Using models of SARS-CoV-2 dynamics to inform vaccine prioritization

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Our Question:

How can mathematical models of SARS-CoV-2 dynamics help us understand the impact of vaccine prioritization **by age**?

Our approach:

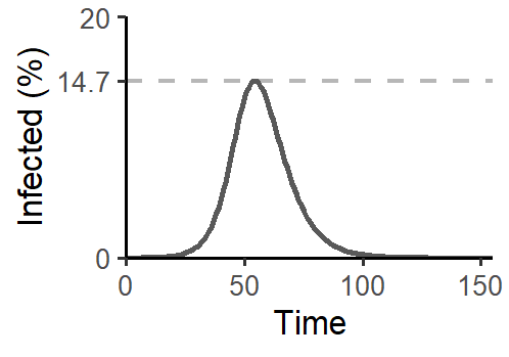
Use an age-structured SEIR model of SARS-CoV-2 dynamics with

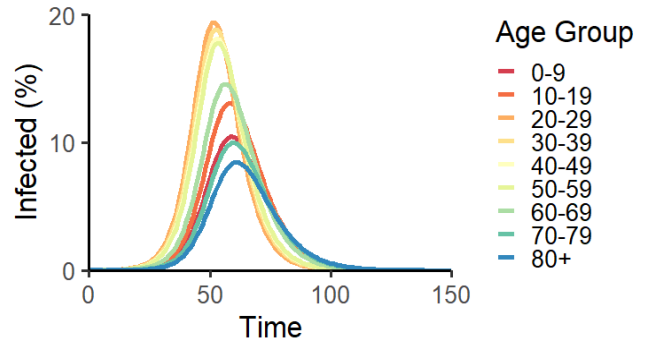
- ➔ country-specific contact matrix
- ➔ population demographics
- ➔ Age-dependent susceptibility
- ➔ Age-dependent IFR

*Results shown in slides are for Belgium, but model can evaluate other countries/regions

We can consider model trajectories

No vaccines:



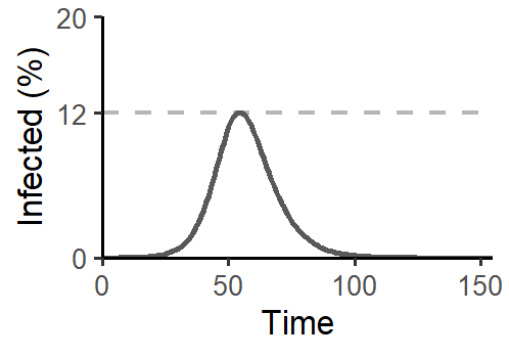


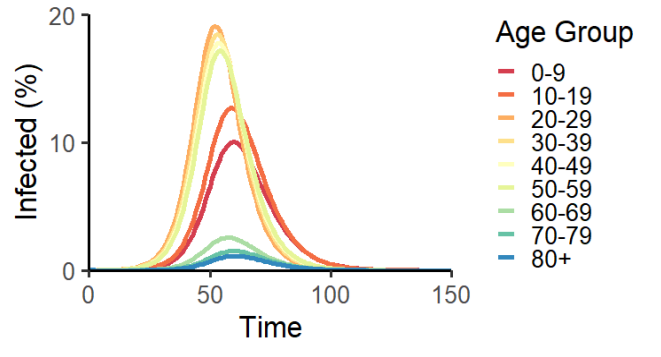
Total Infected: 84%

↓

Total Deaths: 0.56%

Vaccines for 20% of the pop. & distributed to 60+:





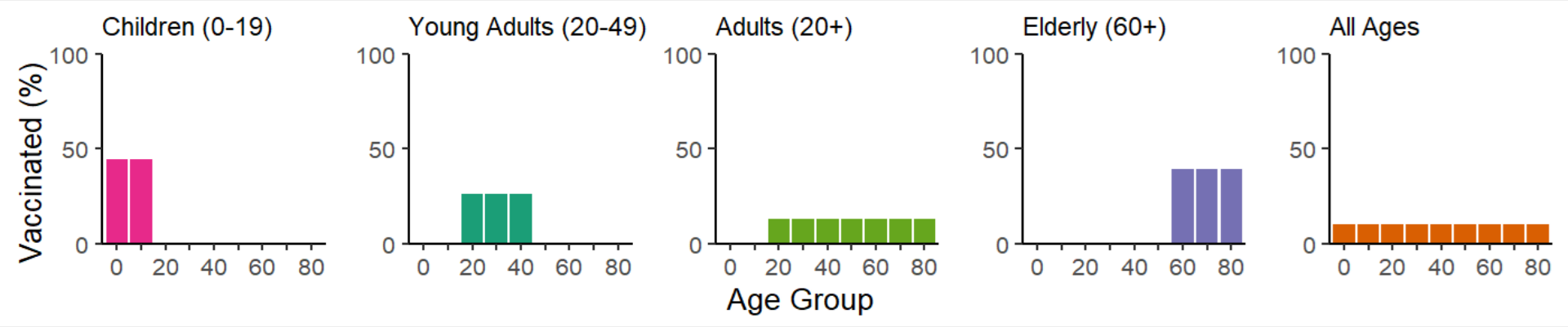
Total Infected: 68%

↓

Total Deaths: 0.11%

This example shows how strategic prioritization to elderly reduces deaths by 80% but reduces cumulative incidence by 19%, for a vaccine that blocks infection & transmission

Framework allows us to simulate the outcomes of different strategies

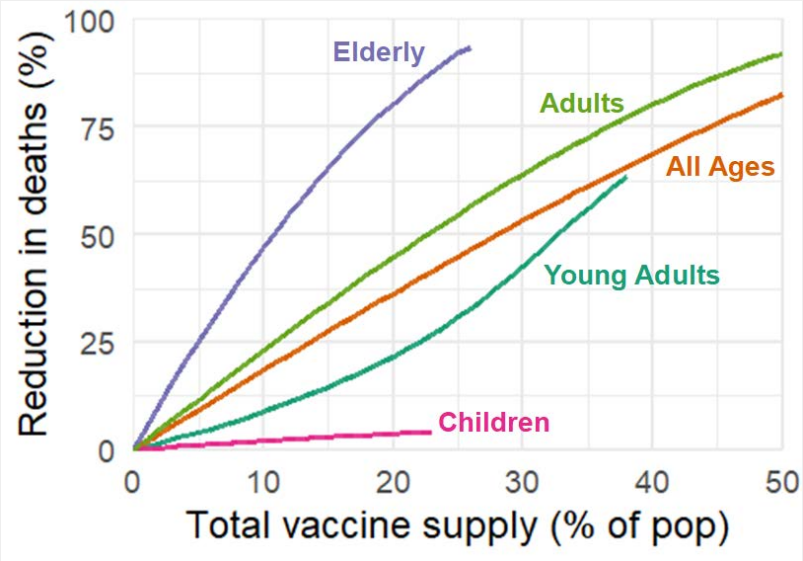


Here we consider five straightforward prioritization schemes based on possible strategies and safety/efficacy guidelines for use.

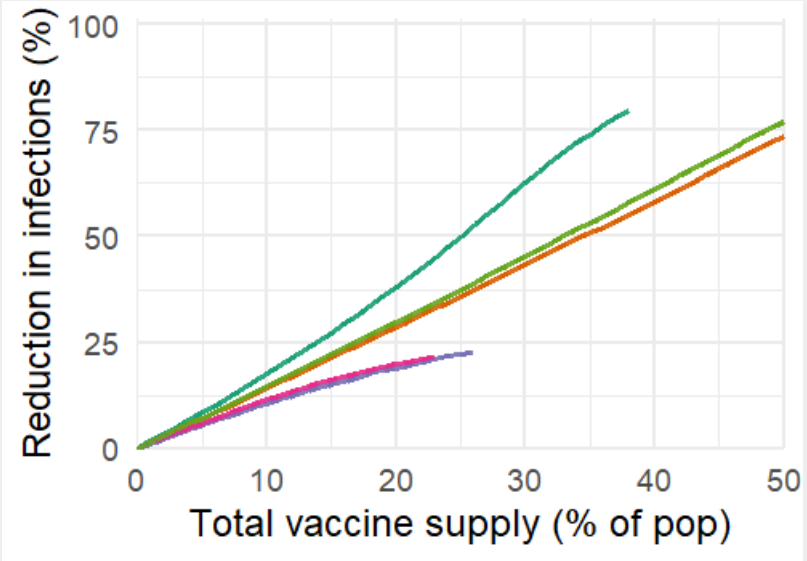
Recommendation depends on target outcome

- ➔ To minimize deaths, prioritize elderly
- ➔ To minimize cumul. incidence, prioritize young adults

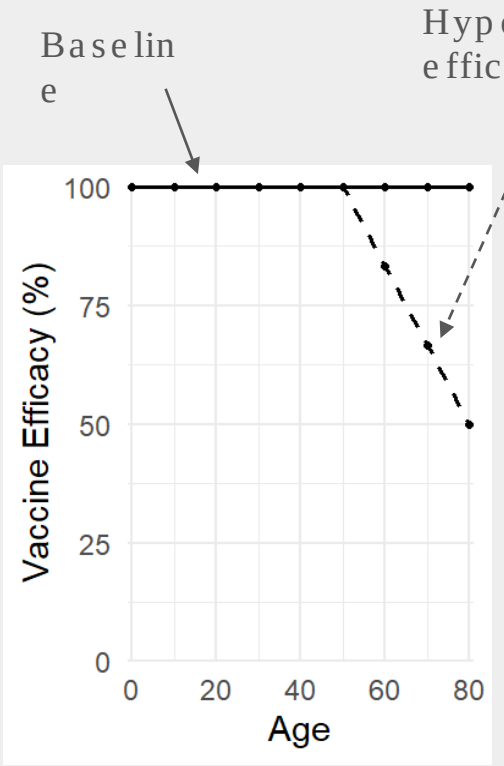
Target: minimize deaths

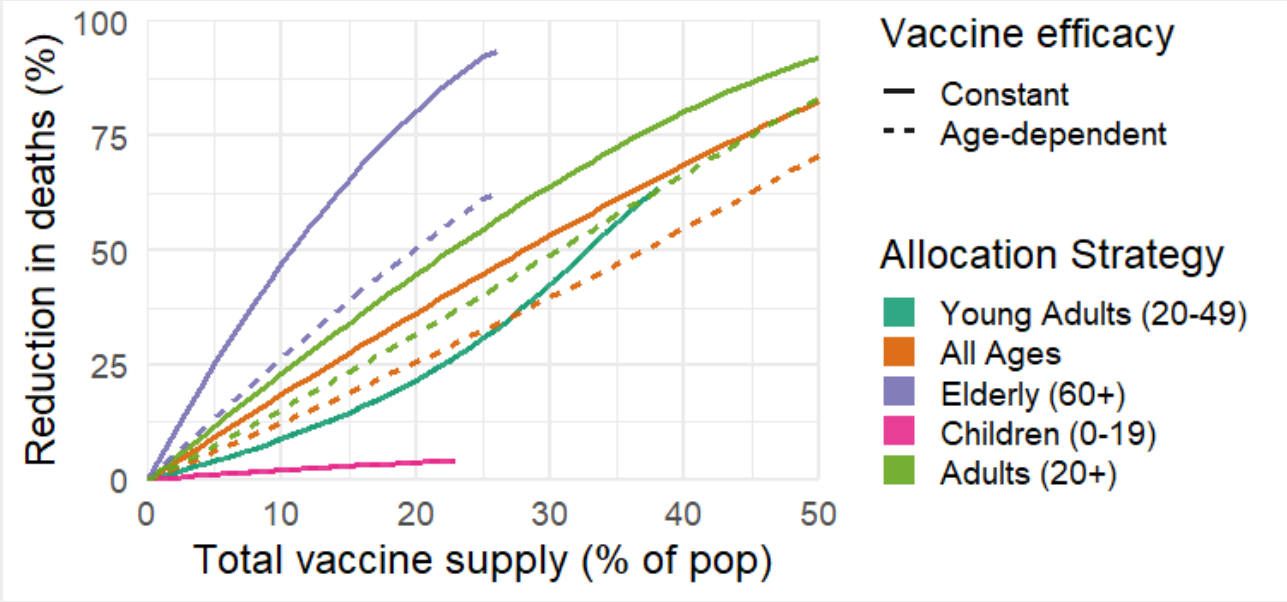


Target: minimize cumul. incidence



Incorporating vaccine efficacy variation by age





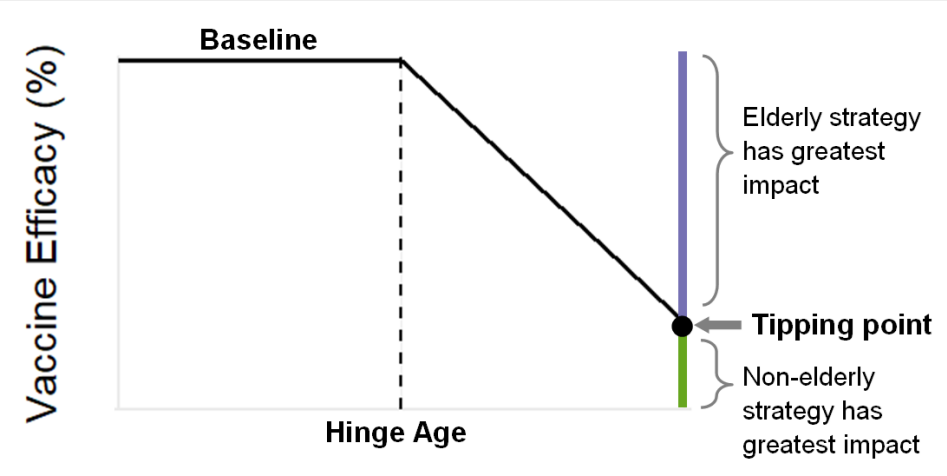
For this vaccine efficacy curve, vaccinating the elderly has the greatest impact on minimizing deaths

slides: assume leaky vaccine
manuscript: also considers all-or-nothing; no difference in recommendations.

Vaccinating young adults remains best strategy for minimizing cases

How low would the efficacy have to be among the elderly to protect them *indirectly*?

- ➔ Depends on # vaccines available & shape of efficacy curve
- ➔ In general, unless the efficacy decreases *significantly* in the elderly in comparison to younger ages, prioritizing elderly remains the best option for minimizing deaths.



Vaccine supply: 15% of pop.

Baseline	Hinge Age	Tipping point
50%	40	/
	50	/
	60	/
75%	40	0.8%
	50	/
	60	/
100%	40	11.7%
	50	3.9%
	60	/

Vaccine supply: 25% of pop.

Baseline	Hinge Age	Tipping point
50%	40	/
	50	/
	60	/
75%	40	2.3%
	50	/
	60	/
100%	40	19.5%
	50	10.2%
	60	/

Incorporating seroprevalence

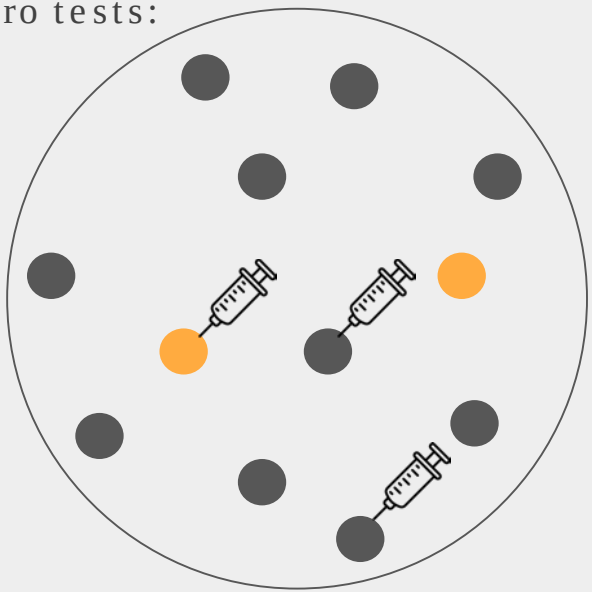
What if we have antibody data from serology studies?

What if the vaccine is only approved for seronegative people?

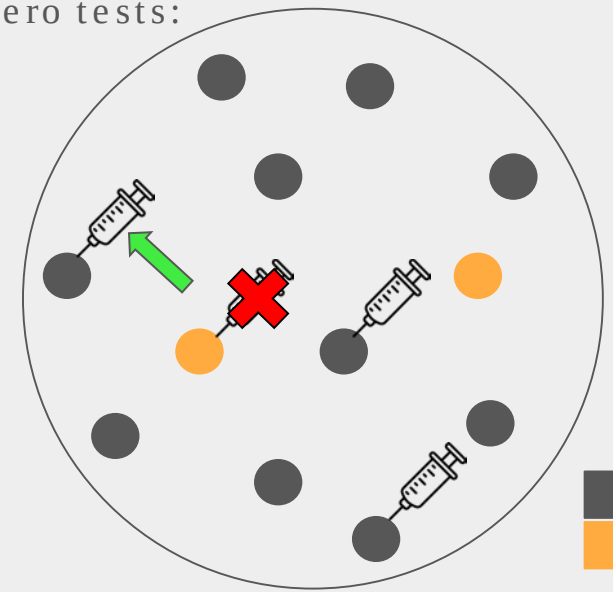
Benefit from pairing serology tests with a vaccination strategy

*assuming antibodies are protective

w/o sero tests:



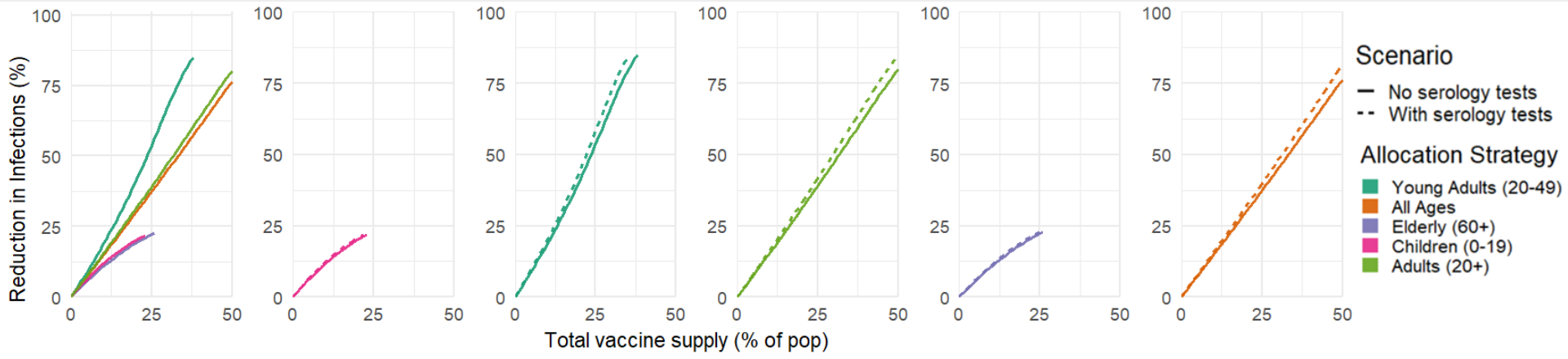
w/ sero tests:



Susceptible

Seropositive

When seroprevalence is low*, the recommended strategy for minimizing infections/deaths remains same



Marginal benefit of paired serological tests depends on **seroprevalence** and **amount of available vaccines**
i.e. benefit is low unless seroprevalence is high

*We included age-stratified seroprevalence (mean = 5.9) estimated from Herzog et. al.

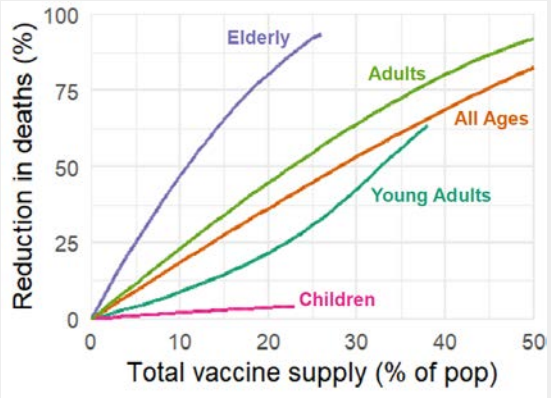
Conclusion

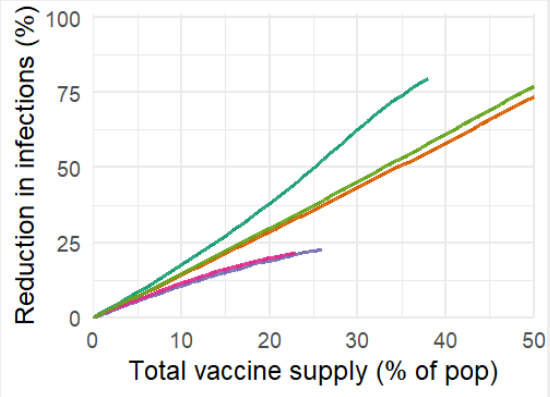
Current model includes:

- ➔ Contact patterns by age
- ➔ Demographics
- ➔ Susceptibility by age
- ➔ Serology
- ➔ Age-variation in vax effectiveness.
- ➔ IFR

Framework enables sensitivity testing.

This work can **evaluate allocation strategies** or **recommend an optimal distribution**.





Needed from vaccine trials to make these decisions based on evidence

- Evidence about efficacy in groups vulnerable to severe outcomes (eg elderly)
- Evidence about efficacy in reducing infection and/or infectiousness

Broader Framework

With data to parameterize, this approach can extend to:

- ➔ Different recommendations for different stratification (e.g. geographic mixing)
- ➔ Different minimization target (hospitalizations, QALY, etc.)
- ➔ Different types of models (Agent-based)
- ➔ Any country or region for which data are available

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Some additional considerations

Caution in prioritizing by race/ethnicity

- It is tempting given disparities in risk
- Potentially inefficient: if herd immunity builds up within disadvantaged communities, they may be lower risk than others by the time we have a vaccine
- This means potentially more doses given to those who are already immune, reducing the benefit per dose
- These arguments are complex, dependent on assumptions and need further thought, but in the heat of this battle my advice would be to avoid potentially divisive decisions whose effects are quite uncertain

International allocation: keep it simple. Two bad ideas:

- Proposed allocation by “need” measured by R(t) or caseloads
  - Ignore delays between allocation and delivery, months during which epidemic can change drastically
  - Are gameable
  - Provide perverse incentives on epidemic control and reporting

- Proposed allocation for HCW use by HCW population per country
  - Further penalizes LMIC with fewer HCW per capita getting fewer vaccines per capita
  - Mistakes reason for allocating to HCW: “value” of a HCW is proportional to how many people they serve.
  - (Pop of HCW)*(# served per HCW)=population.
  - *Thus allocate by population, not HCW population.*

Across countries, Pro Rata Allocation is Rarely Efficient

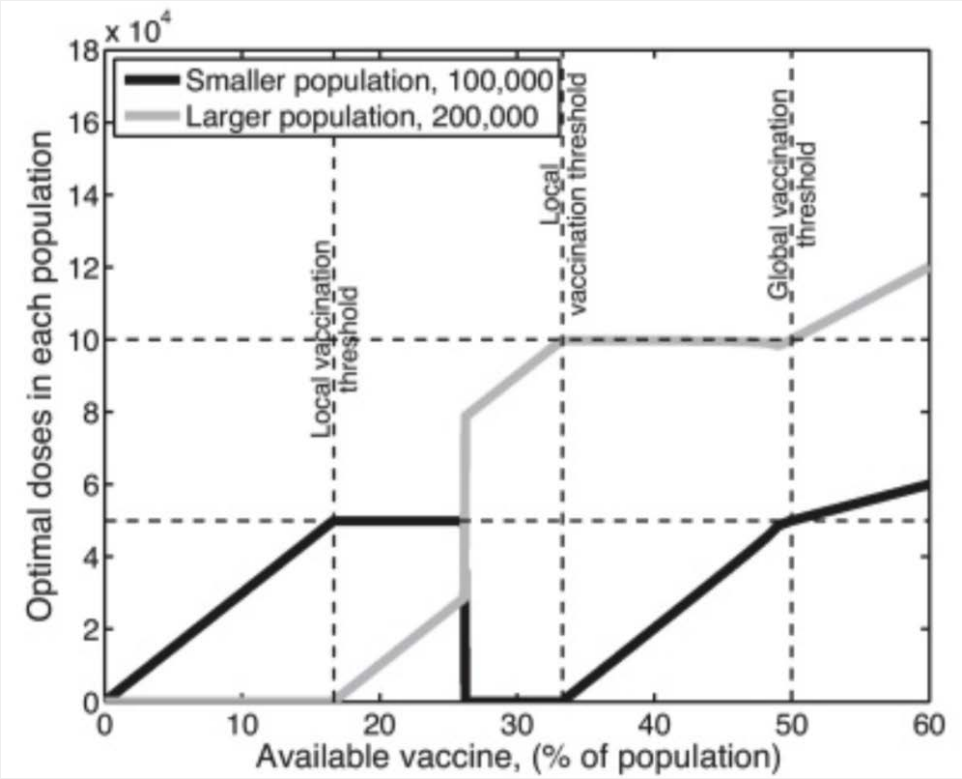
Optimal vaccine allocation rules (for herd immunity):

- Give the vaccine to a population (or subset of populations) where critical vaccination threshold is attainable

- Allocate the remaining doses to another population

- Do not allocate doses to populations beyond their critical vaccination threshold

Implies that simple notions of fair allocation will lose opportunities for herd immunity



Slide from E. Rumpler and K. Joshi

Keeling et al., 2012; Duijzer et al., 2017