

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 affects disease dynamics such as the \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^H, M^S, M^W, M^O denote the contact matrices for **home**, **school**, **work**, and **other** types respectively, then:

- Full social contact matrix:** $M = M^H + M^S + M^W + M^O, \quad M = M^H + M^\Delta$.
- 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:

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

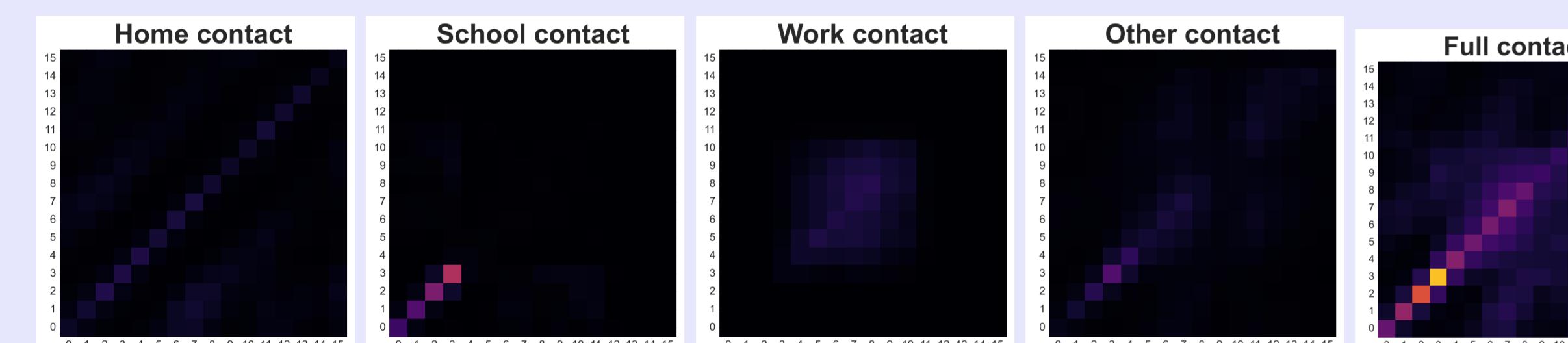


Figure 1. Contact matrices representing the social contact patterns in Hungary, estimated in [4].

Epidemic Model

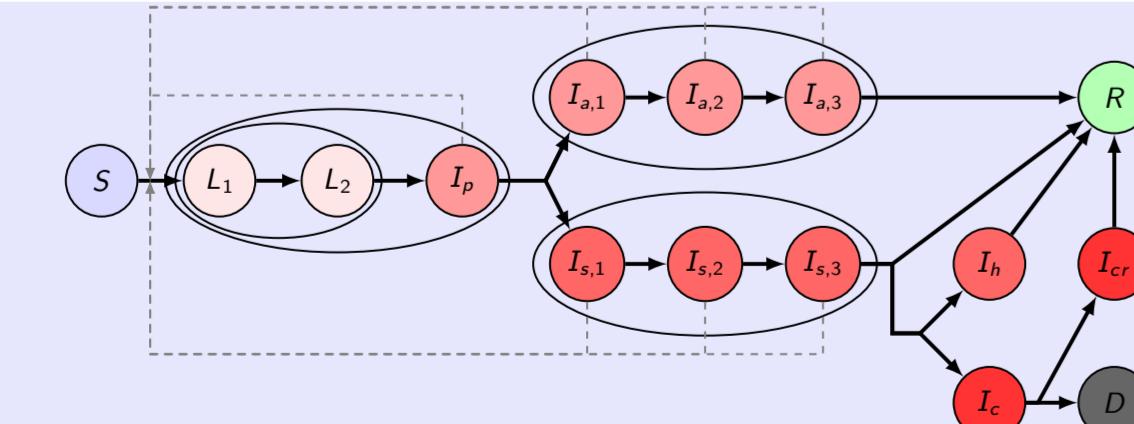


Figure 2. Transmission diagram of the epidemic model from [2]. Black arrows show patient transitions, while dashed arrows indicate possible routes of infection spread.

- Age-Structured Model:** This model incorporates age-dependent parameters.
- Basic Reproduction Number (\mathcal{R}_0):** Calculated using the **Next Generation Matrix** [1].
- Transmission Rate (β_0):** Determined by fixing \mathcal{R}_0 to values [1.2, 1.8, 2.5].
- Susceptibility (σ):** Explored for values [0.5, 1.0] for $1 \leq i \leq 4$.

Our approach

Latin Hypercube Sampling/Partial Rank Correlation Coefficient (LHS/PRCC) to the $K = 136$ parameters: $M = M^H + M^\Delta$

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

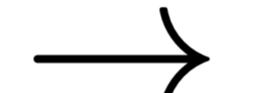
$$M' = M^H + (\mathbb{1} - M_{\text{ratio}}) \odot M^\Delta$$

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

LHS parameter samples

p_1	p_2	\dots	p_K
$p_1^{(1)}$	$p_2^{(1)}$	\dots	$p_K^{(1)}$
$p_1^{(2)}$	$p_2^{(2)}$	\dots	$p_K^{(2)}$
\vdots	\vdots	\ddots	\vdots
$p_1^{(N)}$	$p_2^{(N)}$	\dots	$p_K^{(N)}$



LHS parameter ranks

r_1	r_2	\dots	r_K
$r_1^{(1)}$	$r_2^{(1)}$	\dots	$r_K^{(1)}$
$r_1^{(2)}$	$r_2^{(2)}$	\dots	$r_K^{(2)}$
\vdots	\vdots	\ddots	\vdots
$r_1^{(N)}$	$r_2^{(N)}$	\dots	$r_K^{(N)}$

- LHS table, $N \times K$.
- Simulation outputs, $N \times T$.
- LHS table has intervals $[0, 1 - \kappa]$.
- Assumed $N = 10,000$ simulations.
- To calculate the PRCC values P_k , we **replace each LHS value** with integers $1, 2, 3, \dots, N$ in ascending order.
- Then, we **linearly fit** $2K$ regression models in two rounds.

$$P_k = \rho_{\text{Res}_{1,k}, \text{Res}_{2,k}} = \frac{\text{Cov}(\text{Res}_{1,k}, \text{Res}_{2,k})}{\sqrt{\text{Var}(\text{Res}_{1,k}) \cdot \text{Var}(\text{Res}_{2,k})}}$$

$$\text{Res}_{1,k} = d^{(i)} - \hat{d}_k^{(i)}, \quad \text{Res}_{2,k} = r_k^{(i)} - \hat{r}_k^{(i)}$$

$$\hat{d}_k^{(i)} = a_k^{(0)} + \sum_{j=1, j \neq k}^K a_k^{(j)} r_j^{(i)}, \quad i = 1, \dots, N$$

$$\hat{r}_k^{(i)} = b_k^{(0)} + \sum_{j=1, j \neq k}^K b_k^{(j)} r_j^{(i)}, \quad i = 1, \dots, N$$

Probability values

- Each P_k generates a value \mathcal{T}_k according to the following statistic:

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

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

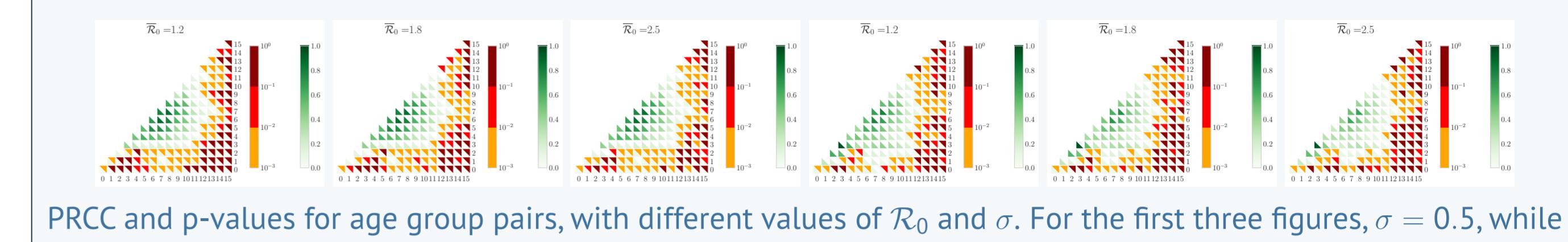
Aggregation approach

$$P_i = \sum_{j=1}^{16} P_{ij} \cdot \xi_{ij} \quad s_i = \sqrt{\left(\sum_{j=1}^{16} P_{ij}^2 \cdot \xi_{ij} \right) - P_i^2}$$

$$\pi_{ij} = \frac{1 - p_{ij}}{\sum_{m=1}^{16} (1 - p_{i,m})}, \quad \xi_{ij} = \frac{P_{ij} \cdot \pi_{ij}}{\sum_{m=1}^{16} P_{i,m} \cdot \pi_{i,m}}$$

$\mathbf{P} = (P_i)_{i=1}^{16}$ is the **age group-wise PRCC values** with their corresponding standard deviations, $\mathbf{s} = (s_i)_{i=1}^{16}$.

Results, Target: \mathcal{R}_0

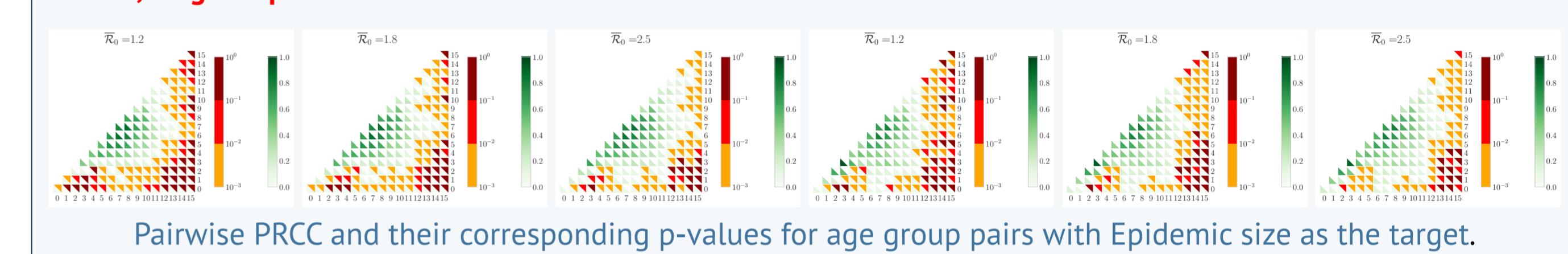


PRCC and p-values for age group pairs, with different values of \mathcal{R}_0 and σ . For the first three figures, $\sigma = 0.5$, while for the remaining figures, $\sigma = 1.0$. The green bars represent PRCC values, while shades of red indicate p-values at various significance levels: < 0.1% (white), 0.1% – 1% (orange), 1% – 10% (red), and > 10% (dark-red).



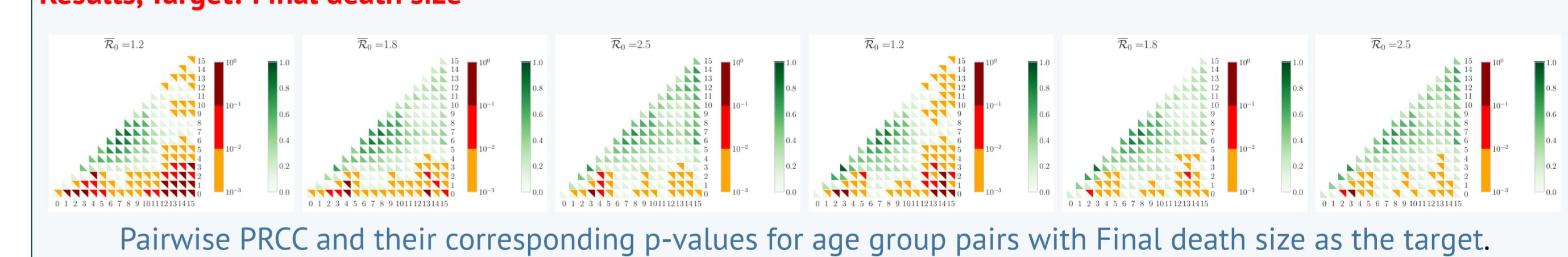
Age group-wise PRCC values, considering various values of \mathcal{R}_0 and σ . The red lines denote error bars, illustrating the standard deviation of the cumulative PRCC values. Cumulative PRCC values below 0.3 are shown in light-green, those between 0.3 and 0.5 in green, and values above 0.5 in dark-green.

Results, Target: Epidemic size

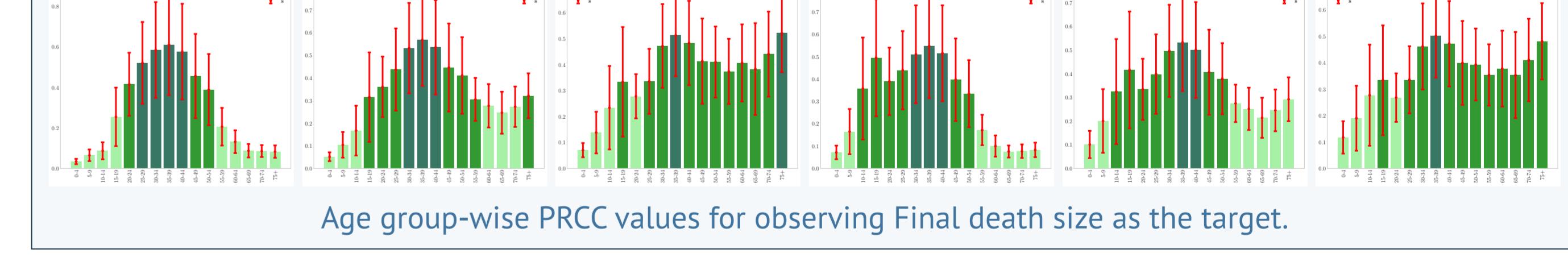


Pairwise PRCC and their corresponding p-values for age group pairs with Epidemic size as the target.

Results, Target: Final death size



Age group-wise PRCC values for observing Epidemic size as the target.



Age group-wise PRCC values for observing Final death size as the target.

References

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