zeta}{U} + 1\right) - C\left(\frac{\omega - \varphi\zeta}{Q} + 1\right). \tag{8.3}$$

For finding intersections $\omega_{R=1}$ with the boundaries of the domain, we obtain

$$\varphi_{\min} = \frac{U}{\zeta}\left(\frac{1-C}{D-B} - 1\right), \quad \omega_{\min} = \zeta\varphi_{\min}, \quad 0 \le \varphi_{\min} \le 1, \tag{8.4}$$

$$\varphi_{\max} = \frac{U}{\zeta}\left[\frac{Q\,(1-C) - C\,(1-\zeta)}{Q\,(D-B) - B\,(1-\zeta)} - 1\right], \quad \omega_{\max} = \varphi_{\max}\zeta + 1 - \zeta, \quad 0 \le \varphi_{\max} \le 1, \tag{8.5}$$

$$\varphi_0 = 0, \quad \omega_0 = Q\left(\frac{D-1}{B-C} - 1\right), \quad 0 \le \omega_0 \le 1 - \zeta, \tag{8.6}$$

$$\varphi_1 = 1, \quad \omega_1 = \zeta + Q\left[\frac{D\zeta + U\,(D-1)}{B\zeta + U\,(B-C)} - 1\right], \quad \zeta \le \omega_1 \le 1. \tag{8.7}$$

For finding the extremes, we set the derivative $\frac{\partial \omega_{R=1}}{\partial \varphi} = \frac{\partial \omega_{R=1}}{\partial X}\frac{\partial X}{\partial \varphi} = 0$. Since X is a linear function with respect to φ, than φ will only appear as a parameter of X in this equation. Therefore, it is advantageous to solve this equation for X and, finally, express the sought-after parameters $\varphi_\pm$ in terms of $X_\pm = X$. The described procedure leads to explicit relationships:

$$X_\pm = \frac{C \pm E}{B}, \quad \varphi_\pm = \frac{U\,(X_\pm - 1)}{\zeta}, \quad \omega_\pm = U\,(X_\pm - 1) + Q\left(\frac{DX_\pm - 1}{BX_\pm - C} - 1\right),$$

$$0 \leq \varphi_\pm \leq 1, \quad \varphi\zeta \leq \omega_\pm \leq \varphi\zeta + 1 - \zeta. \tag{8.8}$$

It is still necessary to retrospectively verify the condition (8.3) for each individual pair of candidates and finally determine the one for which the minimum value of ω is achieved. This pair ω_{opt}, φ_{opt} will be the sought-after global minimum and will determine the optimal strategy for achieving herd immunity.

Now let us take a closer look at the optimal strategy for achieving herd immunity in the situation where vaccinating the younger population is not recommended for other valid reasons (e.g., due to dangerous side effects). In such cases, the herd immunity is achievable only if $R_{\min} \leqslant 1$ for $\Omega_1 = 1$, $\Omega_2 = 0$ ($\varphi = 1$, $\omega = \zeta$). Seeking optimal parameters ω_{opt}, φ_{opt} will be reduced to finding $\Omega_1 = \varphi$ under the condition $\Omega_2 = (\omega - \varphi\zeta)/(1 - \zeta) = 0$, see (6.5), that achieves $R = 1$. This corresponds to substituting $\omega = \varphi\zeta$ into (8.2), which is identical to the calculation in (8.4). Therefore, in this situation, provided that the constraints $0 \leq \varphi_{\min} \leq 1$ and condition (8.3) are met, the optimal strategy for achieving herd immunity is determined by the pair $\varphi_{\text{opt}} = \varphi_{\min}$, $\omega_{\text{opt}} = \zeta\varphi_{\min}$.

In opposite case, where vaccinating the older population is not recommended, herd immunity is achievable only if

$$R_{\min} \leqslant 1 \quad \text{for} \quad \Omega_1 = 0, \quad \Omega_2 = 1 \quad (\varphi = 0, \quad \omega = 1 - \zeta),$$

and seeking optimal parametrization is reduced to calculation (8.6). So, in this case, provided that the constraints $0 \leq \omega_0 \leq 1 - \zeta$ and condition (8.3) are met, the optimal strategy is determined by the pair $\varphi_{\text{opt}} = 0$, $\omega_{\text{opt}} = \omega_0$.

At the end of this subsection, let us briefly examine also the optimal vaccination strategy for the separable model. In subsection 8.1, we concluded that by substituting

$$c_{11} = \Theta_1 c_1, \quad c_{12} = \Theta_1 c_2, \quad c_{21} = \Theta_2 c_1, \quad c_{22} = \Theta_2 c_2,$$

will be separable model only a special case of the non-separable model. Substituting $R = 1$ into (6.7) and expressing ω yields that in the case of the separable model, the function $\omega_{R=1}(\varphi)$ will be linear. In addition, the determinant of the matrix will be $\det\big(\hat{C}\big) = 0$, and therefore, the auxiliary variable

$$B = R_{\text{ref}}^2 \gamma\delta\,(c_{11}c_{22} - c_{12}c_{21}) = 0.$$

With this in mind, to find the global minimum within the valid range ω, φ, it is sufficient to check (8.4), (8.5), (8.6), (8.7) for $B = 0$.

8.3. Impact of contact of younger population on optimal vaccine redistribution

Let us examine the conditions under which

$$\varphi_2 > \varphi_1 \Rightarrow R(\varphi_2) > R(\varphi_1), \quad \varphi_2,\ \varphi_1 \in [0,\ 1]\,, \quad 0 < \omega < 1.$$

We will focus on increasing the contact rate of the younger population, c_2, or c_{22}, and seek additional sufficient conditions under which the reproductive number with respect to the vaccination of the older population would be monotonically increasing. This would mean that, in the case of a limited number of vaccines, prioritizing the vaccination of the older population at the expense of the younger population would result in a higher reproductive number. The following analysis will be carried out under the assumption that none of the model parameters will be 0.

At first, we focus on impact of contact rate of younger c_2 in separable model. By substituting (6.5) into (6.7)

$$R(\varphi) = R_{\text{ref}} \left\{ c_1\Theta_1 \left[1 - \varphi\,(1 - \alpha\sigma\beta)\right] + c_2\Theta_2\gamma\delta \left[1 - \frac{\omega - \varphi\zeta}{1-\zeta}\,(1 - \alpha\beta)\right] \right\},$$

and making adjustments, we obtain that $R(\varphi)$ is a linear:

$$R(\varphi) = \underbrace{\varphi\, R_{\text{ref}} \left[\frac{\zeta}{1-\zeta} c_2\Theta_2\gamma\delta\,(1 - \alpha\beta) - c_1\Theta_1\,(1 - \alpha\sigma\beta)\right]}_{\partial R/\partial\varphi}$$
$$+ R_{\text{ref}} \left[c_1\Theta_1 + c_2\Theta_2\gamma\delta \left(1 - \omega\frac{1-\alpha\beta}{1-\zeta}\right)\right].$$

Now, it is easy to use the condition $\partial R/\partial\varphi = 0$, to determine the decision boundary for c_2:

$$c_{\text{edge}} = \frac{1-\zeta}{\zeta}\frac{\Theta_1 c_1\,(1 - \alpha\sigma\beta)}{\Theta_2\gamma\delta\,(1 - \alpha\beta)}.$$

Assuming

$$\Theta_1,\ \Theta_2,\ \zeta,\ \omega,\ \alpha,\ \beta,\ \gamma,\ \delta,\ \sigma \in (0, 1)\,, \quad c_1,\ R_{\text{ref}} > 0,$$

the condition $\partial R/\partial\varphi > 0$ will be met precisely when $c_2 > c_{\text{edge}}$.

Similarly, it can be shown that in the non-separable model (6.8), it is possible to establish a condition under which a sufficient increase in the contact rate parameter of the younger population with itself c_{22} will result in the same effect of monotonic growth of λ (and therefore growth of $R = R_{\text{ref}}\lambda$ is automatically also presented). While in the separable model, the monotonicity switches suddenly at $c_2 = c_{\text{edge}}$, in the non-separable model, there can be an extreme on the interval $\varphi \in \left[\underline{\varphi}, \overline{\varphi}\right] \subseteq [0,1]$.

First, we will transform (6.9) into linear functions with respect to φ and introduce auxiliary local parameters a, b, c, d (there should be no confusion with the same notation in other chapters).

$$\begin{aligned} X(\varphi) &= \varphi\left(\alpha\sigma\beta - 1\right) + 1 = \varphi \underbrace{\left(\alpha\sigma\beta - 1\right)}_{a} + \underbrace{1}_{b} = \varphi a + b, \\ Y(\varphi) &= \gamma\delta\left[\Omega_2\left(\alpha\beta - 1\right) + 1\right] \\ &= \gamma\delta\left[\tfrac{\omega - \varphi\zeta}{1-\zeta}\left(\alpha\beta - 1\right) + 1\right] \\ &= \omega\gamma\delta\tfrac{\alpha\beta-1}{1-\zeta} - \zeta\varphi\gamma\delta\tfrac{\alpha\beta-1}{1-\zeta} + \gamma\delta \\ &= \underbrace{\varphi\,\zeta\gamma\delta\frac{1-\alpha\beta}{1-\zeta}}_{c} + \underbrace{\gamma\delta\left(\omega\frac{\alpha\beta-1}{1-\zeta} + 1\right)}_{d} = \varphi c + d. \end{aligned} \tag{8.9}$$

Assuming $\zeta,\ \alpha,\ \beta,\ \gamma,\ \delta,\ \sigma \in (0,1)$ the parameters a, b, c, d will be bounded. Furthermore, we assume $c_{11},\ c_{12},\ c_{21},\ c_{22} > 0$. Taking into account all the conditions for the ranges of primary model parameters, we will have $a < 0$, $b = 1$, $c > 0$ (nothing can be said about d from its formula yet), $X(\varphi) > 0$, $Y(\varphi) > 0$, and therefore, $\hat{G} > 0$, see (4.13).

If we can show that for any φ, it is possible to find c_{22} such that $\partial\lambda/\partial\varphi > 0$, then there exists a finite c_{22} that ensures $\partial\lambda/\partial\varphi > 0$ over the entire allowed interval $\varphi \in [0,1]$.

By substituting the functions $X(\varphi)$ and $Y(\varphi)$ into (6.10) and differentiating with respect to φ, we obtain:

$$\begin{aligned} \frac{\partial\lambda}{\partial\varphi} = &\frac{c_{11}a + c_{22}c}{2} \\ &+ \frac{1}{2}\frac{\left[c_{11}\left(\varphi a + b\right) - c_{22}\left(\varphi c + d\right)\right]\left(c_{11}a - c_{22}c\right) + 2\left[2\varphi ac + \left(ad + bc\right)\right]c_{12}c_{21}}{\sqrt{\left[c_{11}\left(\varphi a + b\right) - c_{22}\left(\varphi c + d\right)\right]^2 + 4\left[\varphi^2 ac + \varphi\left(ad + bc\right) + bd\right]c_{12}c_{21}}}. \end{aligned}$$

We will simplify the expression to have a common denominator. Considering $\hat{G} > 0$, the second root in the denominator is a positive real number. Due to this the condition $\partial\lambda/\partial\varphi > 0$ will be met precisely when the numerator is greater than 0:

$$0 < \underbrace{(c_{11}a + c_{22}c)}_{Q_1} \times$$

$$\underbrace{\sqrt{\left[c_{11}\left(\varphi a + b\right) - c_{22}\left(\varphi c + d\right)\right]^2 + 4\left[\varphi^2 ac + \varphi\left(ad + bc\right) + bd\right]c_{12}c_{21}}}_{Q_2}$$

$$+ \underbrace{\left[c_{11}\left(\varphi a + b\right) - c_{22}\left(\varphi c + d\right)\right]\left(c_{11}a - c_{22}c\right)}_{Q_3} + \underbrace{2\left[2\varphi ac + \left(ad + bc\right)\right]c_{12}c_{21}}_{Q_4}.$$

We will now divide the expression on the right into 4 parts: Q_1, Q_2, Q_3, Q_4. Since all the parameters are bounded, the values of these expressions will also be bounded.

The product $Q_1Q_2 > 0 \Leftrightarrow (Q_1 > 0 \text{ and } Q_2 > 0)$ or $(Q_1 < 0 \text{ and } Q_2 < 0)$. Since Q_2 is directly the expression from the denominator for which we already know that $Q_2 \in \mathbb{R}$, $Q_2 > 0$ then $Q_1Q_2 > 0 \Leftrightarrow Q_1 > 0$. This occurs if the condition $c_{22} > -c_{11}a/c$ is satisfied (where $c \neq 0$ directly follows from $c > 0$). Therefore, there exists a sufficiently large c_{22} such that the product Q_1Q_2 will be positive.

Now let us examine the condition for c_{22} to satisfy the inequality $Q_3 + q > 0$ where $q \in \mathbb{R}$. (Its fulfillment will automatically ensure $Q_3 > 0$.) After rearranging, we obtain

$$Q_3 = {c_{22}}^2 c\left(\varphi c + d\right) - c_{22}c_{11}\left[c\left(\varphi a + b\right) - a\left(\varphi c + d\right)\right] + {c_{11}}^2 a\left(\varphi a + b\right).$$

If it were true that $c\left(\varphi c + d\right) > 0$, then

$$\lim_{c_{22}\to\infty} {c_{22}}^2 c\left(\varphi c + d\right) - c_{22}c_{11}\left[c\left(\varphi a + b\right) - a\left(\varphi c + d\right)\right] + {c_{11}}^2 a\left(\varphi a + b\right) + q$$
$$= \lim_{c_{22}\to\infty} {c_{22}}^2 \left\{ c\left(\varphi c + d\right) - \frac{c_{11}\left[c\left(\varphi a + b\right) - a\left(\varphi c + d\right)\right]}{c_{22}} + \frac{{c_{11}}^2 a\left(\varphi a + b\right) + q}{{c_{22}}^2} \right\}$$
$$= \underbrace{c\left(\varphi c + d\right)}_{>0} \lim_{c_{22}\to\infty} {c_{22}}^2 = \infty.$$

So, if $c\left(\varphi c + d\right) > 0$, then there exists, c_{22} for any chosen $q \in \mathbb{R}^+$, a sufficiently large such that $Q_3 + q > 0$. From the previous analysis, it follows that if $c_{22} > -c_{11}a/c$ and $c\left(\varphi c + d\right) > 0$, then $0 < Q_1Q_2 + Q_3 + q$.

The condition $c\left(\varphi c + d\right) > 0$ will be satisfied precisely when $(c > 0$ and $\varphi c + d > 0)$ or $(c < 0$ and $\varphi c + d < 0)$. We know that $c > 0$ directly follows from the ranges of the basic model parameters, but we cannot directly determine the signum of d from its formula (8.9). However, we know that the entire expression $\varphi c + d = Y(\varphi) > 0$ (see again (8.9)) ensures the validity of $c > 0$ and $\varphi c + d > 0$.

Since the expression Q_4 depends only on bounded parameters and it is independent of c_{22}, here is possible to choose q such that $q = Q_4$. In this case, $0 < Q_1Q_2 + Q_3 + q = Q_1Q_2 + Q_3 + Q_4$ and therefore $\partial\lambda/\partial\varphi > 0$.

Thus, we have shown that under the given assumptions, there exists a sufficiently large c_{22} such that over the entire interval $\varphi \in [\underline{\varphi}, \overline{\varphi}] \subseteq [0,1]$, the reproductive number with vaccination of the older population will monotonically increase. Therefore,

$$\exists c_{22} > 0; \quad \varphi_2 > \varphi_1 \Rightarrow R(\varphi_2, c_{22}) > R(\varphi_1, c_{22}); \quad \varphi_2, \varphi_1 \in \left[\underline{\varphi}, \overline{\varphi}\right] \subseteq [0,1].$$

Assuming that the distribution of generation time will be the same for all subpopulations and it will not change in time, a higher reproductive number lead to a higher growth rate of infected individuals (see Chapter 5). Thus, for $R_2 > R_1 \Rightarrow r_2 > r_1$. If the number of hospitalizations is proportional to the number of infected individuals in individual subpopulations, then an increase in the reproductive number will also increase the growth rate of hospitalized individuals (for details, see Chapter 7). This means that with a higher reproductive number R_2, after some time, the total number (as well as the numbers for individual subpopulations) of infected or hospitalized individuals will begin to exceed the corresponding numbers achieved with a lower reproductive number R_1. When we connect this behavior with the result of this subsection, we conclude that with a sufficiently high contact rate of the younger population c_{22} during a sufficiently long period of the exponential phase of the epidemic, hospitalization of individual sub-populations as well as overall hospitalization is minimized when we prioritize the vaccination of the younger population over the older population.

This result is all the more surprising that this state can be achieved even with higher infectivity and susceptibility of the older population compared to the younger population $\delta,\ \gamma < 1$, with the condition that the vaccine in the older population reduces their higher transmissibility ($\sigma < \gamma\delta$) below the transmissibility of vaccinated younger population.

This state can even be achieved despite the higher probability of hospitalization of the elderly, coupled with a higher effectiveness against hospitalization of the elderly, which would compensate for this probability by reducing it below the hospitalization rate of the vaccinated younger population.

This shows that worse disease progression parameters, higher proportional representation of the elderly in the hospitalized population, or higher vaccine effectiveness against infection or hospitalization of the elderly may not be sufficient and valid arguments for prioritizing the vaccination of the older population. Simply because all these circumstances can be overcome by a sufficiently high difference in the contact rates of the younger population compared to the older population.

Of course, this analysis does not provide information about the level of contact rate and the time at which this predicted behavior will manifest. These questions remain open for further investigation. Nevertheless, this behavior of epidemic is not just a mathematical curiosity. For illustration, such a situation in the context of COVID-19 was investigated in articles [9], [30], [17].

9. Conclusion and future work

In this work, we proposed a simple matrix model for the outbreak of an epidemic suitable for analyzing the distribution of vaccines among age groups. The contact pattern of the general population favors interactions within age groups, making the contact matrix non-separable. Therefore, we proposed two model variants using separable and non-separable mixing.

The effects of the vaccine are parameterized by the reduction in infectivity, the reduction in susceptibility, and the reduction in hospitalization of the infected. These parameters may differ for both age groups.

The proposed non-separable model is rich enough to capture non-trivial qualitative and quantitative phenomena during the epidemic outbreak. On the other hand, this matrix model is simple enough to be rewritten as a sequence of explicit relationships and subjected to the analysis of a real variable, which we consider a significant advantage.

In our work, we encountered challenges related to the relationship between generation and time domains and the issue of transient phenomena. We primarily focused on transient phenomena caused by population heterogeneity. Given the scope of this work and the complex relationship between the time domain and the generation domain in modeling an epidemic in a heterogeneous population, we have given up on the explicit reconstruction of the course of the epidemic over time. Despite these challenges, we were able to achieve that the behavior in the generational domain, the determination of the reproduction number, can be used not only for analyzing the epidemic outbreak but also for comparing the steepness of the epidemic with respect to the growth of hospitalizations over time. If the geometric growth of hospitalizations in one scenario is higher than in another, regardless of the shift or initial conditions, after some time, the more rapidly increasing hospitalizations will surpass those with slower growth.

In the model analysis, we focused on the differences between the separable and non-separable models and the impact of contact rates on the optimal vaccine distribution among age groups. Moreover, we showed that, under certain circumstances, all the advantages of vaccinating the older population can be outweighed by the higher contact rate of the younger population.

Our work primarily concentrated on two age groups, assuming a worse disease course for the older population. However, the model can also be used when the younger population is more at risk [21] or when the population is divided based on criteria other than age. Additionally, contact rates of vaccinated and unvaccinated could incorporate also correction due to sociological effects like fear from infection and false assurance from vaccination. Model can be applied to analyze the effects of other medical and non-medical epidemic measures, such as lockdowns, isolating vulnerable communities, or mass use of protective equipment like masks or respirators. The interpretation of parameters may differ, but the mathematical structure of the model will not change.

Some challenges remain open: How to explicitly model the transition from the generation domain to the time domain? How to parameterize such a model based on available real measurements during an epidemic? How to cope with population partially immunized due to prior infection? It might also be interesting to examine the contact rate and the time at which hospitalization rates worsen when the older population is prioritized.

To answer these questions, it may be necessary to examine the proposed model numerically as well.

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