Analytical results

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Reference and general idea

The derivation of R0 for a SIR type model following description of 'Mathematical Tools for Understanding Infectious Disease Dynamics' written by Odo Diekmann, Hans Heesterbeek and Tom Britton. See chapter 7, section 2 'Next-generation matrix for compartmental systems'. We use 4 steps to find the basic reproduction number of a system. 1) Define the infected subsystem, i.e. all equations that include compartments where individuals can get infected. 2) Linearize the subsystem in the disease free equilibrium. 3) Find the next generation matrix (NGM) with large domain (K_L) by writing the linear system as: $\dot{\boldsymbol{x}} = (\boldsymbol{T} + \boldsymbol{\Sigma})\boldsymbol{x}$, here $\boldsymbol{x}$ is a vector containing all states where individuals can get infected, $\boldsymbol{T}$ contains all terms corresponding to transmission and $\boldsymbol{\Sigma}$ all terms corresponding to transitions between compartments. Then: $\boldsymbol{K} = -\boldsymbol{T}\boldsymbol{\Sigma}^{-1}$. 4) The reproduction number is now the dominant eigenvalue of the NGM. We also reference the description of R0 in metapopulations in Philipps S, Rossi D. Mathematical Models of Infectious Diseases: Two-Strain Infections in Metapopulations, and the methodology for calculating R0 used by the authors in Gatto M, Bertuzzo E, Mari L, Miccoli S, Carraro L, Casagrandi R, et al. Spread and dynamics of the COVID-19 epidemic in Italy: Effects of emergency containment measures. PNAS. 2020 May 12;117(19):10484–91.

Infected subsystem

The infected subsystem is the following:

$$\dot{E}_i = \lambda_i S_i - \delta_E E_i \tag{1}$$

$$\dot{P}_i = \delta_E E_i - \delta_p P_i \tag{2}$$

$$\dot{A}_i = (1-f)\delta_p P_i - \gamma_A A_i \tag{3}$$

$$\dot{I}_i = f\delta_p P_i - \kappa_i I_i \tag{4}$$

$$\dot{H}_i = h_i \eta I_i - \gamma_H H_i \tag{5}$$

Where,

$$\lambda_i = \sum_{j=1}^{n} \beta_{ij} \frac{P_j + A_j + I_j + H_j}{N_j} \tag{6}$$

where $\beta_{ij} = \tau C_{ij}$ with τ being the probability of infection for a contact with an infected person, and C_{ij} is the average number of contacts of an individual of class i with an individual of class j.

Parametrization of the contact matrix

We estimated the average number of contacts of individuals of class i in the camps, $\bar{c}_i$, and we parametrized the contact matrix assuming that, in a well-mixed population, these contacts will be distributed among classes relative to the fraction of individuals within each class, i.e.

$$C_{ij} = \bar{c}_i N_j / N, \tag{7}$$

with N the total population size. A well-mixed population will be considered the null model, and parameters derived under the null model assumptions are indexed with the superscript 0, e.g. the null contact matrix is C^0_{ij}. The type of interventions that we consider, aim to reduce either the average number of contacts a class i (e.g. self-isolation) or the accessibility of class i to class j (e.g. shielding strategies). We model the first type of intervention introducing the parameter ϵ_{ij}, representing the fraction of the average number of contacts observed in the null model that prevail after the intervention: $\bar{c}_i = \epsilon_{ij}\bar{c}^0_i$. Similarly, we model the second type of intervention with the matrix m_{ij}, representing the fraction of population j visible to population i after the intervention. The contact matrix resulting from management strategies can therefore be written with respect to the null model as:

$$C_{ij} = \epsilon_{ij} m_{ij} \bar{c}^0_i N_j / N = \epsilon_{ij} m_{ij} C^0_{ij} = M_{ij} C^0_{ij}, \tag{8}$$

and the matrix M_{ij} will be called the managament matrix. Given this parameterization, we substitute in the expression for lambda (Eq. 6) to obtain for a model including management strategies

$$\lambda_i = \frac{\tau}{N} \sum_{j=1}^{n} \epsilon_{ij} \bar{c}^0_i m_{ij} \left(P_j + A_j + I_j + H_j\right) \tag{9}$$

Estimation of the Next Generation Matrix

We start considering the subsystem containing the infectious population and, to facilitate notation, let us consider the following ordering of the variables in the vector $x = (E_1, ..., E_M, P_1, ..., P_M, A_1, ..., A_M, I_1, ..., I_M, H_1, ..., H_M)$, with M the number of population classes. We are interested in the parametrization of the null model, which will serve as a baseline to estimate the parameter τ, which is unknown, and that does not change when interventions are introduced. For the null model, Eq. 9 becomes

$$\lambda_i = \frac{\tau}{N} \sum_{j=1}^{n} \bar{c}_i^0 \left(P_j + A_j + I_j + H_j\right).$$

Following this notation, the linearized system can be written in the form $\dot{\boldsymbol{x}} = (\boldsymbol{T} + \boldsymbol{\Sigma})\boldsymbol{x}$, where:

$$\boldsymbol{T} = \tau \begin{bmatrix} \mathbf{0} & \boldsymbol{\Theta} & \boldsymbol{\Theta} & \boldsymbol{\Theta} & \boldsymbol{\Theta} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} \end{bmatrix} \tag{10}$$

is the transmission matrix, with $\boldsymbol{\Theta} = \mathrm{diag}(p_i \bar{c}_i^0)\boldsymbol{U}$, $p_i = N_i/N$, and $\boldsymbol{U}$ being the all-ones matrix of size M. The transition matrix is

$$\boldsymbol{\Sigma} = \begin{bmatrix} -\delta_E \boldsymbol{I} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \delta_E \boldsymbol{I} & -\delta_p \boldsymbol{I} & \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & (1-f)\delta_p \boldsymbol{I} & -\gamma_A \boldsymbol{I} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & f\delta_p \boldsymbol{I} & \mathbf{0} & -\mathrm{diag}(\kappa_i)\boldsymbol{I} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} & \eta\,\mathrm{diag}(h_i)\boldsymbol{I} & -\gamma_H \boldsymbol{I} \end{bmatrix} \tag{11}$$

Where $\boldsymbol{I}$ and $\mathbf{0}$ are the identity and null matrices of size M, and $\kappa_i = ((1 - g_i - h_i)\gamma_I + h_i\eta + g_i\alpha)$. We next compute the inverse of the transition matrix

$$\boldsymbol{\Sigma^{-1}} = \begin{bmatrix} -\frac{1}{\delta_E}\boldsymbol{I} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} \\ -\frac{1}{\delta_p}\boldsymbol{I} & -\frac{1}{\delta_p}\boldsymbol{I} & \mathbf{0} & \mathbf{0} & \mathbf{0} \\ -\frac{(1-f)}{\gamma_A}\boldsymbol{I} & -\frac{(1-f)}{\gamma_A}\boldsymbol{I} & -\frac{1}{\gamma_A}\boldsymbol{I} & \mathbf{0} & \mathbf{0} \\ -f\,\mathrm{diag}(\frac{1}{\kappa_i})\boldsymbol{I} & -f\,\mathrm{diag}(\frac{1}{\kappa_i})\boldsymbol{I} & \mathbf{0} & -\mathrm{diag}(\frac{1}{\kappa_i})\boldsymbol{I} & \mathbf{0} \\ -\frac{f\eta}{\gamma_H}\mathrm{diag}(\frac{h_i}{\kappa_i})\boldsymbol{I} & -\frac{f\eta}{\gamma_H}\mathrm{diag}(\frac{h_i}{\kappa_i})\boldsymbol{I} & \mathbf{0} & -\frac{\eta}{\gamma_H}\mathrm{diag}(\frac{h_i}{\kappa_i})\boldsymbol{I} & -\frac{1}{\gamma_H}\boldsymbol{I} \end{bmatrix} \tag{12}$$

The NGM with large domain can now be found by $\boldsymbol{K_L} = -\boldsymbol{T}\boldsymbol{\Sigma}^{-1}$, however, as we know that each individual that gets infected first will go to the E compartment we can instead calculate the NGM with small domain, $\mathbf{K}_\mathrm{S}$ that only

consists of the E compartment [Heffernan]. We do this by removing from T the rows that correspond to the other compartments and from Σ^{-1} the columns APG: This could be more elegantly explained defining an epsilon matrix We then find:

$$\boldsymbol{K_S} = \tau \left[\left(\frac{1}{\delta_P} + \frac{(1-f)}{\gamma_A} \right) \boldsymbol{\Theta} + \text{diag} \left(\frac{f}{\kappa_i} (1 + \frac{h_i \eta}{\gamma_H}) \right) \boldsymbol{\Theta} \right].$$

Estimation of τ

The reproduction number can be obtained from the maximum of the absolute value of all eigenvalues of $\boldsymbol{K_S}$, i.e. $R_0 = |\lambda_1|$. In our model all parameters are known except the probability of infection per contact, τ. We estimate the probability distribution of τ generating realizations of R_0 and $\tilde{K_S} = K_S/\tau$ assuming a well mixed population as null model and solving for τ:

$$\tau = \frac{R_0}{|\tilde{\lambda}_1^0|}, \tag{13}$$

where $|\tilde{\lambda}_1^0|$ is the maximum of the absolute values of all eigenvalues of $\tilde{K_S}$, when the contact matrix is estimated under the null model, i.e. $\bar{c}_i = \bar{c}_i^0$.

Parametrization of the interventions

Shielding a population

In the following, we analyse the effect of shielding certain fraction f_S of the population, mostly vulnerable. In practice, this is made dividing the camp in two areas, a "green" zone (denoted g) for vulnerable population and an "orange" zone (o) for the remaining population. These two populations could eventually interact via a "neutral" zone under controlled conditions. In particular, we will consider that members of both populations will meet maintaining 2m of distance and using contention measures such as masks, reducing the infectivity an 80% [Ref], i.e. $\hat{\tau} = 0.2\tau$. In addition, only a limited number of family members c_{fam} will be allowed to interact per each person shielded in the green area per day. Finally, people getting into the neutral zone will be tested (how?), and hence symptomatic patients will be excluded from the zone, reducing the transmission probability.

The model implies a reduction in the number of contacts between classes of the green zone and the orange zone, but not in the mean number of contacts that each individual has per day, therefore $\bar{c}_i$ does not vary. We model this redistribution of the contacts with the parameter ϵ_{ij} as follows:

$$\begin{aligned} \epsilon_{ij} &= \rho c_{\text{fam}}/\bar{c}_i \quad (i,j \text{ in different areas}) \\ \epsilon_{ij} &= 1 - \rho c_{\text{fam}}/\bar{c}_i \quad (i,j \text{ in same area}). \end{aligned}$$

If we assume that the relatives from the orange zone visiting the neutral zone are always different, $f_{\mathrm{o,fam}} = c_{\mathrm{fam}} \frac{N_{\mathrm{g}}}{N_{\mathrm{o}}}$ will be the fraction of the orange population susceptible of visiting the neutral zone and we define ρ as:

$$\rho = \begin{cases} 1 & \text{if } i \in \mathrm{g} \\ f_{\mathrm{o,fam}} & \text{if } i \in \mathrm{o} \end{cases}$$

[1]

The next step is to model the probability of interaction between a member of the class i and the class j, depending on whether they belong to the same or a different area. Since in the intervention classes are constrained to interact in the demarcated areas, once one individual is within a given area she will observe an increased likelihood of finding members of the classes permitted to visit that area with respect to the null model. In particular, the proportion N_i/N of individuals for class i in the null model will become N_i/N_{X} with N_{X} the total number of individuals in the area $X = \{\mathrm{o}, \mathrm{g}\}$. This leads to the following factors for m_{ij}:

$$\begin{aligned} m_{ij} &= \left(\tfrac{N_i}{N_{\mathrm{X}}}\right) / \left(\tfrac{N}{N_i}\right) = \frac{N}{N_{\mathrm{X}}} \quad (i, j \text{ in same area } X) \\ m_{ij} &= \left(\tfrac{N_i}{N_{\mathrm{Y}}}\right) / \left(\tfrac{N}{N_i}\right) = \frac{N}{N_{\mathrm{Y}}} \quad (i \in X \text{ and } j \in Y) \end{aligned}$$

Maximum number of family members permitted

[APG, the following should be reviewed, it is unfinished] We considered until now that people from the orange area visiting the neutral zone will be always different within the same week. An interesting question for management is how to keep the fraction of the orange population using the neutral zone as small as possible to minimize the spread of the infection. This relies on the assumption that, since symptomatic members are excluded from the neutral zone, increasing this fraction increases the chances for assymptomatic individuals to visit the neutral zone. As we will see immediately, this observation could be used to improve the management strategies.

To illustrate this point we note that the fraction of the orange population getting in contact with the green population can be estimated through the quantity $0.2\epsilon_{ij} m_{ij}$ $(i \in \mathrm{o})$, which we aim to keep lower than one. Expanding this expression we obtain

[1] We could saturate this fraction making it equal to one when every member eventually visits the neutral zone:

$$\rho = \begin{cases} 1 & \text{if } i \in \mathrm{g} \\ f_{\emptyset,\mathrm{fam}} \left(1 - \mathrm{H}(f_{\mathrm{o,fam}} - 1) \frac{f_{\mathrm{o,fam}} - 1}{f_{\mathrm{o,fam}}}\right) & \text{if } i \in \mathrm{o} \end{cases}$$

with the Heaviside function $\mathrm{H}(f_{\mathrm{o,fam}} - 1) = 1$ if $f_{\mathrm{o,fam}} \geq 1$.

$$c_{\text{fam}} < 5\sqrt{\bar{c}_i \frac{N_{\text{o}}}{N}}$$

with a value of ≈ 17 individuals per day for the adult class and assuming 20% of the population shielded. Note that the estimation heavily relies on the efficiency of the protection measures.

The clan's dilemma

In the previous section, we considered that the family members visiting were always different. However, if the population in the camps is structured in large families (hereafter clans) it opens the question of whether it would be more beneficial to keep all members of the same clan in the same area or in different areas. If all members of the same clan live in the same zone, there would be little need to interact with members of the other zone, hence reducing c_{fam}. However, since the capacity of the green zone is limited, shielding whole clans may lead to leaving other clans completely outside of the green zone, even if the strategy may be better to minimize the overall impact in the population. On the other hand, if clans are split, it increases the chances that the same relatives visit the neutral zone several times. Under the assumption that minimizing the number of different people would reduce the probability of infection, this could also be a positive strategy.