Sensitivity analysis of contact related interventions for modeling epidemics.

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Introduction

- **Age-Dependent Transmission:** We explore how interactions vary across age groups, utilizing a population contact matrix.
- **Parameter Sensitivity:** Even slight changes in parameters significantly affect disease dynamics such as $\mathcal{R}_0$ and epidemic size.
- **Understanding Impact:** Employing sensitivity analysis, we decode the impact of these parameter variations on disease propagation.
- **Innovative Techniques:** Through Latin Hypercube Sampling (LHS) and the Partial Rank Correlation Coefficient (PRCC) method, we unravel the sensitivity of contact matrix elements.
- **Enhanced Precision:** We introduce a novel approach to aggregate PRCC values, elevating the precision of pairwise sensitivity analysis.

Social Contact Matrices

If $M^{\mathrm{H}}, M^{\mathrm{S}}, M^{\mathrm{W}}, M^{\mathrm{O}}$ denote the contact matrices for home, school, work, and other types respectively, then:

- **Full** social contact matrix:

$$M = M^{\mathrm{H}} + M^{\mathrm{S}} + M^{\mathrm{W}} + M^{\mathrm{O}},$$

$$M = M^{\mathrm{H}} + M^{\Delta}.$$

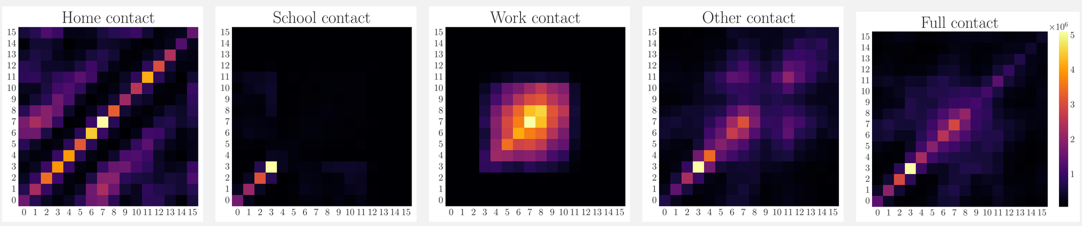
- Formally, for a **population vector** $\mathcal{P}$:

$$\mathcal{M}^{(i,j)}\mathcal{P}_j = \mathcal{M}^{(j,i)}\mathcal{P}_i,$$

$\mathcal{M}^{(i,j)}$ is the **element** of the matrix at (i, j),
$\mathcal{P}_i$ is the **number of people** in age group i.

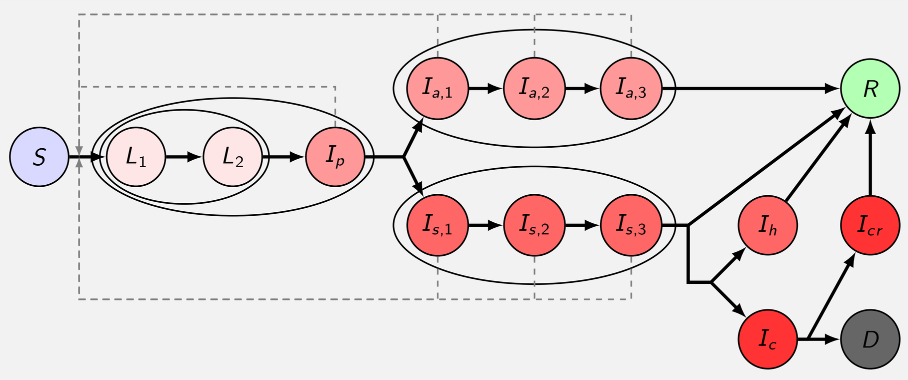
- **Symmetrize** the contacts:

$$M^{(i,j)} = \frac{1}{2\mathcal{P}_j}\left(\mathcal{M}^{(i,j)}\mathcal{P}_j + \mathcal{M}^{(j,i)}\mathcal{P}_i\right).$$



Total social contact patterns in Hungary.

Epidemic Model



- **Age-Structured Model**: This model incorporates age-dependent parameters.
- **Basic Reproduction Number ($\mathcal{R}_0$)**: Calculated using the Next Generation Matrix.
- **Transmission Rate (β_0)**: Determined by fixing $\mathcal{R}_0$ to values $[1.2, 1.8, 2.5]$.

Our approach

Concept: Perform a sensitivity analysis on the elements of the contact matrix.

- Due to dependence, we consider only the **upper triangular elements**.
- Assumed reproduction numbers, $\overline{\mathcal{R}}_0 = [1.2, 1.8, 2.5]$.
- Considered *target variables, T*: $\mathcal{R}_0$ and Final death size.

Approach: **Latin Hypercube Sampling/Partial Rank Correlation Coefficient (LHS/PRCC)** to the $k = 136$ **parameters**: $M = M^{\mathrm{H}} + M^{\Delta}$.

- **Sample only** M^{Δ} i.e. $k = 136$ elements on the interval $[0, 1]$ to get M_{ratio}.

$$M' = M^{\mathrm{H}} + (\mathbb{1} - M_{\text{ratio}}) \odot M^{\Delta}$$

- $\mathbb{1} \in \mathbb{R}^{16\times 16}$ refers to matrix $[1]_{i,j=1}^{16}$, $\odot$ denotes **element-wise product calculation.**
- $M_{\text{ratio}} \in [0,1]^{16\times 16}$, $M_{\text{ratio}}^{(i,j)} = M_{\text{ratio}}^{(j,i)}$.

- Since when $\mathcal{R}_0 < 1$, there is no epidemic, we generate samples with $\mathcal{R}_0 \geq 1$.
- Thus, $\mathbb{1} - M_{\text{ratio}} = \kappa \cdot \mathbb{1}, \kappa \in [0, 1]$.

LHS

LHS Parameter Samples				Outputs			
p_1	p_2	$\cdots$	p_K	s_1	s_2	$\cdots$	s_T
$p_1^{(1)}$	$p_2^{(1)}$	$\cdots$	$p_K^{(1)}$	$s_1^{(1)}$	$s_2^{(1)}$	$\cdots$	$s_T^{(1)}$
$p_1^{(2)}$	$p_2^{(2)}$	$\cdots$	$p_K^{(2)}$	$s_1^{(2)}$	$s_2^{(2)}$	$\cdots$	$s_T^{(2)}$
$\vdots$	$\vdots$	$\ddots$	$\vdots$	$\vdots$	$\vdots$	$\ddots$	$\vdots$
$p_1^{(N)}$	$p_2^{(N)}$	$\cdots$	$p_K^{(N)}$	$s_1^{(N)}$	$s_2^{(N)}$	$\cdots$	$s_T^{(N)}$

- LHS table, $N \times k$.
- LHS table intervals, $[0, 1 - \kappa]$.
- Simulation outputs, $N \times T$.
- Assumed $N = 10{,}000$ simulations.

PRCC

LHS Parameter Ranks				Output Ranks			
r_1	r_2	$\cdots$	r_K	d_1	d_2	$\cdots$	d_T
$r_1^{(1)}$	$r_2^{(1)}$	$\cdots$	$r_K^{(1)}$	$d_1^{(1)}$	$d_2^{(1)}$	$\cdots$	$d_T^{(1)}$
$r_1^{(2)}$	$r_2^{(2)}$	$\cdots$	$r_K^{(2)}$	$d_1^{(2)}$	$d_2^{(2)}$	$\cdots$	$d_T^{(2)}$
$\vdots$	$\vdots$	$\ddots$	$\vdots$	$\vdots$	$\vdots$	$\ddots$	$\vdots$
$r_1^{(N)}$	$r_2^{(N)}$	$\cdots$	$r_K^{(N)}$	$d_1^{(N)}$	$d_2^{(N)}$	$\cdots$	$d_T^{(N)}$

- For PRCC values P_k, **replace LHS table values** with ascending integers.
- Then, we **linearly fit** $2k$ regression models in two rounds:
  - First variable d is used as target,
  - Then models are fitted for each r_i as output variable, $i = 1, 2, \ldots, k$.

Probability values

$$\mathcal{T}_k = P_k\sqrt{\frac{N-2-k}{1-P_k^2}} \sim t_{N-2-k}$$

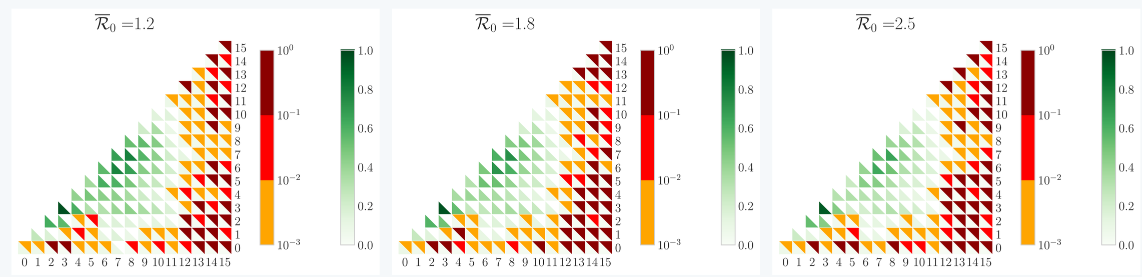
- $N - 2 - k$ **degrees of freedom** and P-values, p_k,
- Then p_k, can be computed from $\mathcal{T}_k$; $p_k \in [0, 1]$.

Aggregation approach

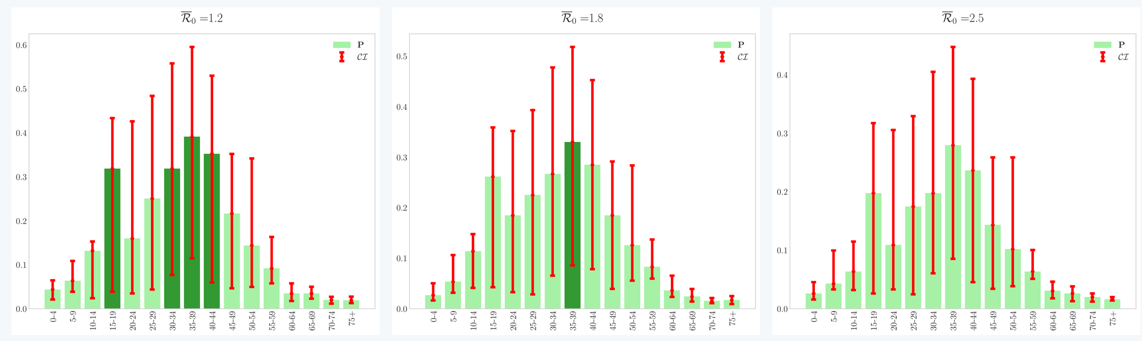
$$\xi_{i,j} = \frac{1 - p_{i,j}}{\sum_{m=1}^{16}(1 - p_{i,m})}$$

- Median, **P** is calculated with respect to $\xi_{i,j}$ along with their corresponding lower and upper quartiles, establishing confidence interval bounds, $\mathcal{CI}$.
- The **P** shows age group-wise PRCC values, with $\mathcal{CI}$ indicating their **variations**.

Results, Target: $\mathcal{R}_0$

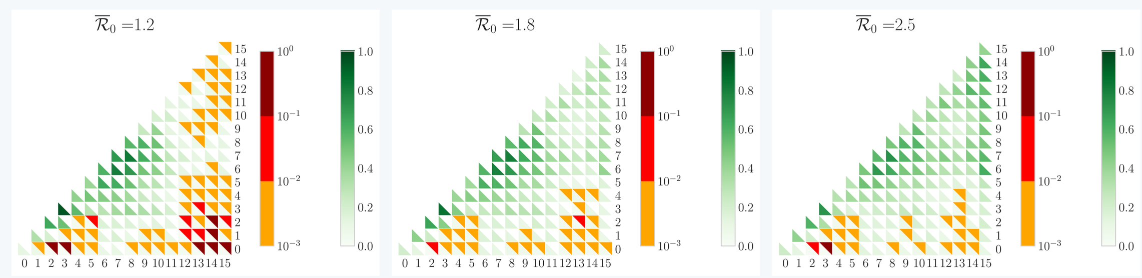


For age group pairs, P_k and p_k are depicted with varying values of $\mathcal{R}_0$. The green bars represent P_k, while shades of red indicate p_k at different significance levels: $< 0.1\%$ (white), $0.1\% - 1\%$ (orange), $1\% - 10\%$ (red), and $> 10\%$ (dark-red).

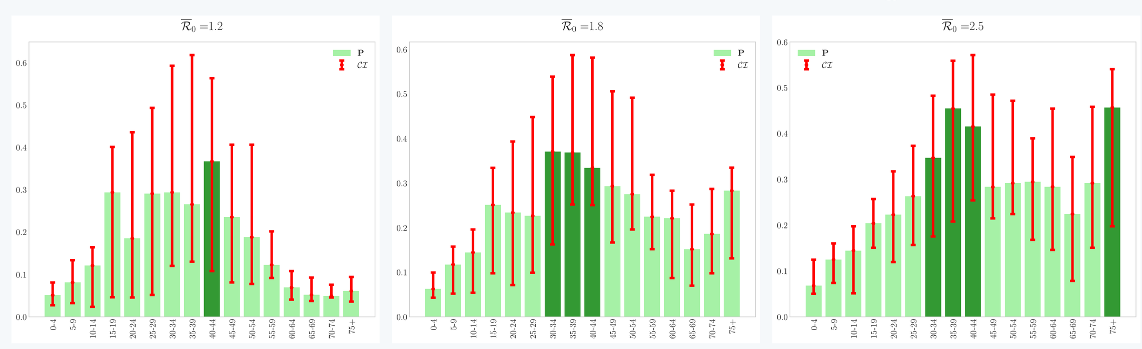


Considering various values of $\overline{\mathcal{R}}_0$, the red lines denote the lower and upper quartiles of the **P**. Values below 0.3 are shown in light-green, those between 0.3 and 0.5 in green, and values above 0.5 in dark-green.

Results, Target: Final death size



For age group pairs, the corresponding p_k values and P_k with the final death size as the target.



The corresponding $\mathcal{CI}$ for **P** when observing the final death size as the target.

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