Vaccine Prioritization & Dose Sparing Strategies by Age & Serostatus

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With a limited supply of vaccine, do the most good you can.

Motivation: COVAX estimates only around 1/4 of the world's adult population will be vaccinated by the end of 2021.

With a limited supply of vaccine, do the most good you can.

Method 1: Vaccine prioritization

Adjust the order in which people receive the vaccine.

Examples:

- HCW → 70+ → 60+ → 50+ → general public
- HCW → under 60 → general public

With a limited supply of vaccine, do the most good you can.

Method 1: Vaccine prioritization

Adjust the order in which people receive the vaccine.

Examples:

- HCW → 70+ → 60+ → 50+ → general public
- HCW → under 60 → general public

Method 2: Dose sparing

Adjust the dosing or dose scheduling.

Examples:

- Two half-doses
- Increase spacing between doses
- Give seropositives 0 or 1 dose.

Today:

1. How can we use models to inform **vaccine prioritization** strategies?

2. Why might proposed **dose sparing** strategies be wise (or unwise)?

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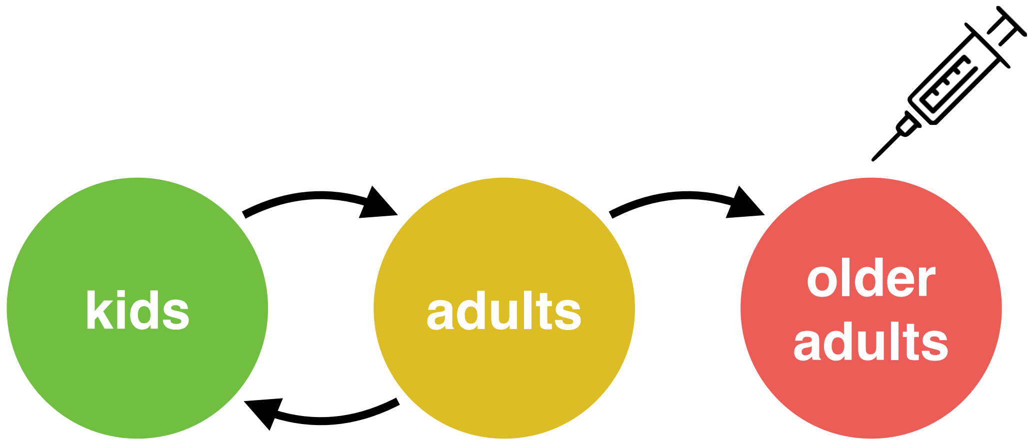
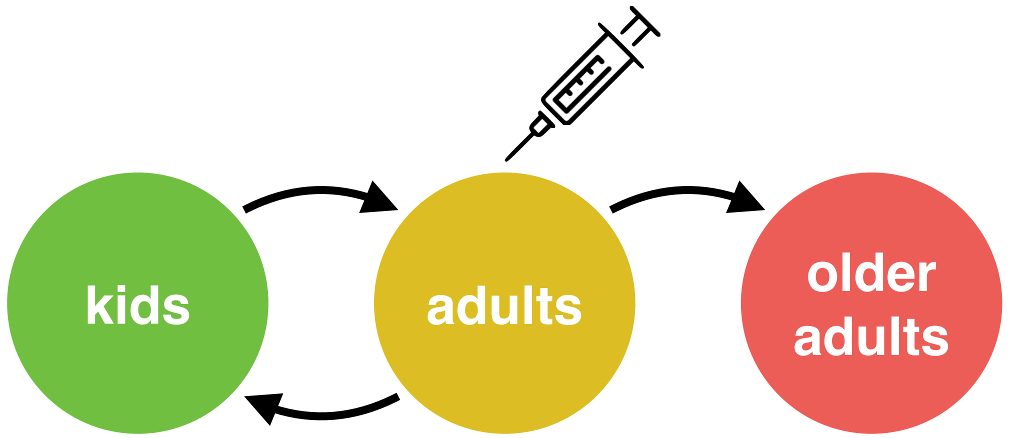
General concepts

Direct Protection



Protect the vulnerable

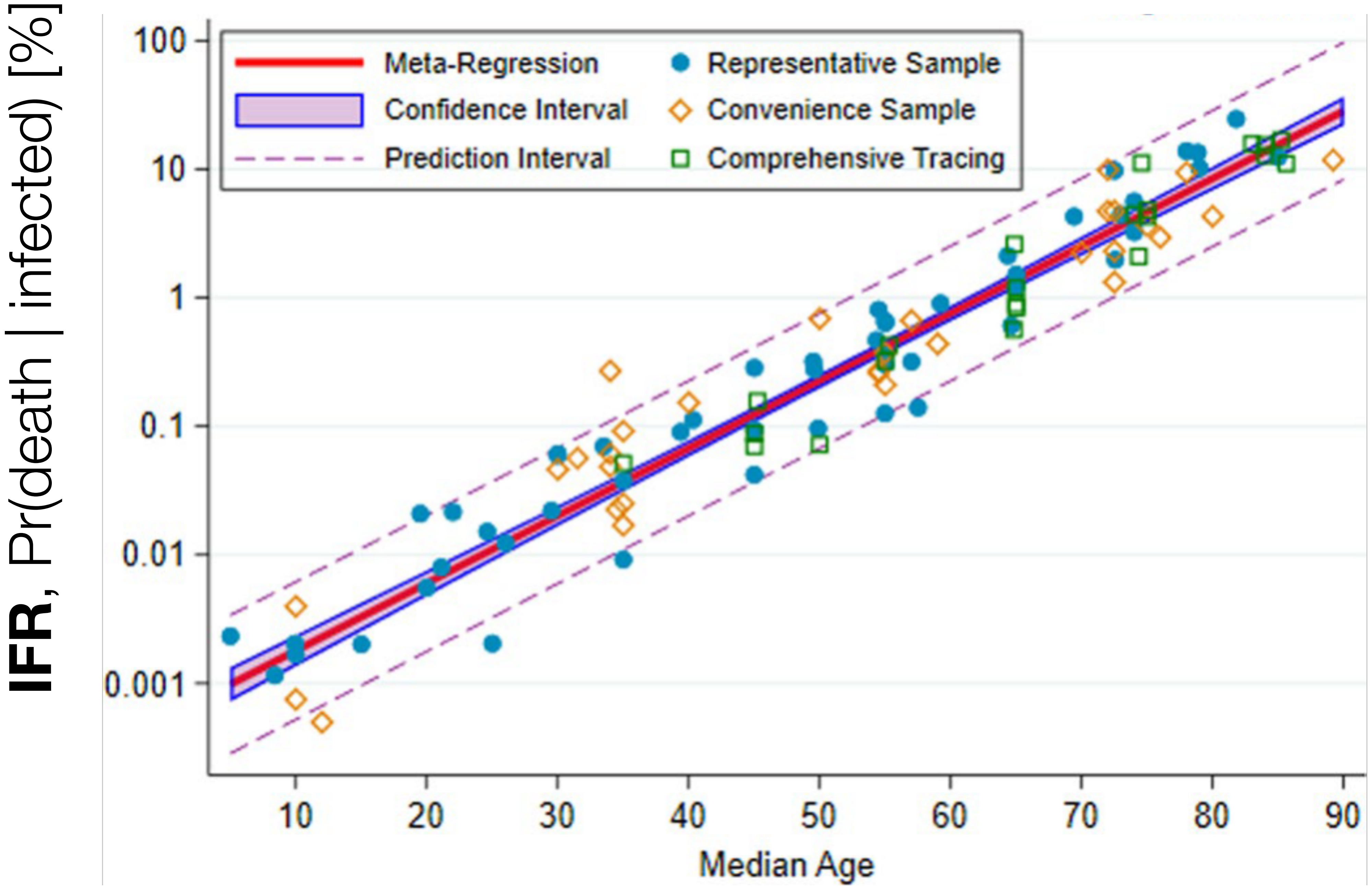
Indirect Protection



Break the backbone of transmission

How should we approach COVID-19 prioritization?

Infection Fatality Ratio (IFR) grows exponentially with age



Levin, Meyerowitz-Katz, et al. Eur J Epidemiol. 2020

Our Question:

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

Approach:

We use a model of SARS-CoV-2 dynamics to evaluate the impact of different prioritization strategies on

- cumulative incidence
- mortality
- years of life lost

Requirements

To be useful, this model must…

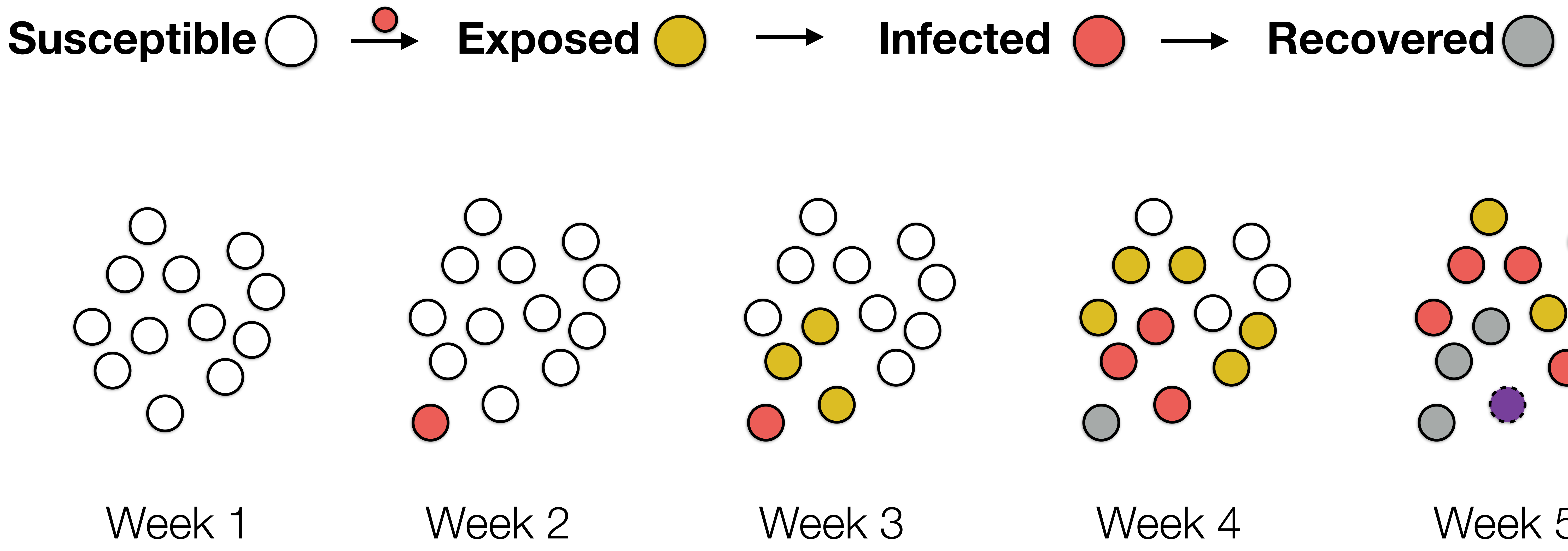
1. Model the spread of the disease.

2. Incorporate differences in contact patterns, susceptibility, and fatality rates by age.

3. Include various knowns and unknowns about the current portfolio of COVID-19 vaccines.

4. Include the ability to “roll out” the vaccine according to different strategies.

The SEIR model for the spread of SARS-CoV-2:



The SEIR model for the spread of SARS-CoV-2:

Susceptible → **Exposed** → **Infected** → **Recovered**

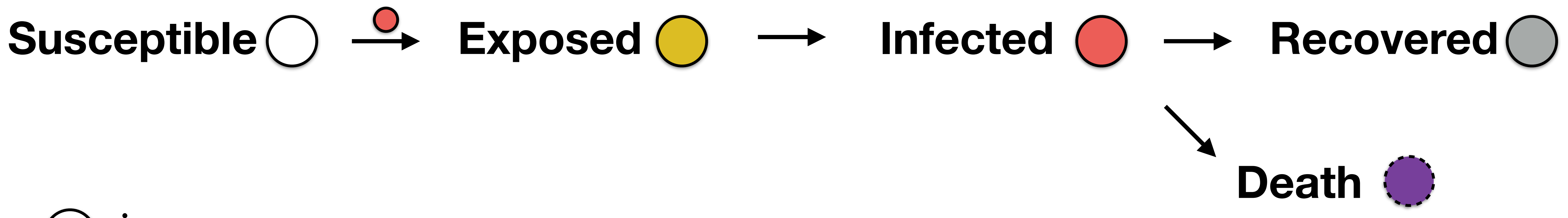
$$\dot{S} = -\beta S I$$

$$\dot{E} = \beta S I - d_E^{-1} E$$

$$\dot{I} = d_E^{-1} E - d_I^{-1} I$$

$$\dot{R} = d_I^{-1} I$$

The SEIR model for the spread of SARS-CoV-2:



$$\dot{S} = -\beta SI$$

$$\dot{E} = \beta SI - d_E^{-1}E$$

$$\dot{I} = d_E^{-1}E - d_I I$$

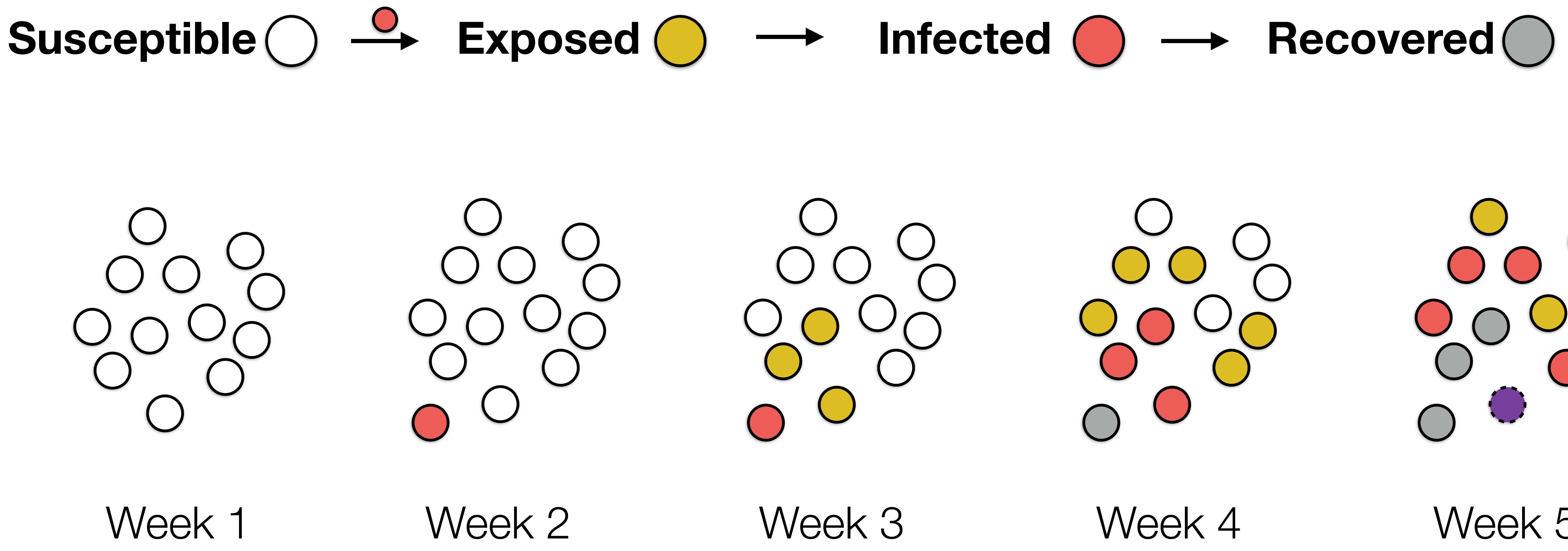
$$\dot{R} = d_I^{-1}I\,(1 - IFR)$$

$$\dot{\Omega} = d_I^{-1}I\,(IFR)$$

Lots of analyses & variations exist, including:

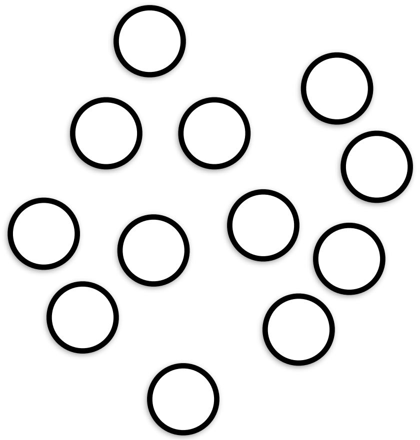
- inclusion of **social distancing** (e.g. CDPHE team's models)
- **reversion** to susceptibility (flu)
- **birth** & population turnover (measles)
- inclusion of a parallel model for **mosquitos** (malaria, dengue)
- put dynamics on a **contact network** (gonorrhea)

The SEIR model for the spread of SARS-CoV-2:

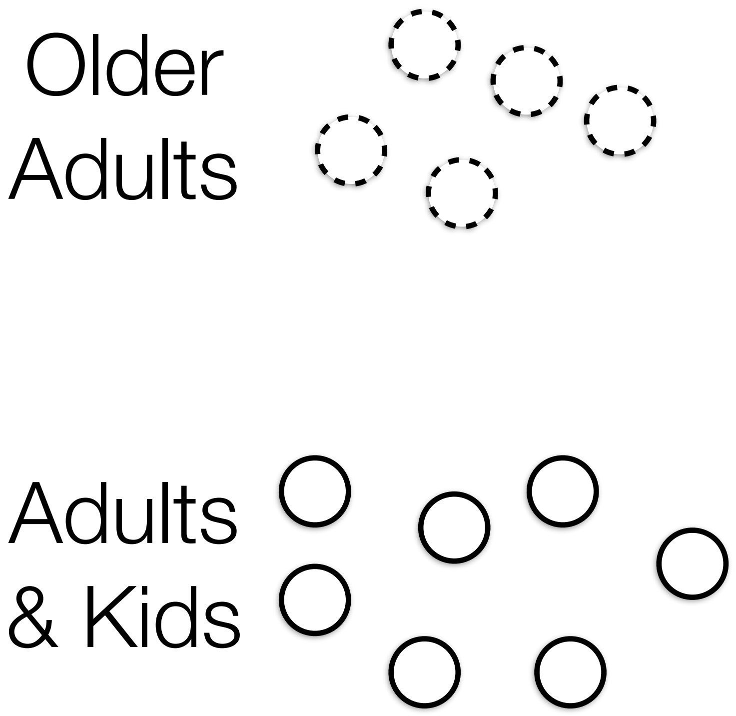


This is a good model, but it’s too simple—if the model treats everyone the same, we can’t use it to answer questions about prioritization.

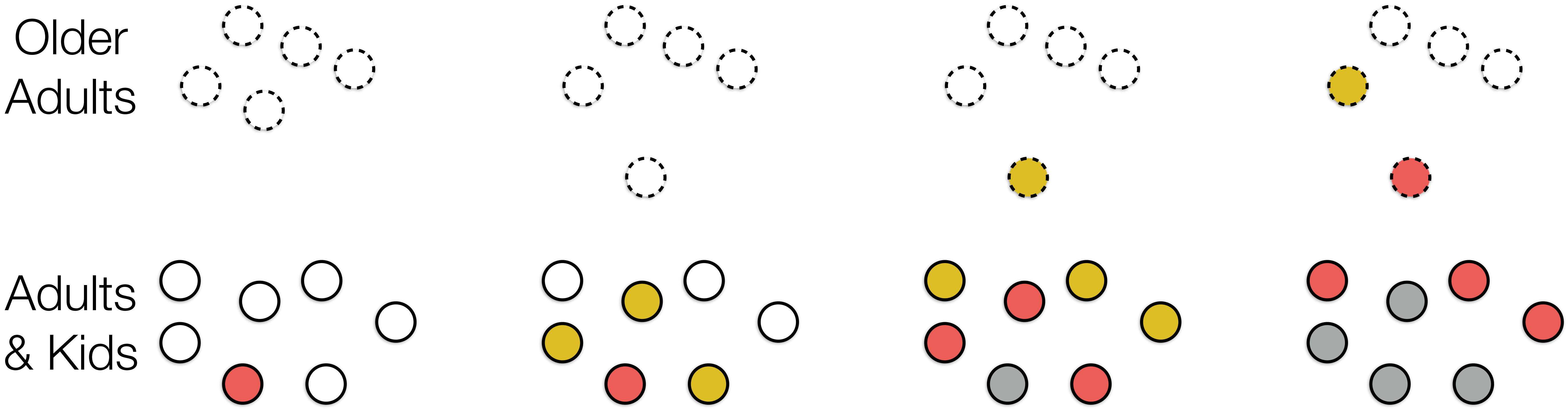
The age-stratified SEIR model.



The age-stratified SEIR model.

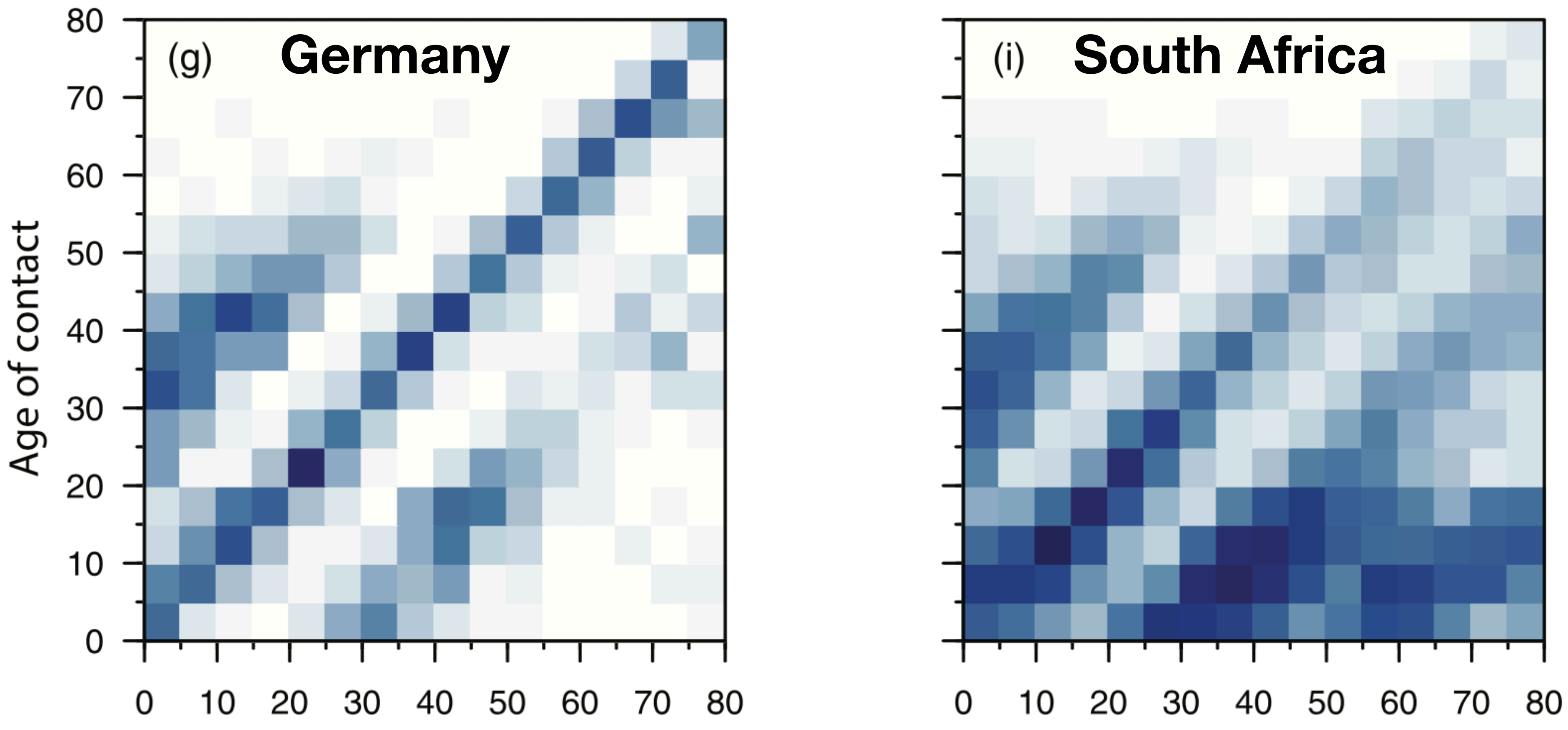


The age-stratified SEIR model.



Key idea: if we knew the mixing rates between these age groups, we could prioritize the vaccine to maximize protection.

Contact matrices allow for age-stratified SEIR models



The POLYMOD study and others like it have mapped age-contact structure across countries.

→ an SEIR model *within* each age group, and a network of mixing *between* age groups.

Mossong et al, *PLOS Medicine, 2008*
Prem et al, *PLOS Computational Biology, 2016/2020*

The age-stratified SEIR model.

Let the age groups be indexed by i.

Let the per person *force of infection* on group i be given by λ_i :

$$\lambda_i = u_i \sum_j c_{ij} \left(\frac{I_j}{N_j - \Omega_j} \right)$$

Pr(a group j individual is infected)

susceptibility of people in group i
Pr(get infected | exposure)

# of group j's that a
group i contacts per time

The age-stratified SEIR model.

$$\lambda_i = u_i \sum_j c_{ij} \left(\frac{I_j}{N_j - \Omega_j} \right)$$

$$\dot{S}_i = -\lambda_i S_i$$

$$\dot{E}_i = \lambda_i S_i - d_E^{-1} E_i$$

$$\dot{I}_i = d_E^{-1} E_i - d_I I_i$$

$$\dot{R}_i = d_I^{-1} I_i \, (1 - IFR_i)$$

$$\dot{\Omega}_i = d_I^{-1} I_i \, (IFR_i)$$

Notes:

- All the coupling is bundled up and hidden away in λ_i
- Note that we went from 5 “compartments” to 5m (# age groups).
- We have assumed age-dependent IFR and susceptibility.
- But we have assumed that latent period & infectious duration are not age dependent.

Requirements

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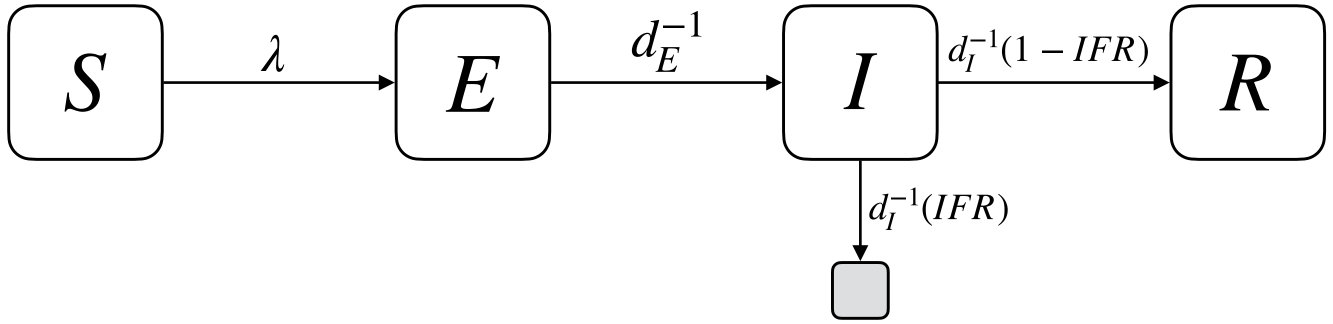
How do we model a vaccine?

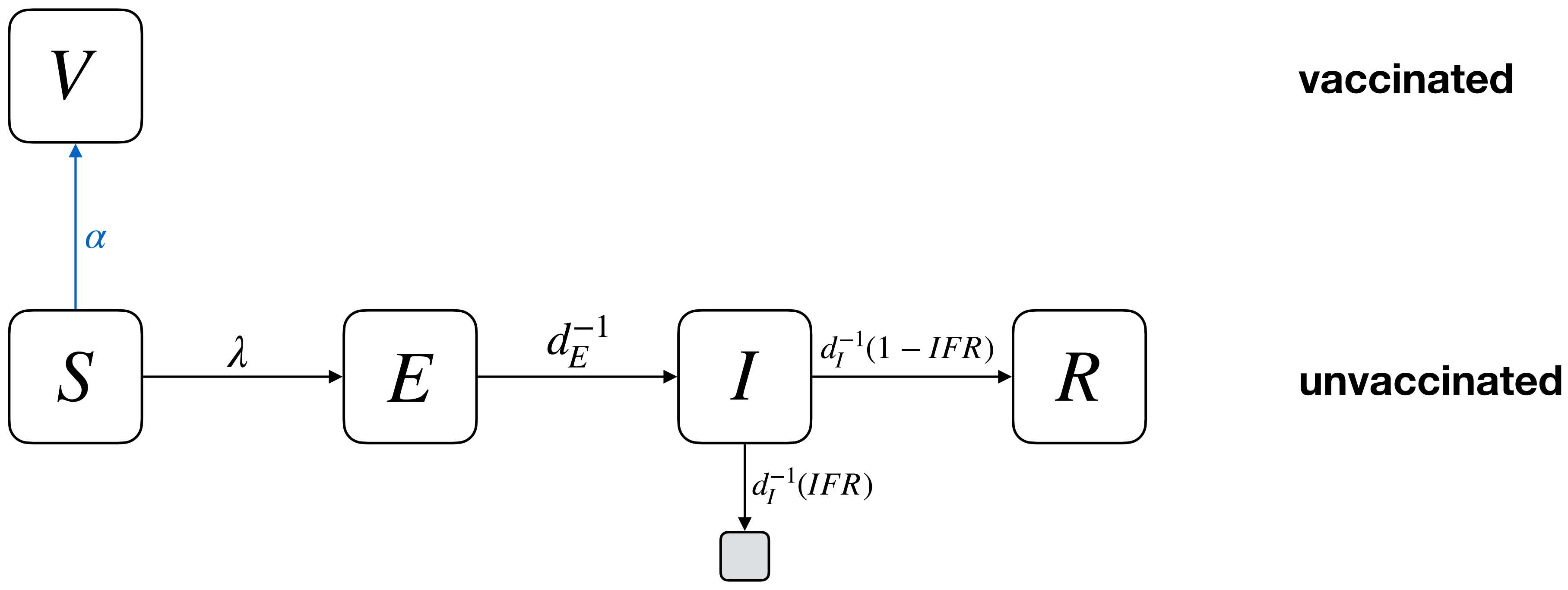
(Let’s get cooking with just a single population.)



unvaccinated

How do we model a vaccine?

(Let’s get cooking with just a single population.)



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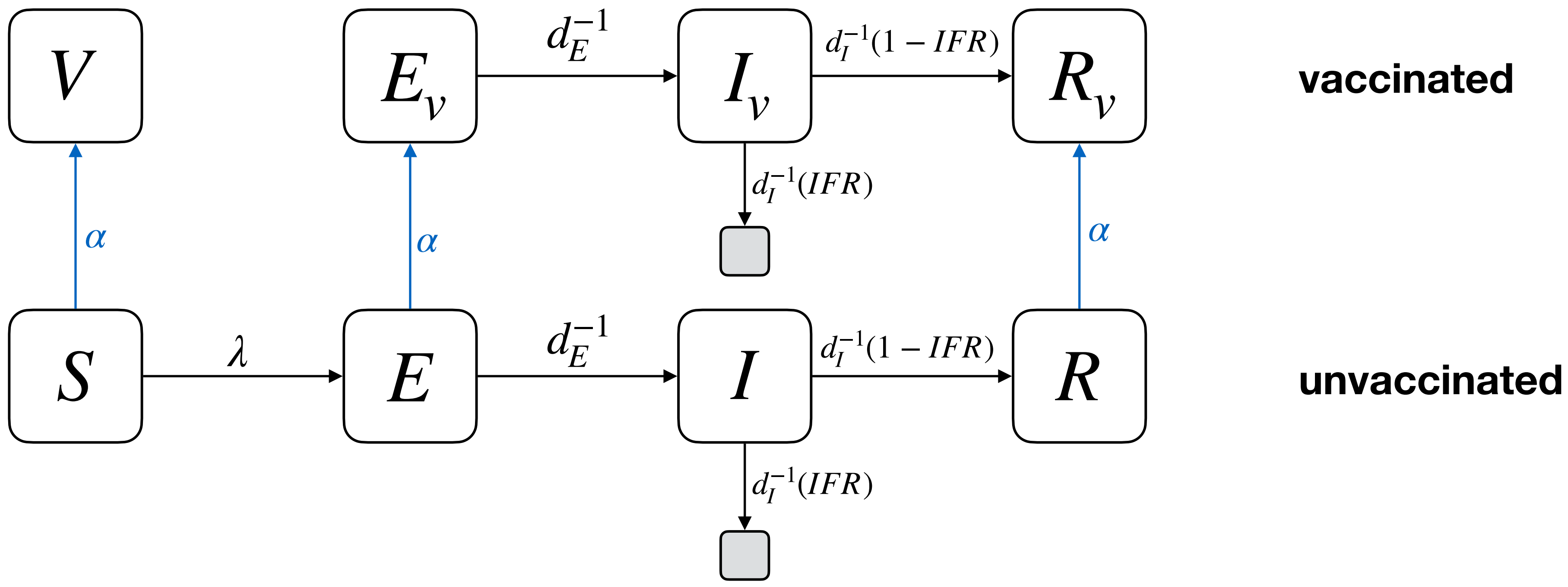
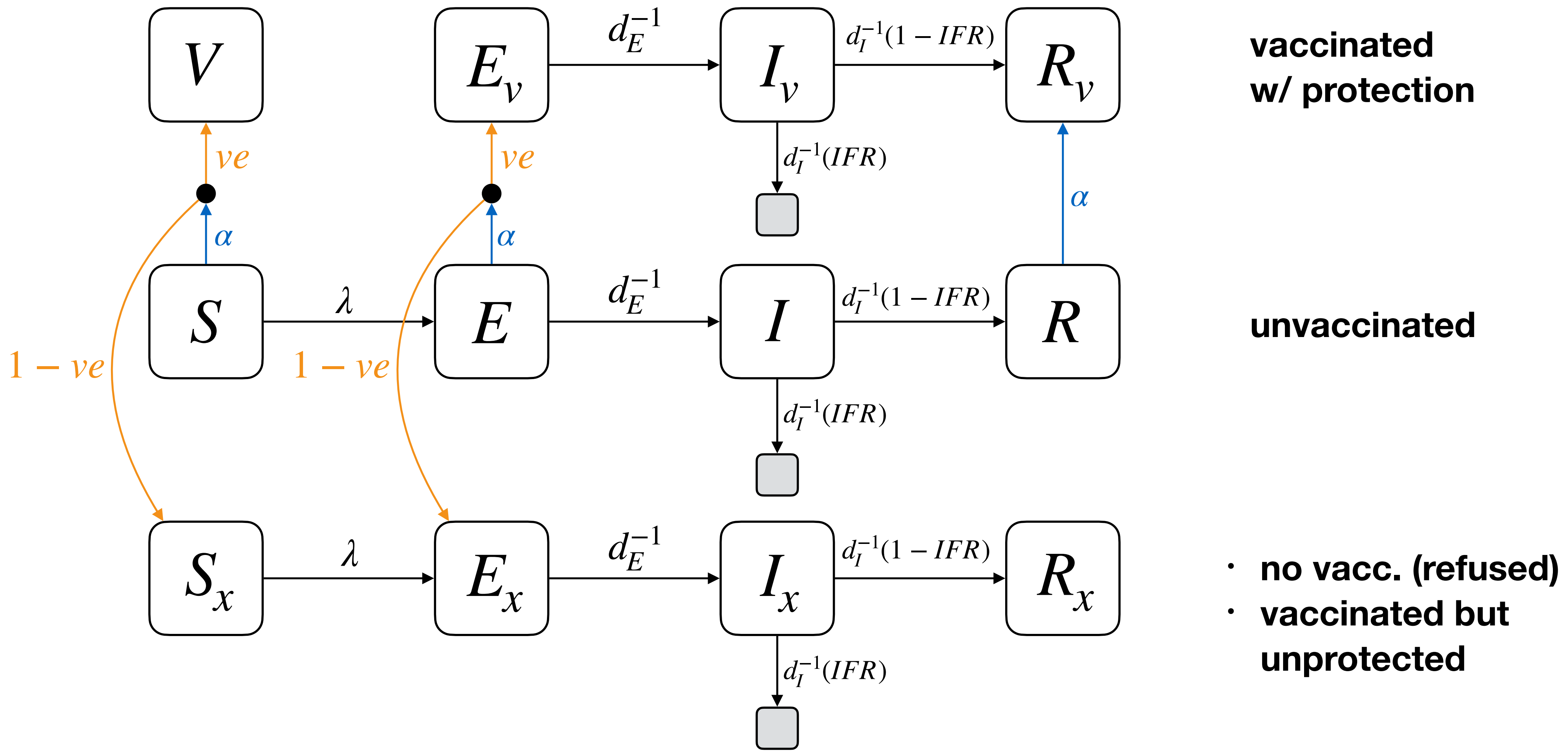


This model is great, but…real vaccines have imperfect *vaccine efficacy*.

How do we model a vaccine?

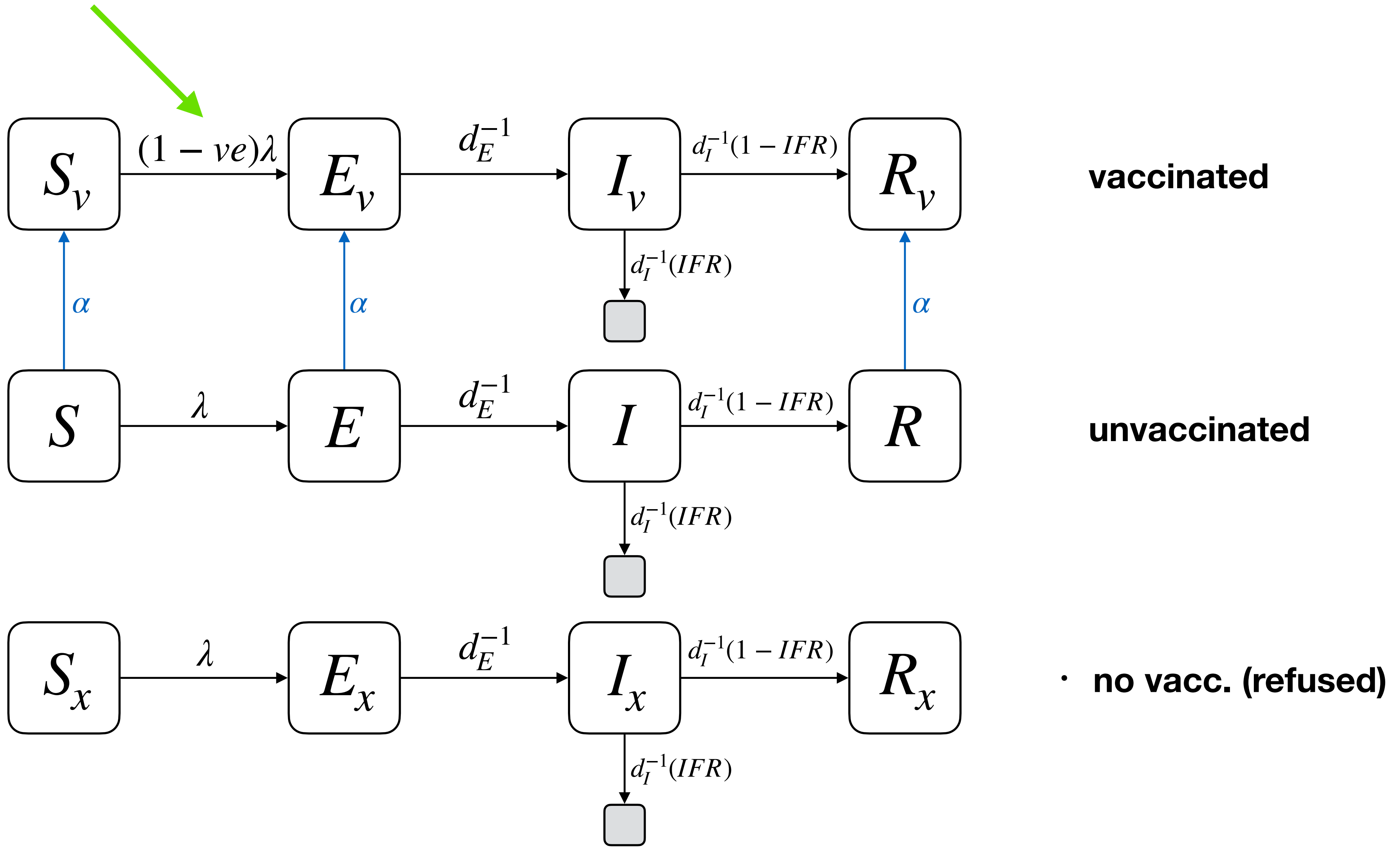
Now, a fraction ve get protection, while $1 - ve$ do not.



This is called an *all-or-nothing* model for vaccine efficacy.

How do we model a vaccine?

Instead, we could have *all* vaccinated folks get ve partial protection.



This is called a *leaky* model for vaccine efficacy.

The New York Times

Covid-19 Vaccines › | Who's Winning the Vaccination Race? | Vaccine Questions | Rollout by State | How 9 Vaccines Work

Here's Why Vaccinated People Still Need to Wear a Mask

The new vaccines will probably prevent you from getting sick with Covid. No one knows yet whether they will keep you from spreading the virus to others — but that information is coming.

45

Scientists worry that if vaccinated people are silent spreaders of the virus, they may keep it circulating in their communities, putting unvaccinated people at risk. Max Whittaker for The New York Times

By Apoorva Mandavilli

Published Dec. 8, 2020 Updated Dec. 9, 2020

Will the vaccine block transmission?

If it did/didn't, how would we model it?

Various ways to model *vaccine efficacy*

Let ve_p be the ***p**rotective* efficacy. It measures:

If you are infected, how well protected are you from severe disease or death?

Let ve_s be the ***s**usceptibility reducing* efficacy. It measures:

If you come into contact with an infected person, by how much will your probability of becoming infected decrease?

Let ve_I be the ***i**nfectiousness reducing* efficacy. It measures:

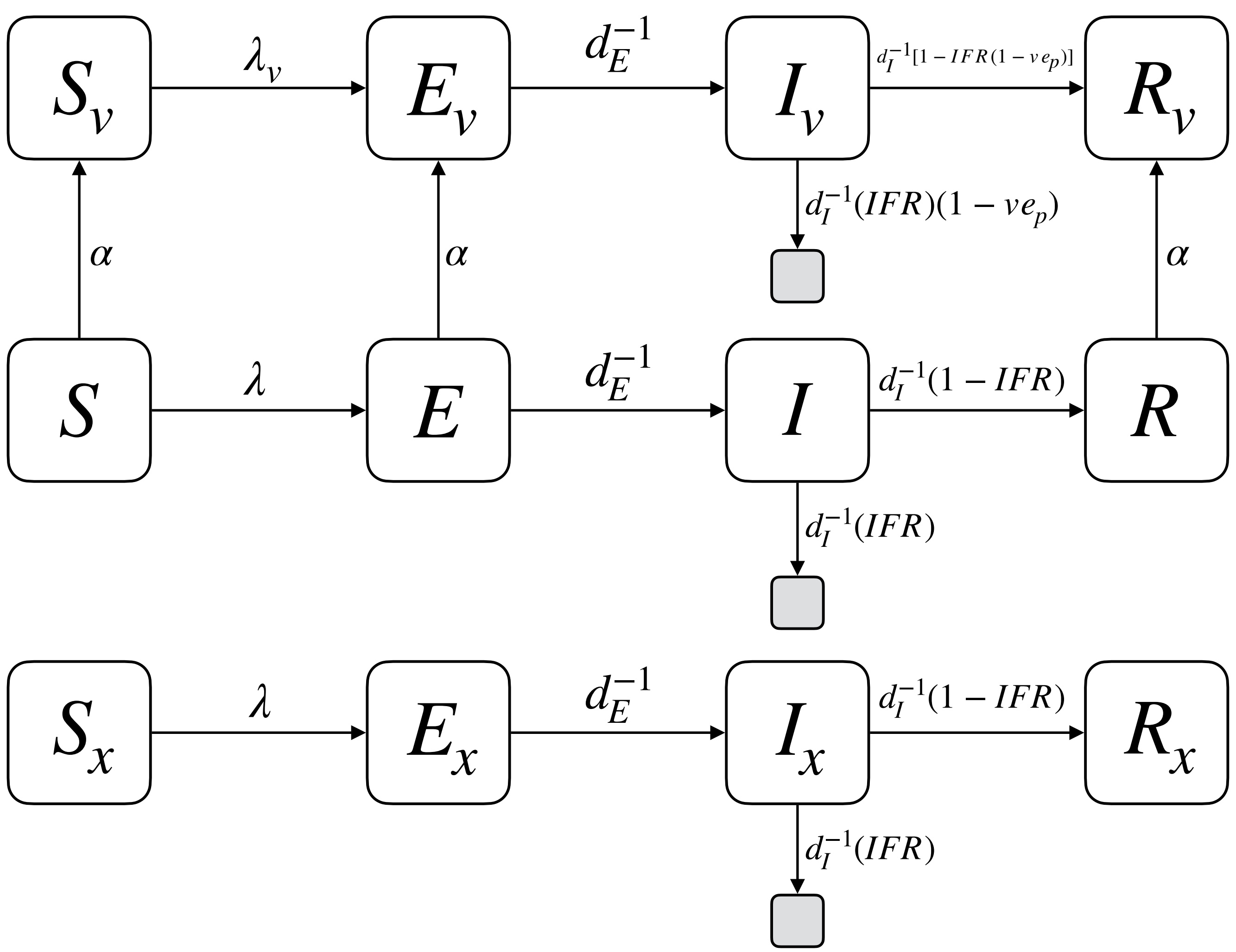
If you are infected, by how much will your outward infectivity be decreased?

NB: in Pfizer/Moderna trials, they measured disease outcomes.

$$ve \approx 1 - (1 - ve_s)(1 - ve_p)$$

How do we model a vaccine?

We can incorporate vaccine effects on susceptibility, infectivity, and protection



vaccinated

$$\lambda_{i,v} = u_i \sum_j c_{ij} \left(\frac{I_j + I_{j,x} + I_{j,v}(1 - ve_I)}{N_j - \Omega_j} \right) (1 - ve_s)$$

unvaccinated

$$\lambda_i = u_i \sum_j c_{ij} \left(\frac{I_j + I_{j,x} + I_{j,v}(1 - ve_I)}{N_j - \Omega_j} \right)$$

no vacc. (refused)

This is a *partial transmission blocking* model. But it's still a model!

Various modeling choices:

Let's suppose that the vaccine has efficacy $VE = 90\,\%$.

Model 1: the vaccine provides full protection from infection to 9 in 10 people.
[1 in 10 get no protection.]

Model 2: the vaccine provides 90% protection from infection to everyone.

Model 3: the vaccine reduces clinical disease by 90%, and affects transmission to a varying degree.

Various modeling choices:

Let's suppose that the vaccine has efficacy $VE = 90\,\%$.

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all or nothing vaccine model

Model 2: the vaccine provides 90% protection from infection to everyone.

leaky vaccine model

Model 3: the vaccine reduces clinical disease by 90%, and affects transmission to a varying degree.

variable transmission-blocking model

NB: unclear which is the right model—we tried all, to see if answer changed.

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Incorporating vaccine rollout

We choose:
1. a set of age demographics to prioritize.
2. a rollout speed (% total population per day).

The vaccine is then rolled out [proportionally] to those age groups, until 70% have received the vaccine—30% refuse. After the priority phase: no prioritization.

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Sources of variation & uncertainty

Vaccine:
- Overall efficacy [parameter]
- Decreased efficacy by age [parameters]
- Limited approval by age [rollout constraints]
- Ability to block transmission [parameter]

Population:
- country-specific age-contact matrices [Prem et al.]
- country-specific age demographics [UNWPP]
- fraction seropositive individuals by age [New York DPH, Bajema et al]

Infection:
- Age-varying susceptibility [Davies]
- Age-varying infection fatality rate (IFR) [Levin]

Policy Choices

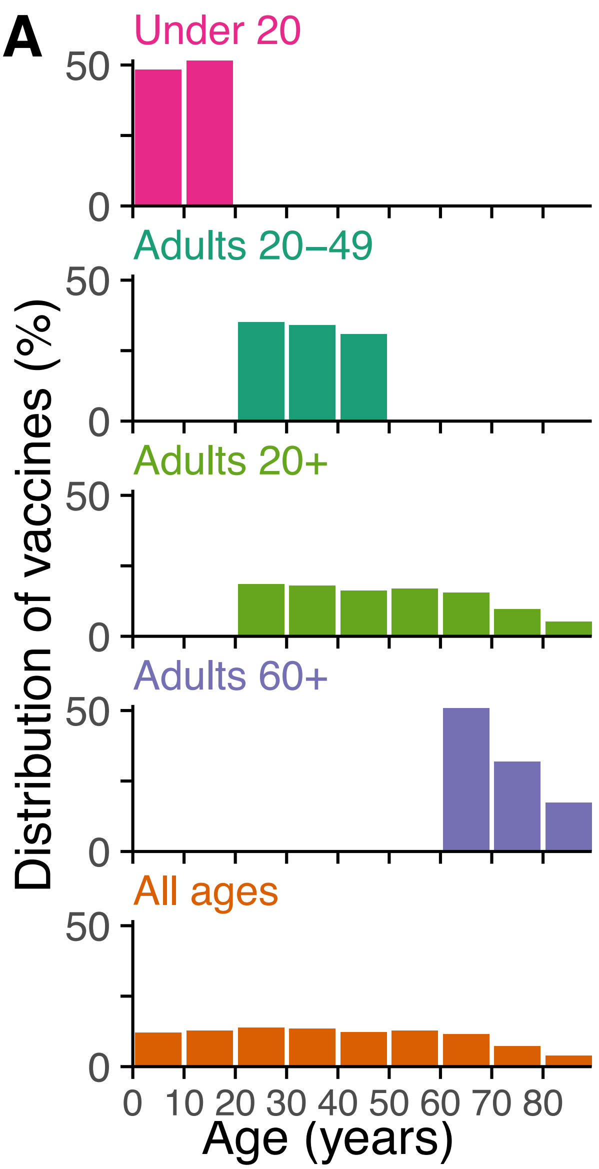
Prioritization:

- Who gets the vaccine first? [strategies]

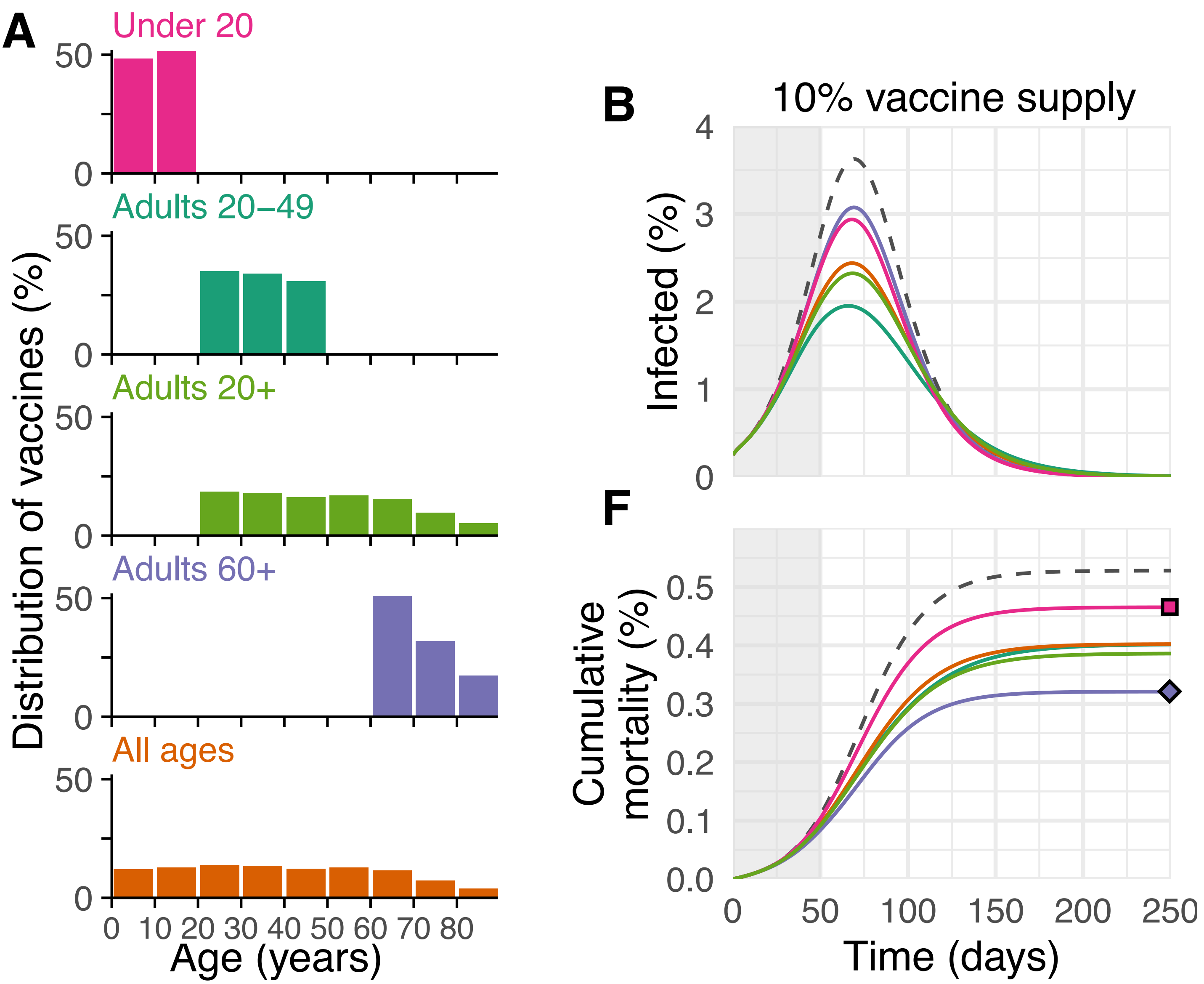
Policy & Rollout:

- What is the vaccine supply?
- How fast will it be rolled out?
- What will transmission rates be held [down] to during vaccine rollout?
- What fraction of the population will refuse the vaccine? [Gallup, December 2020, 30%]

Modeling framework

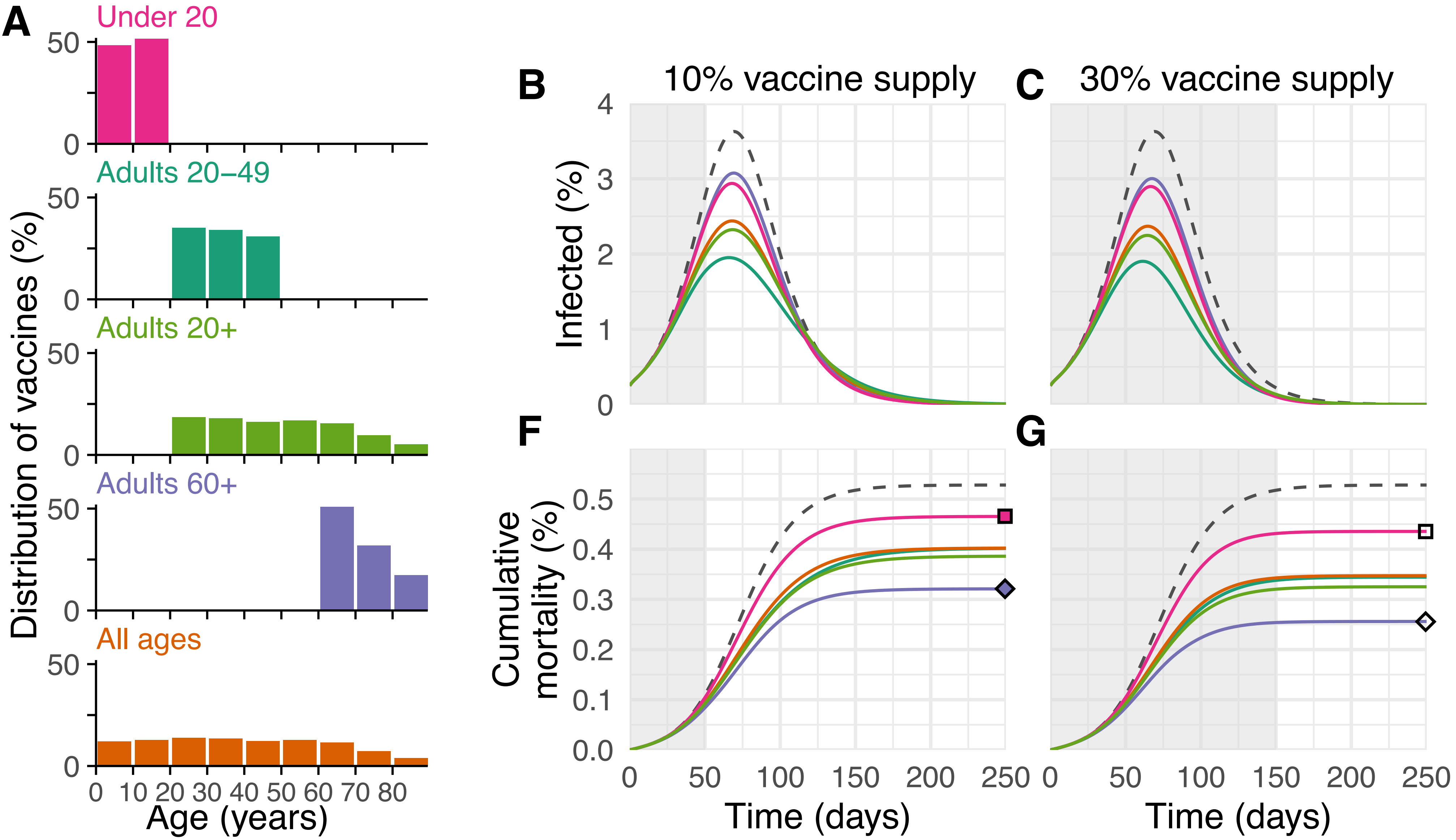


Modeling framework



0.2% of the population vaccinated per day, all-or-nothing and transmission-blocking vaccine, VE 90%. $R_0 = 1.5$ (Scn. 2) and $R_0 = 1.15$ (Scn. 1), USA

Modeling framework



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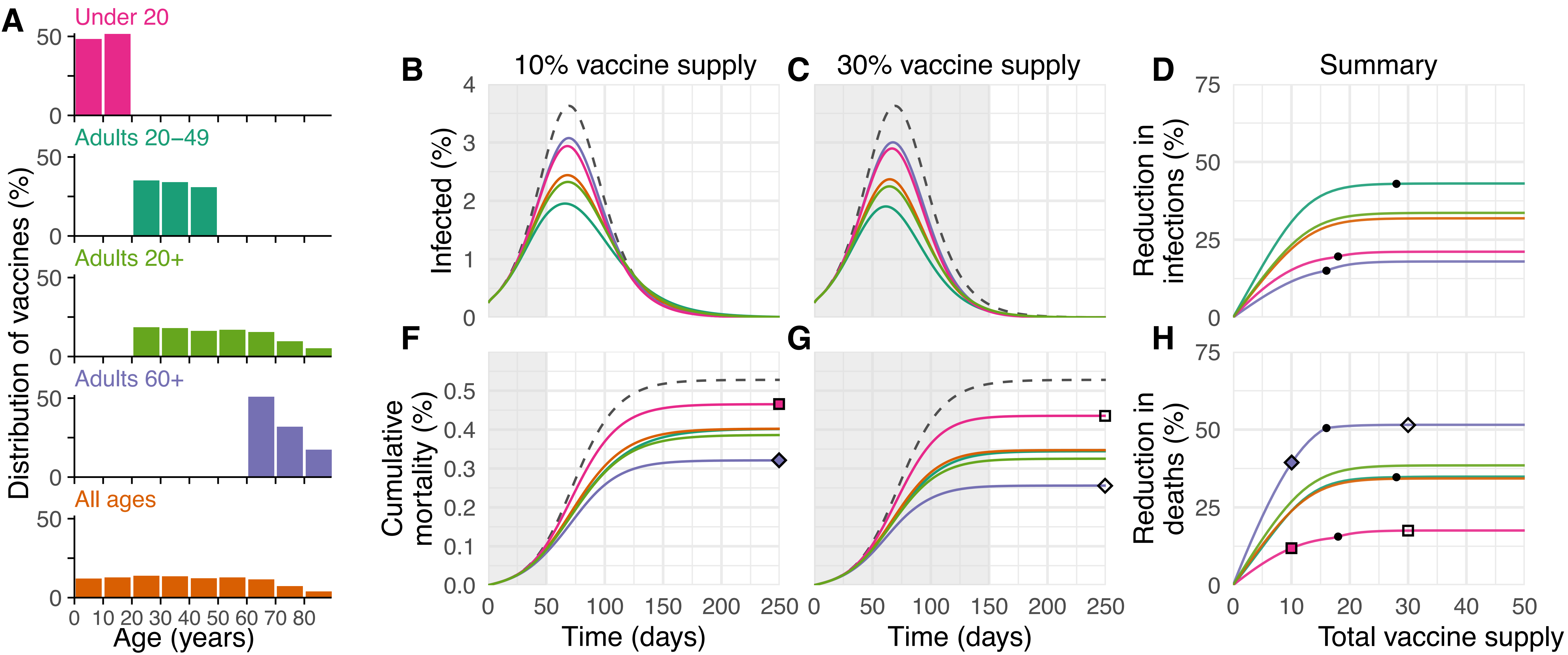

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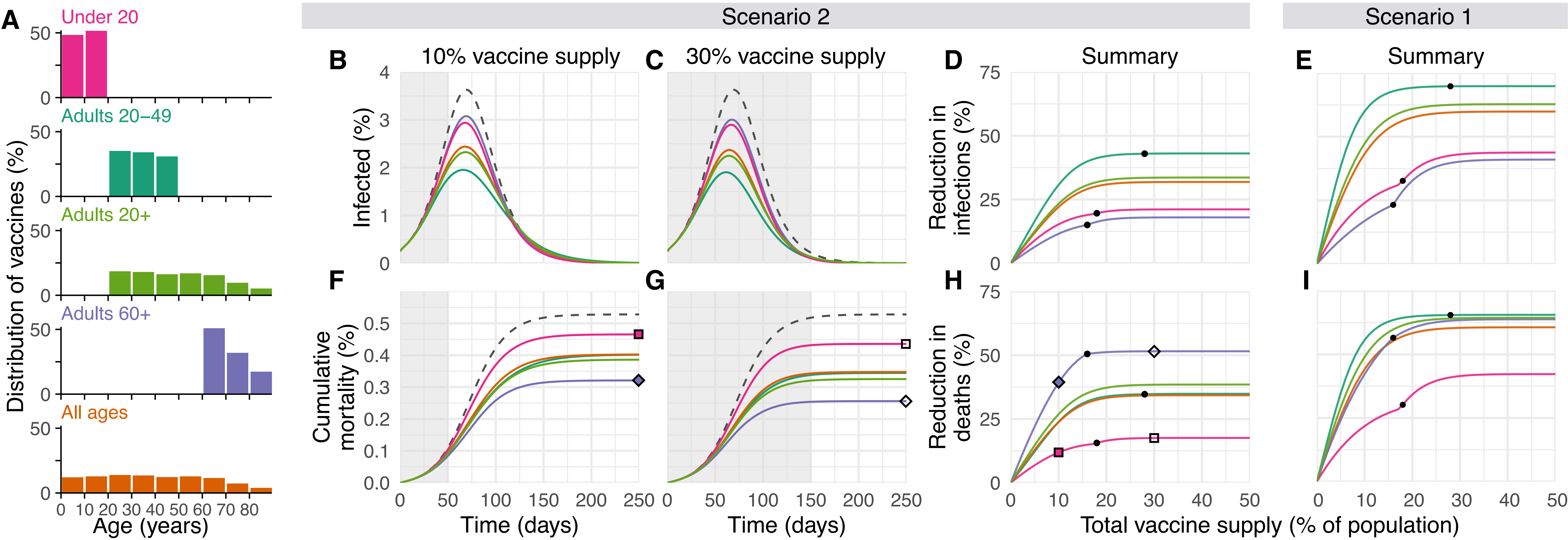
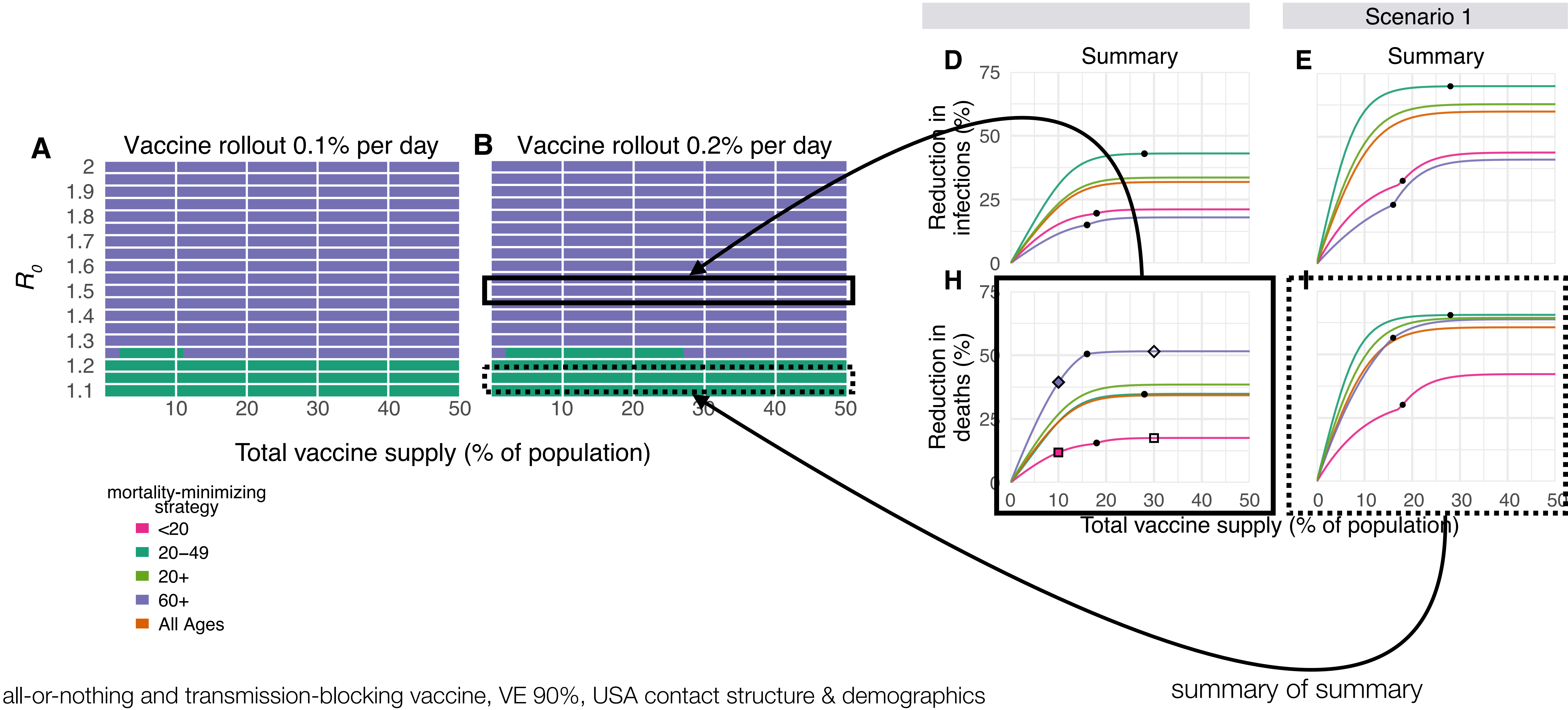


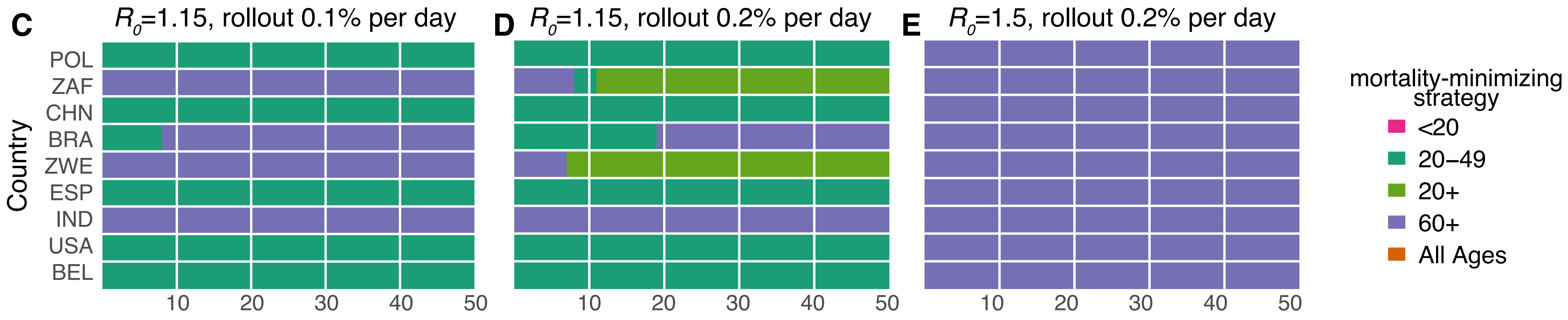
0.2% of the population vaccinated per day, all-or-nothing and transmission-blocking vaccine, VE 90%. $R_0 = 1.5$ (Scn. 2) and $R_0 = 1.15$ (Scn. 1), USA

How does transmission rate affect recommendations?



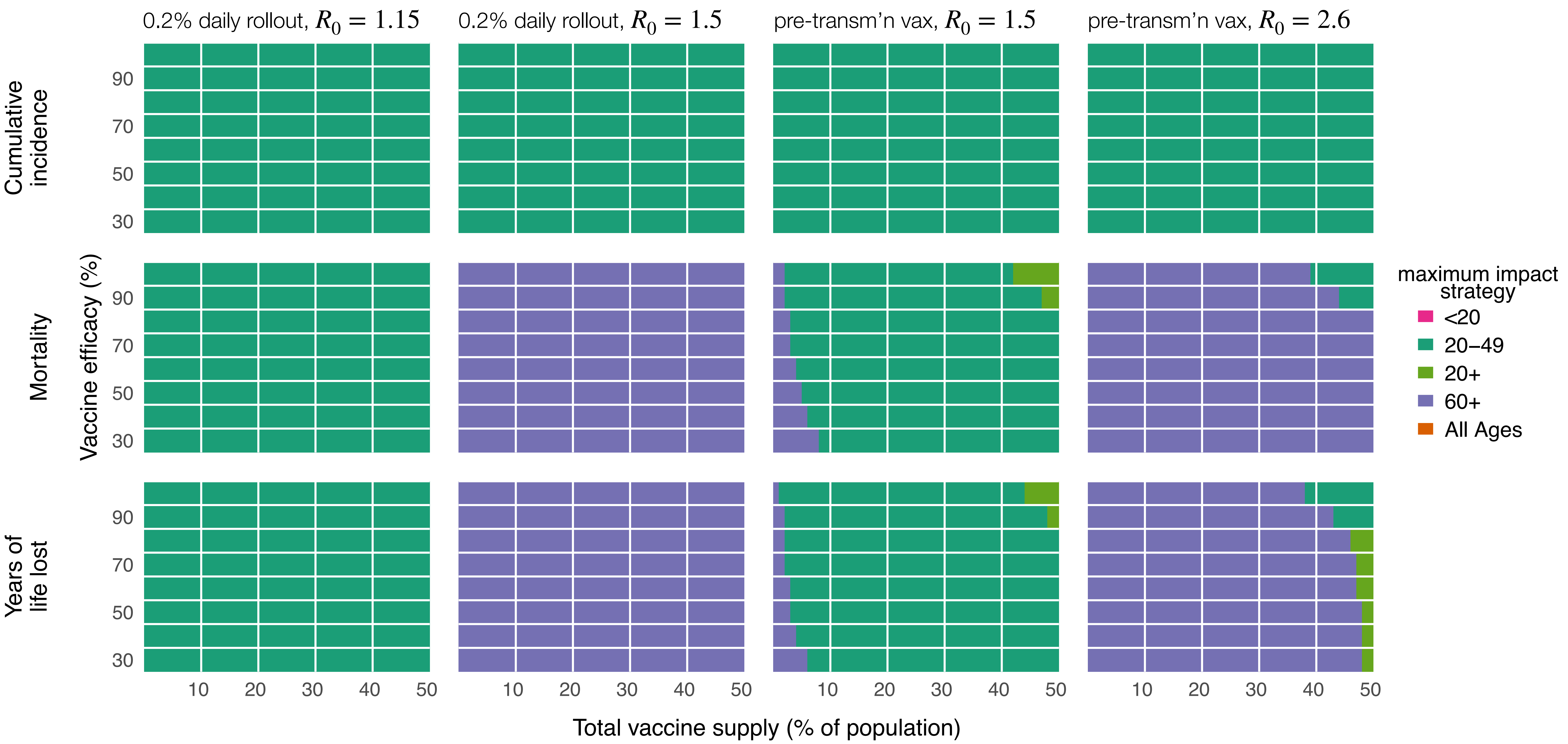
all-or-nothing and transmission-blocking vaccine, VE 90%, USA contact structure & demographics

How does country affect prioritization?



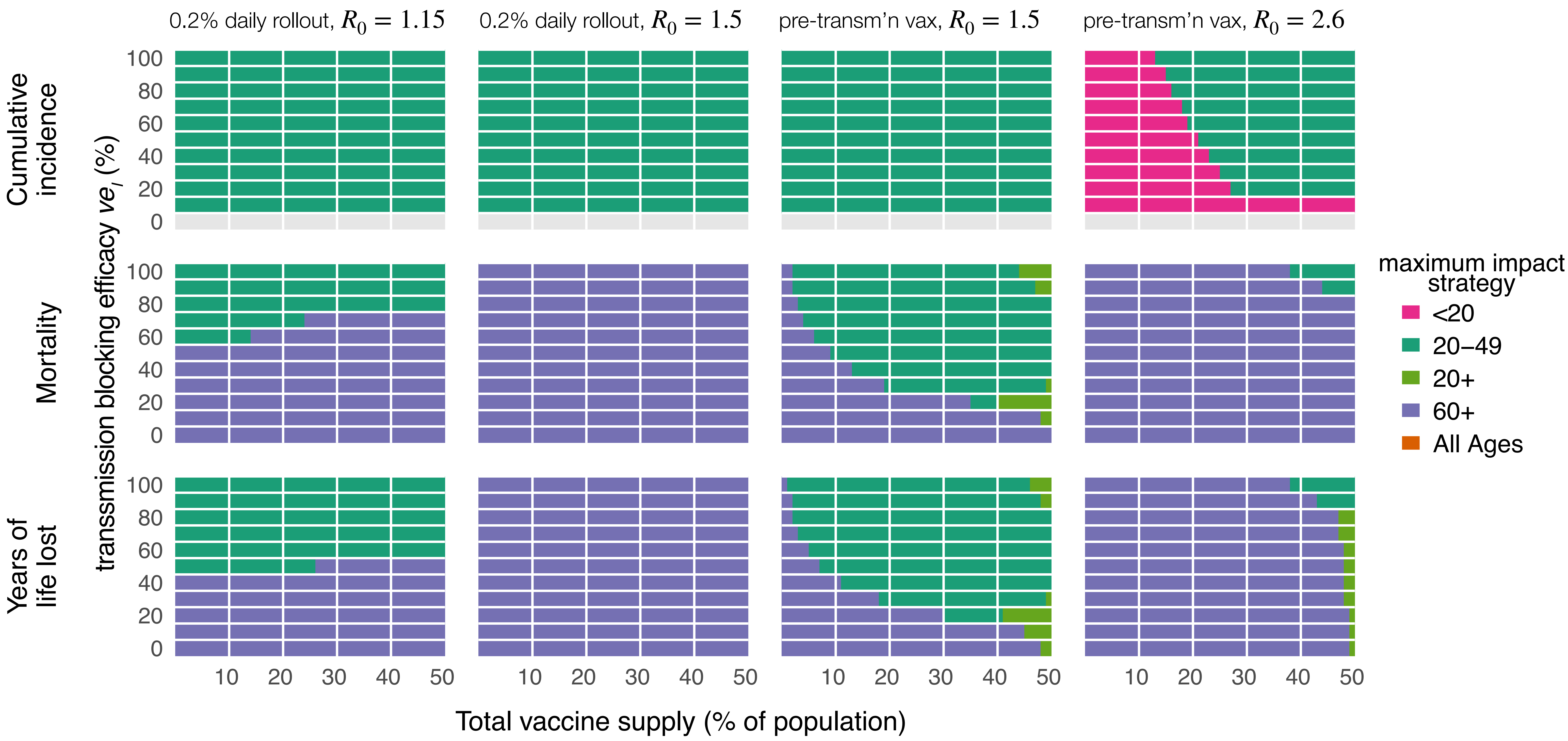
all-or-nothing and transmission-blocking vaccine, VE 90%

How does vaccine efficacy affect prioritization?



all-or-nothing and transmission-blocking vaccine, USA contact structure & demographics

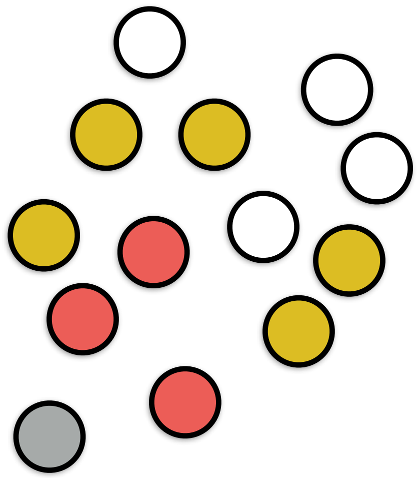
Pfizer/Moderna without perfect transmission blocking?



Discussion

Over most scenarios & settings:

- Minimize mortality by vaccinating adults 60+ first.
- Unless: (1) low R, fast rollout, and excellent transmission blocking or (2) dramatic declines in efficacy among older adults [not shown]



Over most scenarios & settings:

- Minimize incidence by vaccinating adults 20-49 first.

Model-informed COVID-19 vaccine prioritization strategies by age and serostatus
Bubar, Reinholt, Kissler, Lipsitch, Cobey, Grad, Larremore
Science, **371**(6532) abe6959 (2021)

Concerns about SARS-CoV-2 evolution should not hold back efforts to expand vaccination
Cobey, Larremore, Grad, Lipsitch
preprint, 2021

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