SAND2022-14528C

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A Practical Application of Global Sensitivity Analysis for Stochastic Epidemiology Models in Support of Policy Decisions

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October 18, 2022

SES 2022, Texas A&M University, College Station, TX

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Motivation

We want to understand the benefit of vaccine prioritization strategies in communities with different demographics and connectivity.

- We anticipate that variability in communities structures may require prioritization of different vaccination strategies.
- Network models are very useful in capturing the variability across community structures.
- That variability inherent to the stochastic model is yet another source of uncertainty.

How do we provide proper treatment of uncertainty quantification so that we trust the results of global sensitivity analysis?

Outline

The Model: Sandia’s Adaptive Recovery Model (ARM)

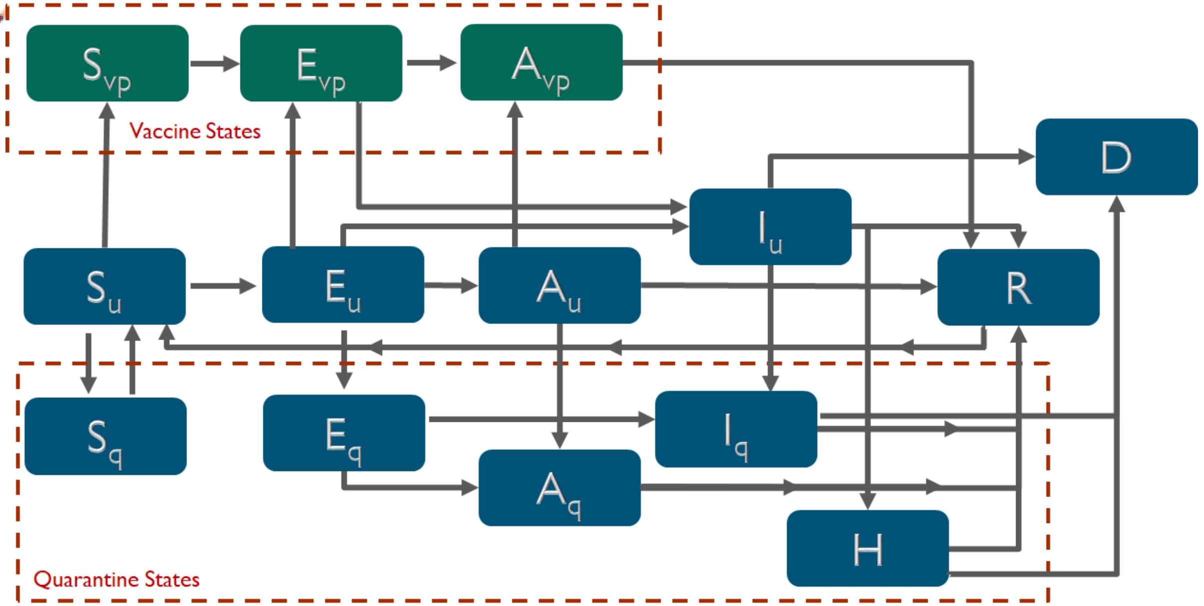
Global Sensitivity Analysis: in Support of Vaccine Prioritization Strategies

Sobol’ Indices of Stochastic Models

Vaccination Prioritization Strategy Analysis

Adaptive Recovery Model

Sandia's Adaptive Recovery Model (ARM)



S_*: Susceptible

E_*: Exposed

A_*: Asymptomatic-Infectious

I_*: Infectious-Symptomatic

R: Recovered

H: Hospitalization

D: Disease-related Deaths

Intervention Strategies

- Vaccination strategies
- Quarantine
- Use of PPE
- Contact tracing
- Random testing

Force of Infection: $\lambda(t) = \beta\kappa \frac{\eta_A A(t) + I(t) + \eta_H H(t)}{Total\_Pop}$

Network-based representation

- Network prioritization for transmission
- Heterogeneous node properties can include information on age and comorbidities
- Stochastic process is used to model disease progression

Disease transmission parameters are based on age.

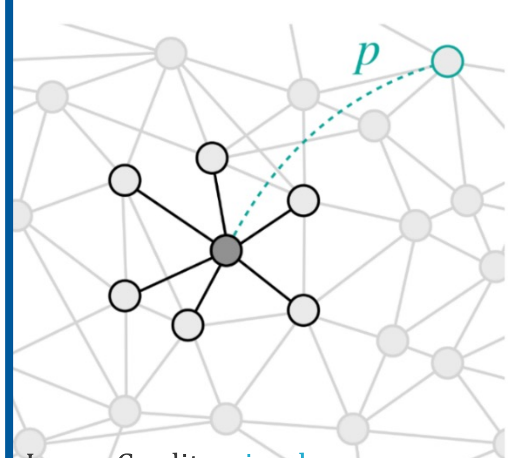
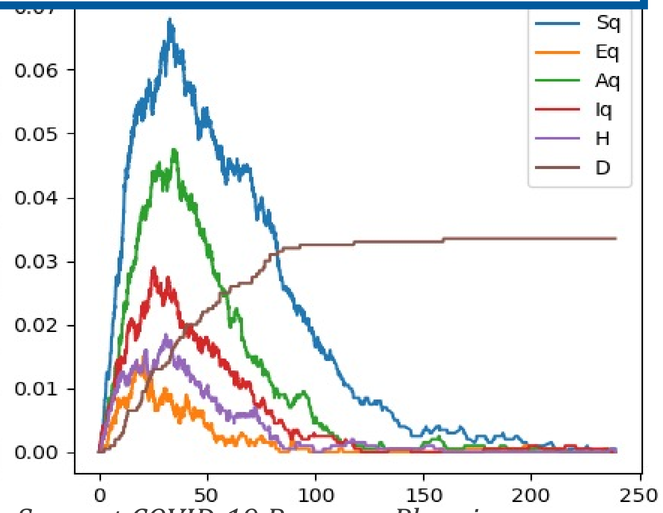


Image Credit: seirsplus



Beyeler, Acquesta, Klise, Makvandi, and Finley 2020). Adaptive Recovery Model: Designing Systems for Testing, Tracing, and Vaccination to Support COVID-19 Recovery Planning, SAND2020-11014, Sandia National Laboratories, Albuquerque, NM

Centers for Disease Control and Prevention, COVID-19 Pandemic Planning Scenarios, https://www.cdc.gov/coronavirus/2019-ncov/hcp/planning-scenarios.html

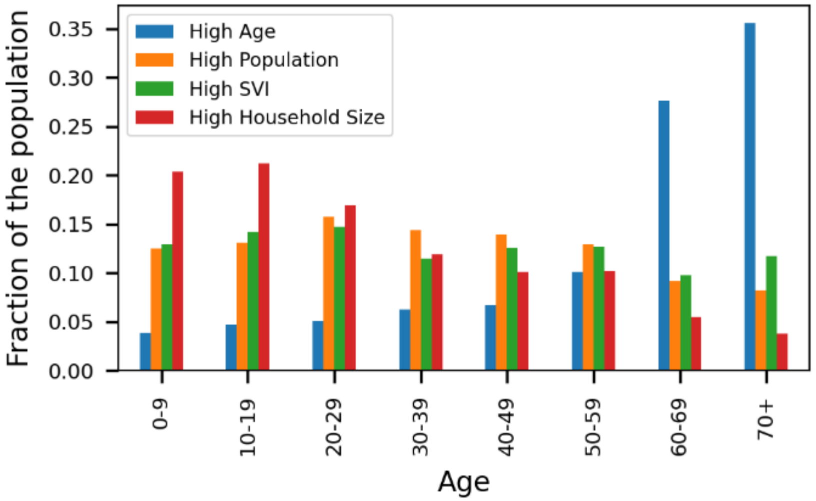
Variability in Community Networks Structures

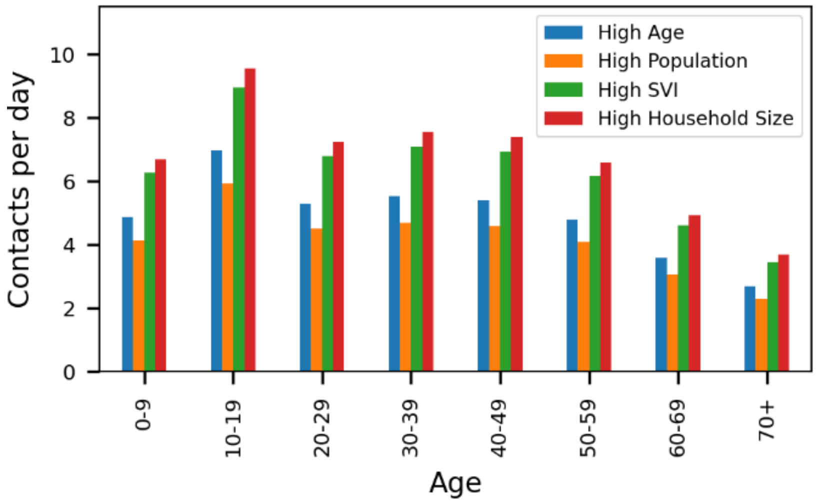
Table 1: **Communities based on U.S. counties having high SVI, high average age, high average household size, or high population (criteria for selection shown in bold).**

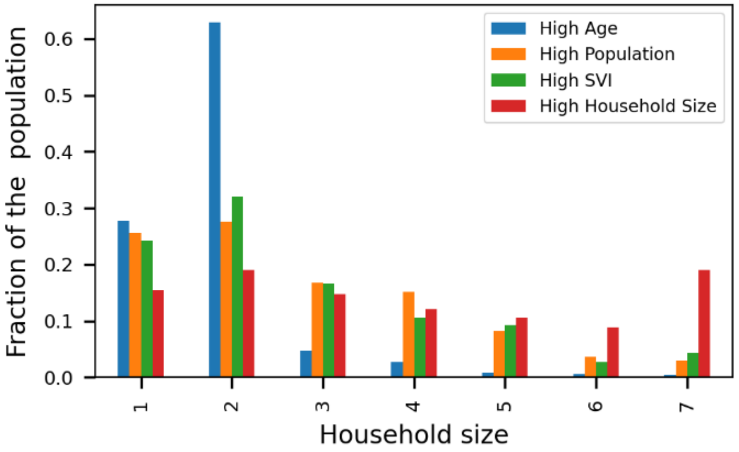
Community	County, State	Average Age (yr)	Population (people)	SVI (unitless)	Average Household Size (people)
High Age	Sumter, FL	**58.557**	113,589	0.236	1.894
High Population	Los Angeles, CA	37.400	**10,057,155**	0.768	2.754
High SVI	Duval, TX	38.616	11,510	**0.999**	2.746
High Household Size	Oglala Lakota, SD	29.299	14,263	0.994	**3.863**

Community networks based on county level census data

FARZ algorithm is used to generate networks from census data and empirical contact data within age groups.

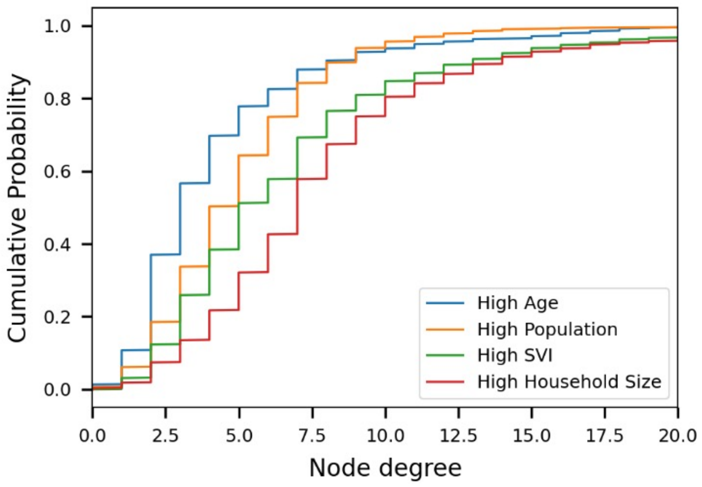




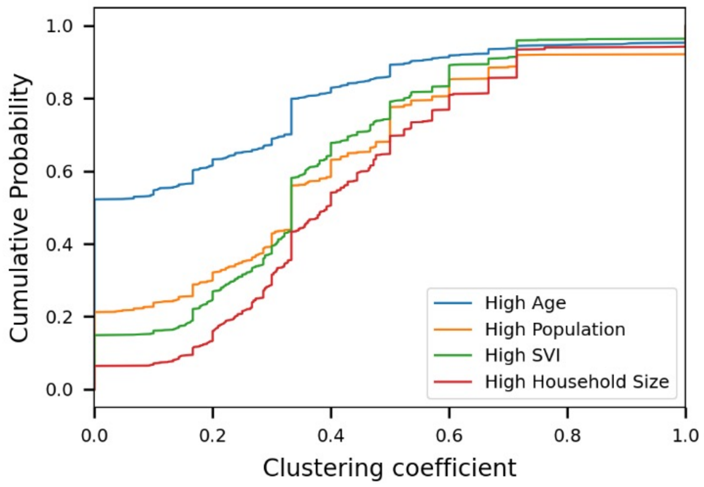


Centers for Disease Control and Prevention, CDC/ATSDR Social Vulnerability Index, https://www.atsdr.cdc.gov/placeandhealth/svi/index.html
Fagnan, Abnar, Rabbany, and Zaiane, Modular networks for validating community detection algorithms," arXiv preprint arXiv:1801.01229, 2018.
Mossong et al, 2008, Social contacts and mixing patterns relevant to the spread of infectious diseases, PLoS Medicine, 5(3)

Variability in Community Networks

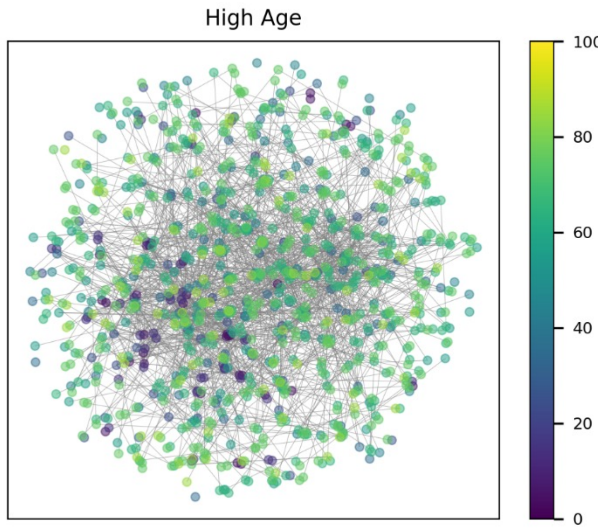


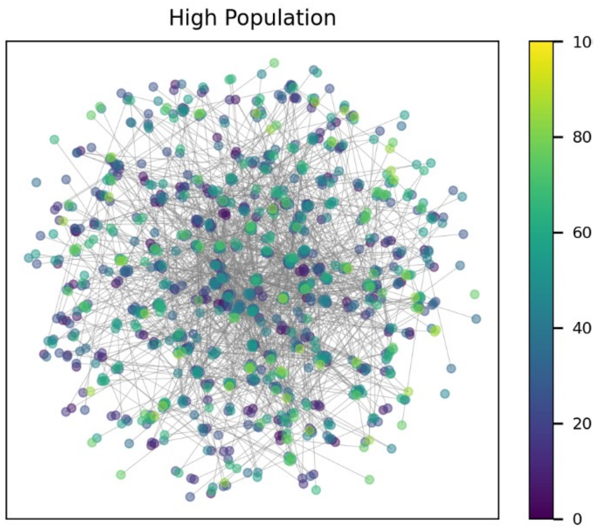
Node degree, clustering coefficient, and graphics show distinct differences between communities

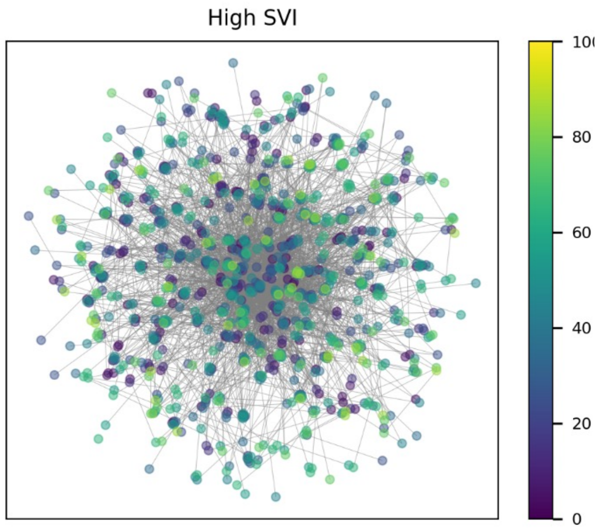


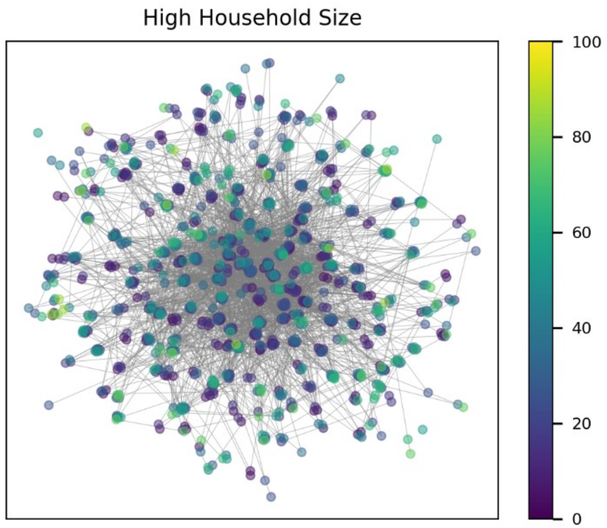
Higher age,
Lower connectivity community

Lower age,
Higher connectivity community









Global Sensitivity Analysis in Support of Vaccination Prioritization Strategies

Global Sensitivity Analysis

Formal mathematical method for apportioning the influence that sources of uncertainty have on the output uncertainty.

Objective	What is the analysis objective for partition the influence that sources of uncertainty have on a model/system output uncertainty?

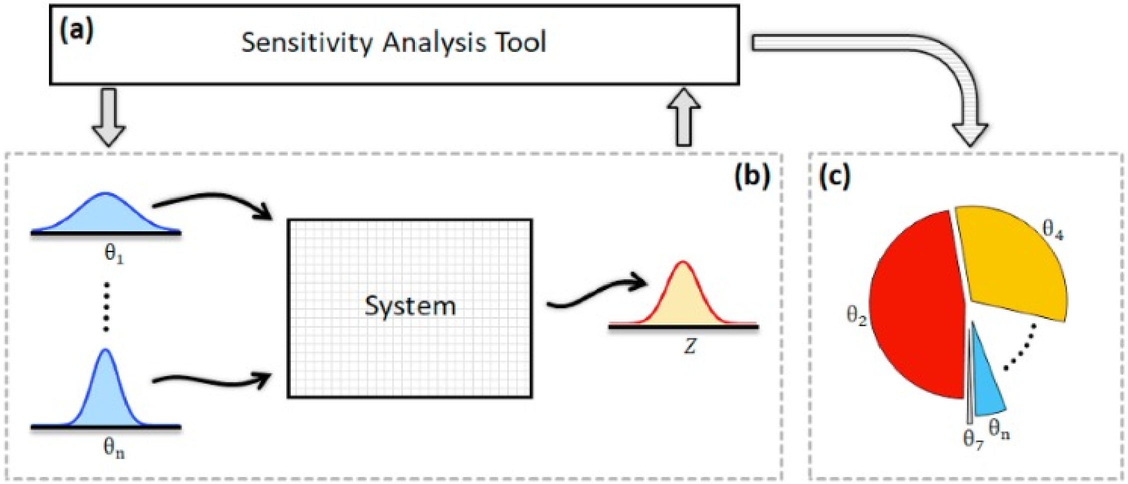


Image Credit: **Razavi et. al.** *The future of sensitivity analysis: An essential disciple for systems modeling and policy support.* 2021

Inputs	**System**	**Output**
Sampling techniques: for capturing variability from input uncertainty.	Proper treatment for controlled and uncontrolled sources of random behaviors.	Target scalar variable outcome for which output uncertainty will be measured.

Global Sensitivity Analysis in Support of Vaccine Strategy Prioritization

Objective: For each community type, how are vaccine prioritization strategies impacted by vaccine willingness, mask use/effectiveness, and community interactions (i.e., network initializations)?

Vaccine prioritization strategies

- **Random vaccination**
- **Number of contacts**: high daily contacts to low
- **Age**: oldest to youngest
- **Household size**: large households to small households
- **Ring vaccination**: Based on contact with known cases

Vaccine willing: percent of the population that is willing to be vaccinated
Mask use/effectiveness: combines the probability that an individual wears a mask and the protection from the mask.
Network Initialization: a random seed controls initialization and network structure of the community.

Variable	Type	Values
Community	Categorical	High Age, High Population, High SVI, High Household Size
Vaccine Prioritization	Categorical	Random, Number of Contacts, Age, Household size, Ring
Vaccine Willingness	Continuous	$\mathcal{U}[0.1,0.9]$
Mask Use/Effectiveness	Continuous	$\mathcal{U}[0,0.8]$
Random Seed	Discrete	$\mathbb{N} \cap [0,9]$

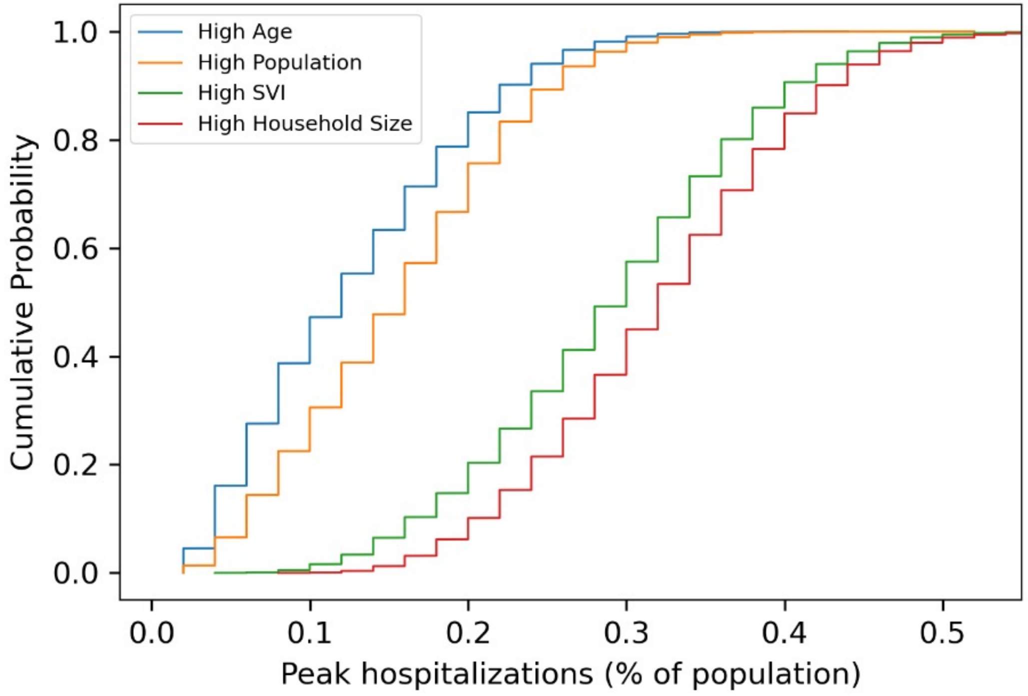
Output: Quantity of Interest (QoI)

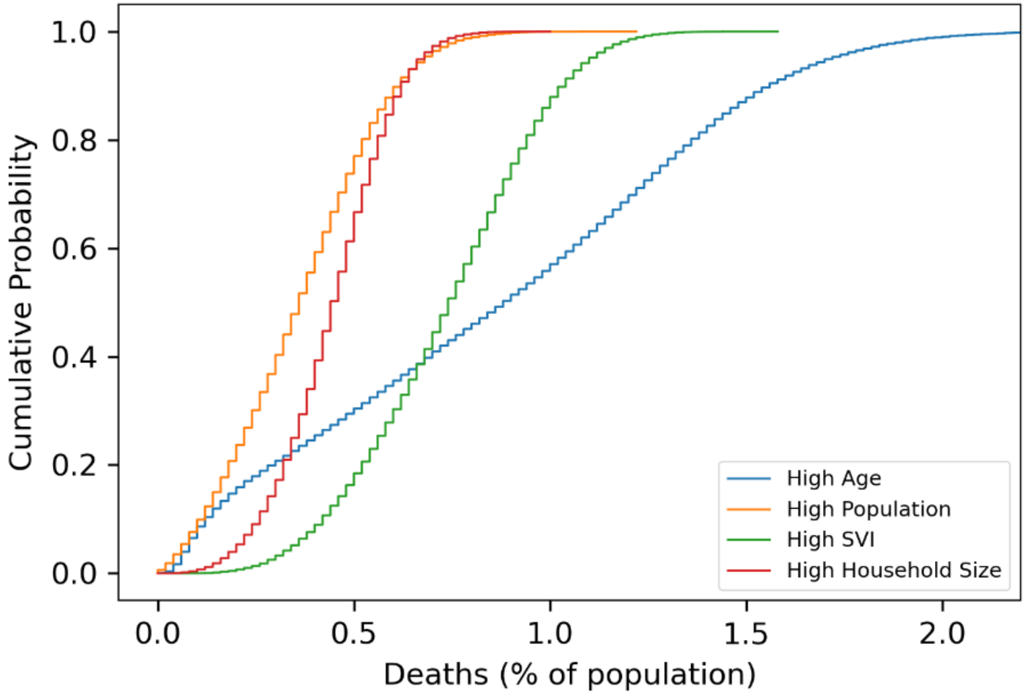
Peak Hospitalizations
Highest within the
High SVI and High Household Size communities.

- These communities have higher connectivity (high node degree and clustering coefficient) and higher number of contacts per day among older people.

Disease-related Deaths
Highest within the High Age community

- While High Age communities are more isolated the older population has high mortality risk.
- High SVI communities also have an older population with high mortality risk





* Distributions include results from all simulation results

Sobol’ Indices for Stochastic Models

Sobol' Indices: Deterministic Model

Sobol Indices are a variance-based approach to global sensitivity analysis (GSA)

Determinisitic Computer Model:

$$Z = f\big(\boldsymbol{X}(t;\Theta)\big)$$

such that

$$\Theta = \{\theta_1, \theta_2, \dots, \theta_n\}\text{: Parameters}$$

and

$$Z\text{:Quantity of Interest (QoI)}$$

Sobol' Indices:

Each parameter θ_i represents a variate that is sampled from a random variable, e.g., $\theta_i^j \in \mathcal{N}(\mu, \sigma^2)$ for $1 \leq i \leq n$

$$S_u = \frac{Var(\mathbb{E}[Z|\boldsymbol{\Theta}_u])}{Var(Z)}$$

Where

$$u \in \mathcal{P}(\{1,2,\dots,n\})$$

The power set derived from the set of integer indexes 1 to n.

First Order Sobol' Indices:

$$u = \{k\} \text{ for } k \in \{1,2,\dots,n\}$$

Total Order Sobol' Indices:

$$u = \{k\}^c, T_k = 1 - S_u$$

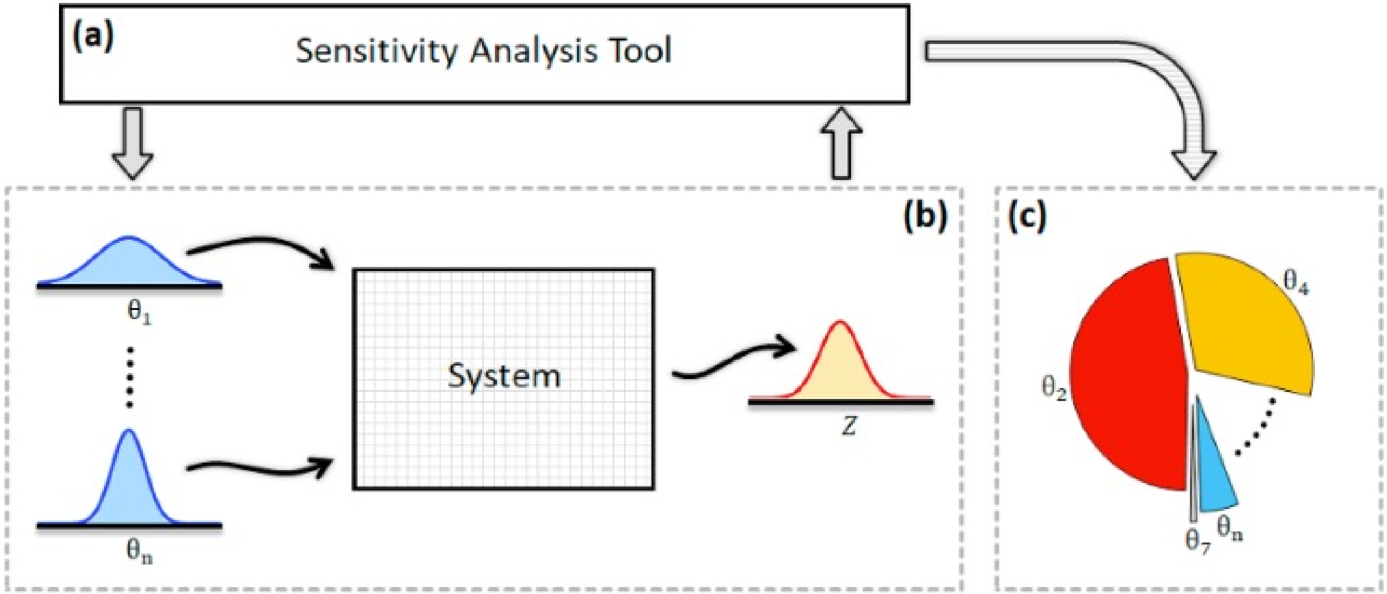


Image Credit: **Razavi et. al.** *The future of sensitivity analysis: An essential disciple for systems modeling and policy support.* 2021

Sobol' Indices: Stochastic Model

Sobol Indices are a variance-based approach to global sensitivity analysis (GSA)

Stochastic Computer Model:

$$Z = f(\boldsymbol{X}(t;\boldsymbol{\Theta});\boldsymbol{\mathcal{W}})$$

such that

$\boldsymbol{\Theta} = \{\theta_1, \theta_2, \dots, \theta_n\}$: Parameters

$\boldsymbol{\mathcal{W}} = \{w_1, w_2, \dots, w_p\}$: Randomized behavior of the model

and

Z: quantity of interest (QoI)

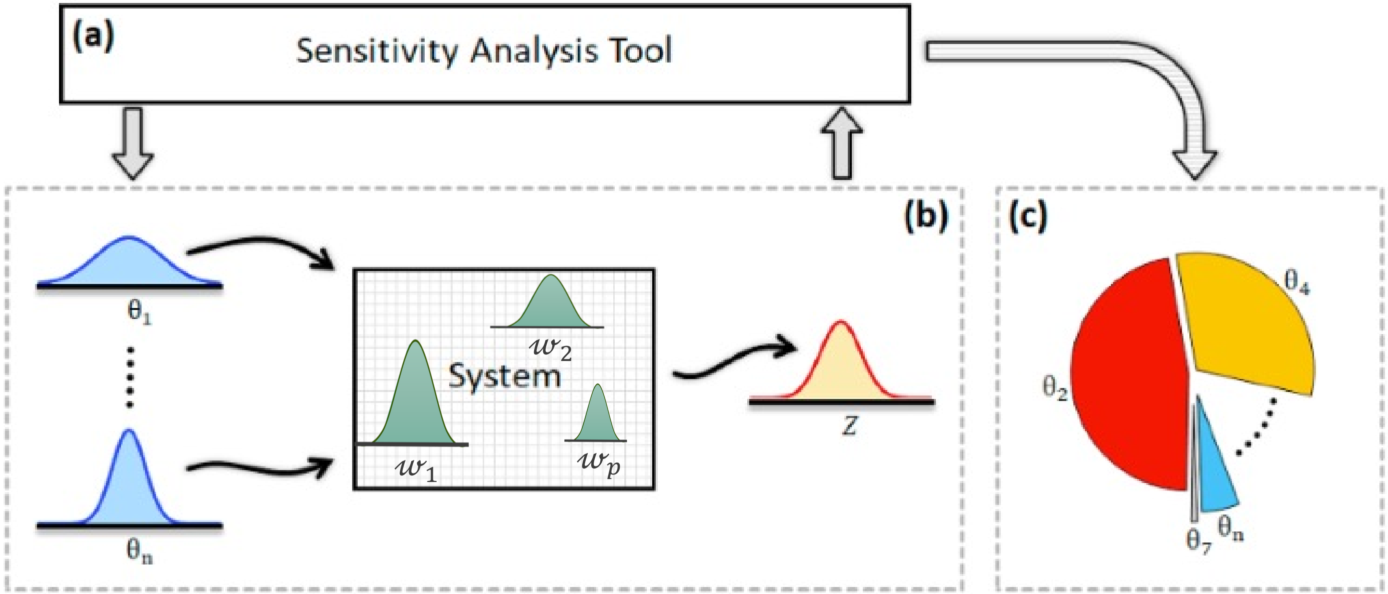


Image Credit: **Razavi et. al.** *The future of sensitivity analysis: An essential disciple for systems modeling and policy support.* 2021

For each variate sample for $\boldsymbol{\mathcal{W}}^{\boldsymbol{k}} = \{w_1^k, w_2^k, \dots, w_p^k\}$ results in one realization of the stochastic system Z^k.
Yet the variability of $\boldsymbol{\Theta}$ can still be measured such that:

$$S_u^k = \frac{Var(\mathbb{E}[Z^k|\boldsymbol{\Theta}_u])}{Var(Z^k)}$$

For sufficient sampling of $\boldsymbol{\mathcal{W}}$**,** results in the uncertainty of the Sobol' indices, i.e., $Var(S_u)$**.**

Hart, J.L., Alexanderian, A. and Gremaud, P.A., 2017. Efficient computation of Sobol'indices for stochastic models. *SIAM Journal on Scientific Computing*, *39*(4), pp.A1514-A1530.

Vaccine Prioritization Strategy Analysis Under Uncertainty

1. **[Scenario]** For each combination of community type and vaccination strategy [20 Total]:

   {High Age, High Population, High SVI, High Household Size}
   and
   {Random, Age, Number of Contacts, Household size, Ring}

   a. **[Stochastic Model Uncertainty]** Fix the random seed to set network initialization: $\mathcal{w}^k \in \mathbb{N} \cap [0,9]$

      i. **[Sobol' Indices]**

         1. Generate Saltelli Sampling, 2×2^8 variates, for two random variables:
            a. Vaccine Willingness, $\theta_1 \sim \mathcal{U}[0.1, 0.9]$
            b. Mask use/effectiveness, $\theta_2 \sim \mathcal{U}[0, 0.8]$
         2. For each Saltelli sample of $\mathbf{\Theta}^j$ and fixed $\mathcal{w}^k$ run the simulated model to get 2×2^8 realizations:
            a. Peak Hospitalizations, $\{Z_H\}^k$
            b. Disease-related Deaths, $\{Z_D\}^k$
         3. Calculate the Sobol' Indices for the k^{th} realization of the stochastic system:

$$\{S^k_{\theta_1}, S^k_{\theta_2}, S^k_{\theta_1\theta_2}, T^k_{\theta_1}, T^k_{\theta_2}\}$$

   b. **Repeat** for $\mathcal{w}^k \in \mathbb{N} \cap [0,9]$
2. **Repeat** for all 20 combinations

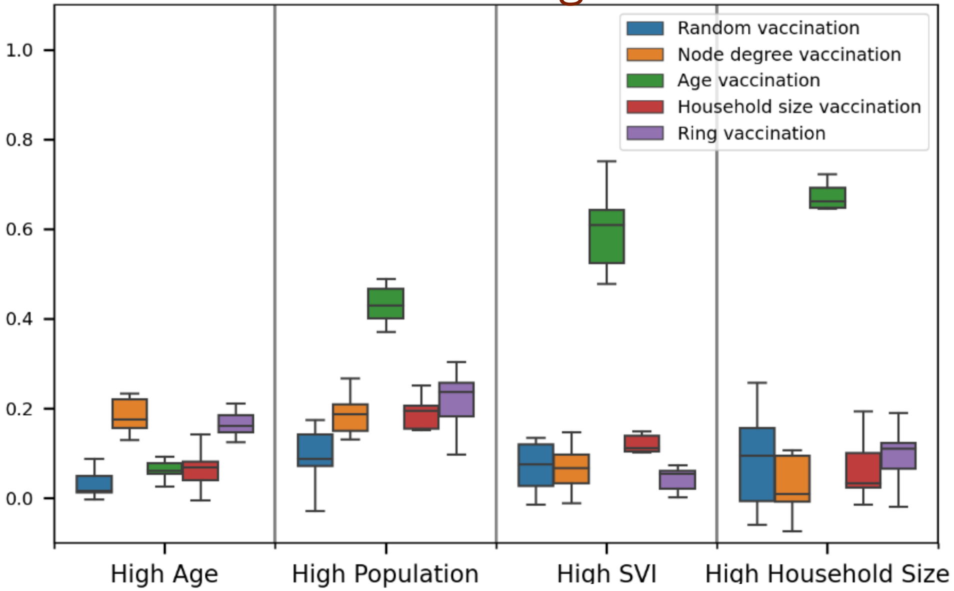
307,200 Simulations of Stochastic Network Model

Vaccination Strategy Prioritization Analysis

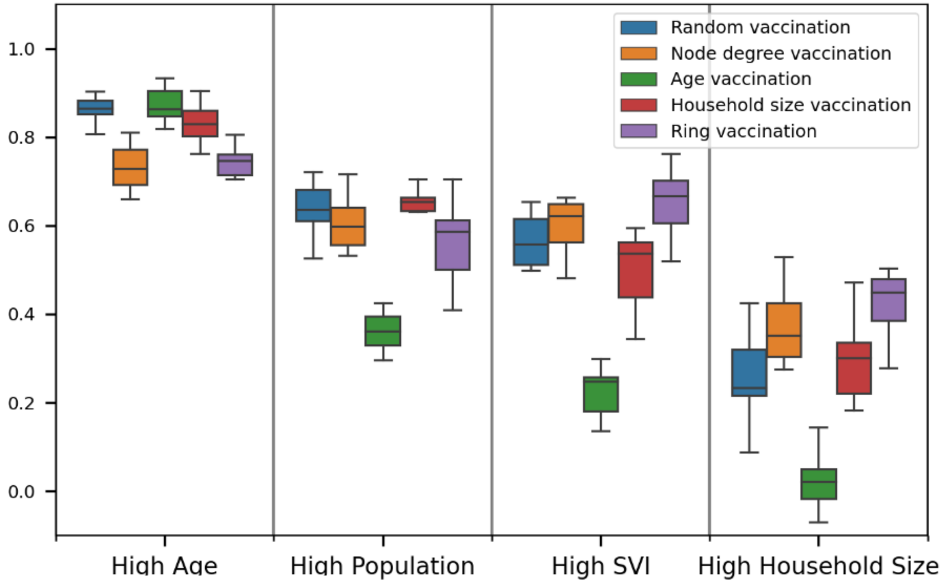
Sensitivity of Disease Related Deaths with respect to:

Vaccine Willingness

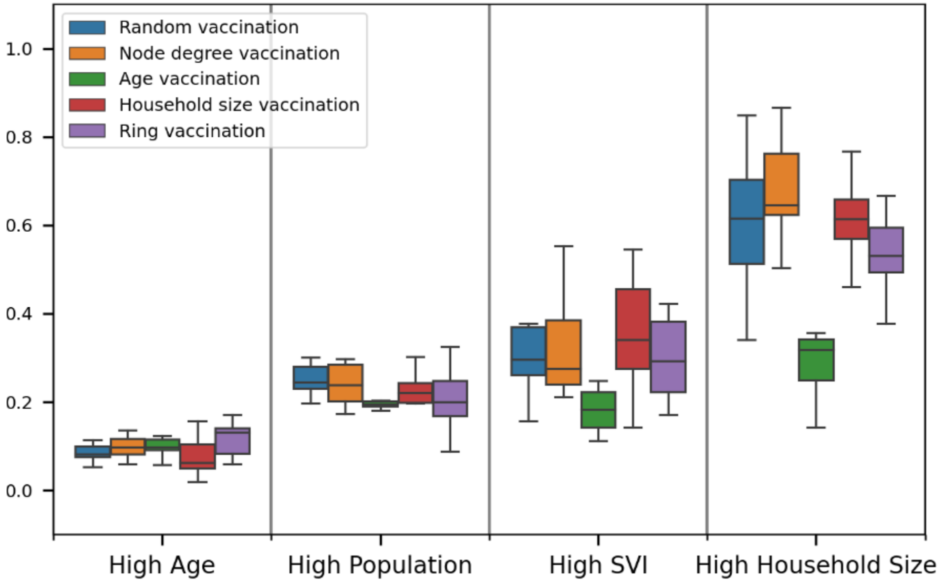
First-Order



Mask Use/Effectiveness



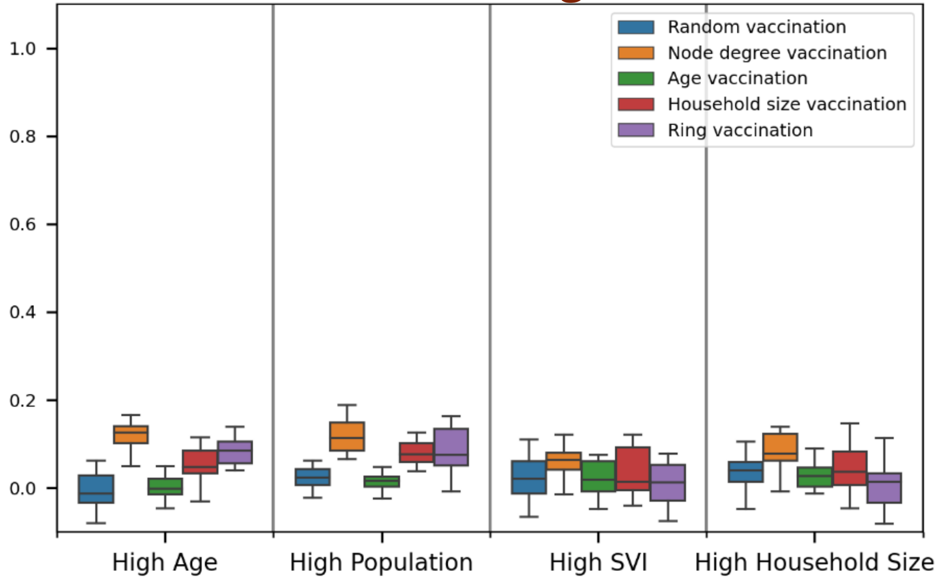
Second-Order



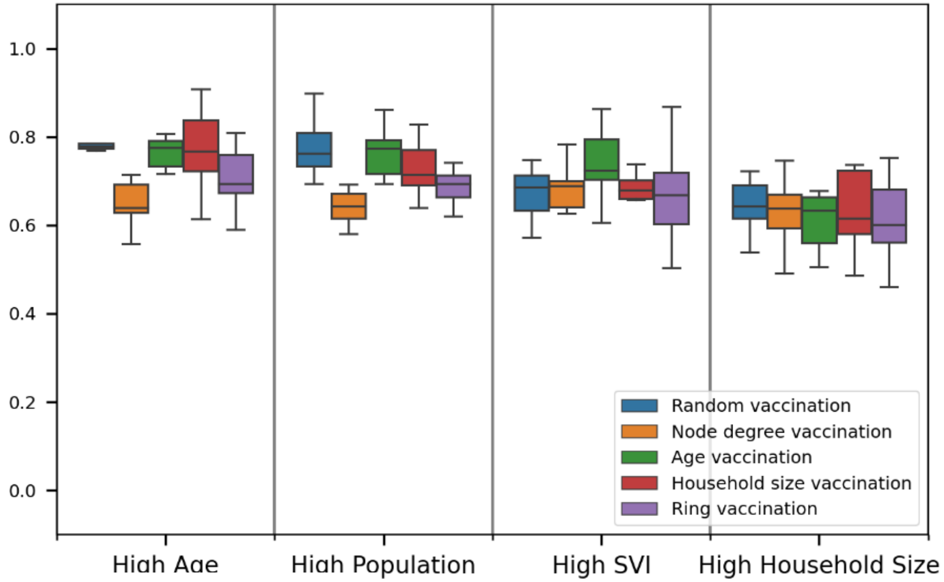
Sensitivity of Peak Hospitalizations with respect to:

Vaccine Willingness

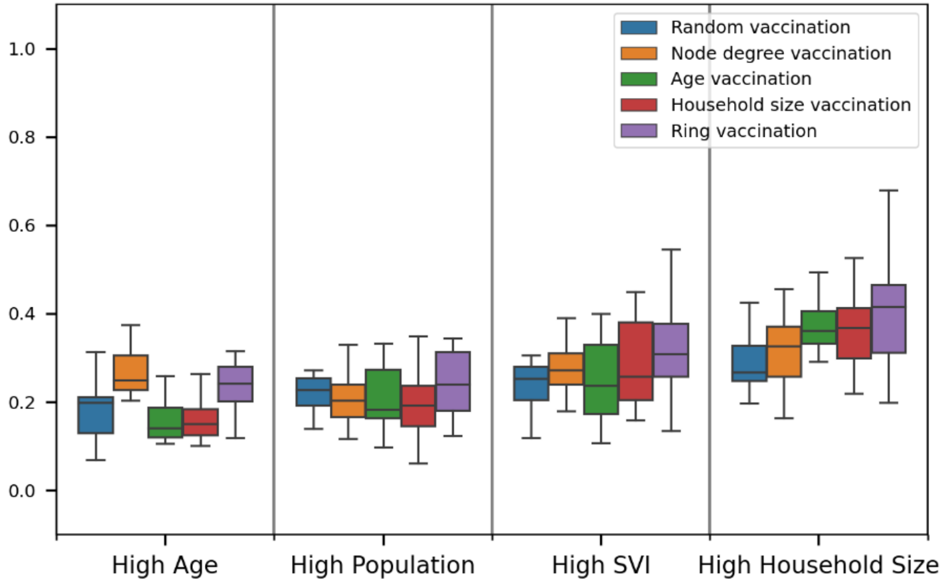
First-Order



Mask Use/Effectiveness



Second-Order



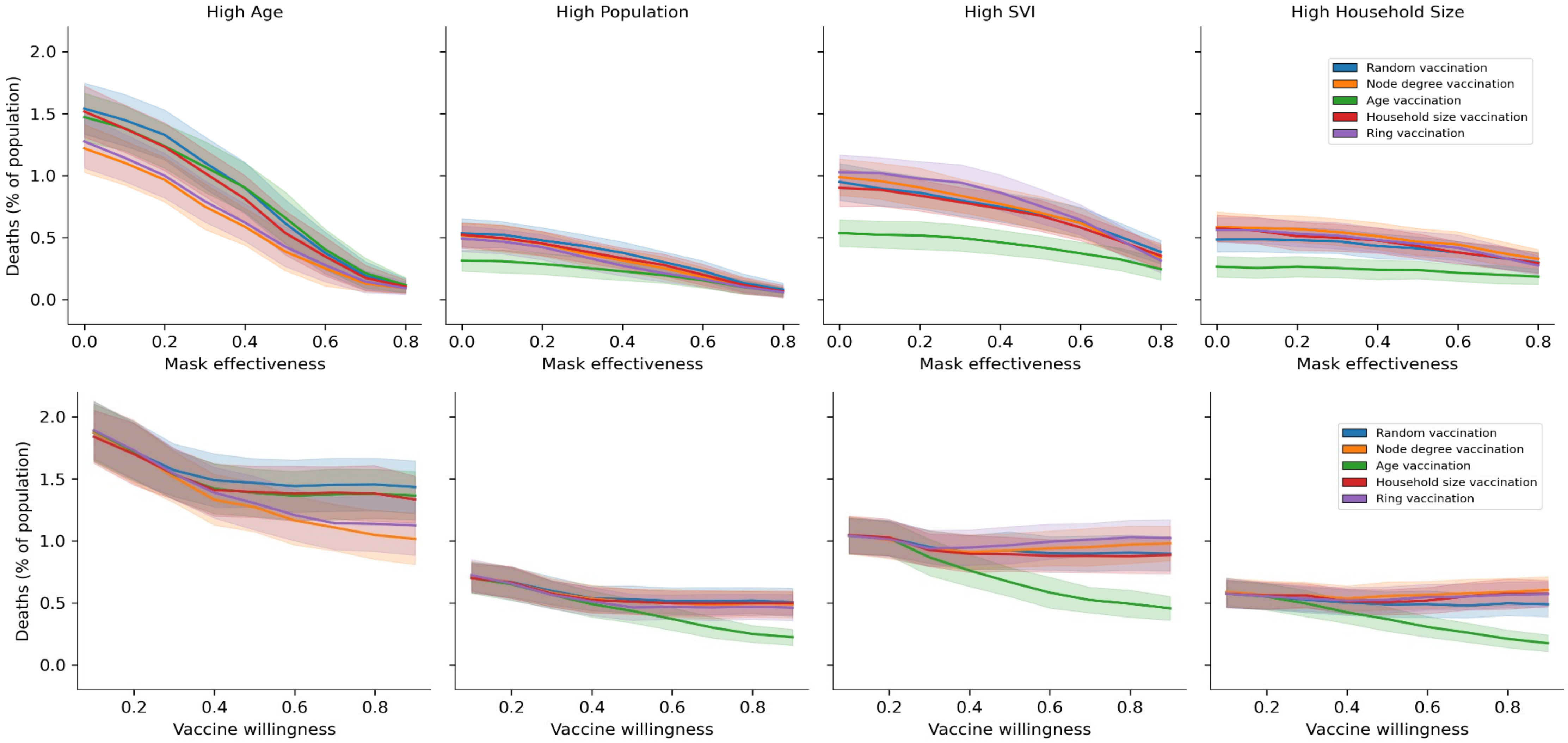
Regression Analysis from Simulation Replicates: Disease-related Deaths

Higher age,
Lower connectivity community

Lower age,
Higher connectivity community

$0.6 \leq$ Vaccine Willing ≤ 0.8
$0.0 \leq$ Mask Use/Eff ≤ 0.8

$0.1 \leq$ Vaccine Willing ≤ 0.9
$0.0 \leq$ Mask Use/Eff ≤ 0.2



Conclusions and Future Work

Conclusions and Future Work

We have shown that global sensitivity analysis can be used to analyze the variability in benefits of vaccine prioritization strategies in communities with different demographics and connectivity.

- Distinguishing sources of uncertainty between parameter and model behavior is essential for proper treatment of global sensitivity analysis.
- Different communities and strategies will have different results.
- Different objective (i.e., QoI) will have different results.

Next Steps:

- Utilizing a surrogate to run sufficient simulations that will measure the uncertainty of our Sobol' indices.
- Add additional sources of uncertainty, e.g., disease state transmissions.

Thank You for Your Time and Attention!

For questions or follow-up discussions:

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Back-up Slides

Inputs: Vaccine Availability, Queue, and Prioritization

Vaccine availability

- A peak of 3.38 million doses per day were administered in the U.S. [1]
- If that rate was sustained, that is equivalent to a vaccine availability of 7.2% of the population each week.
- This analysis assumes vaccine availability covers 5% of the population each week

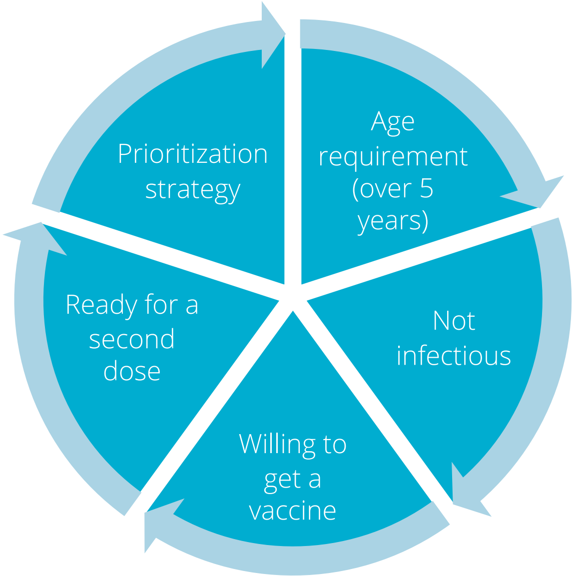
Vaccine queue based on the following

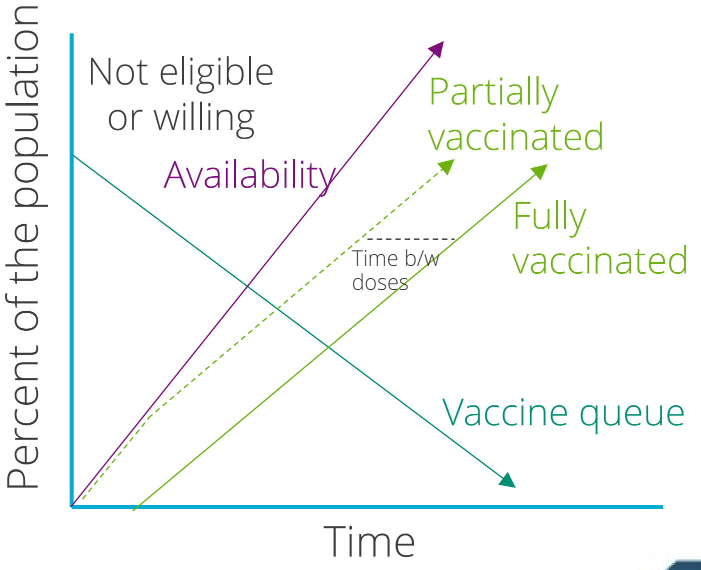
- ✓ Willing to be vaccinated
- ✓ Eligible (over age 5)
- ✓ Not infectious
- ✓ 2 weeks between doses
- ✓ Meet prioritization criteria (below)

Vaccine prioritization strategies

- **Age**: oldest to youngest
- **Household size**: large households to small households
- **Number of contacts**: Social butterflies to isolated people
- **Ring vaccination**: Based on contact with known cases
- **Random vaccination**

Vaccine Queue





[1] The New York Times, See How Vaccinations Are Going in Your County and State, https://www.nytimes.com/interactive/2020/us/covid-19-vaccine-doses.html