Age-specific mortality and immunity patterns of SARS-CoV-2

Megan O’Driscoll

Introduction: IFR

- Infection fatality ratio (IFR) - the proportion of infected individuals that die from their infection

- This can translate the number of deaths to the total number of underlying infections (very helpful for viruses with lots of undetected infections!)
    - Total infections = Total deaths / IFR

- Used in epidemiological modelling to estimate mortality burdens, inform healthcare planning, etc.,.

Introduction: IFR of SARS-CoV-2

- Very clear trend of increasing severity with age

- Complicated by large burdens of SARS-CoV-2 in nursing homes, with very different dynamics than general population
    - Greater frailty
    - Potential for much higher attack rates

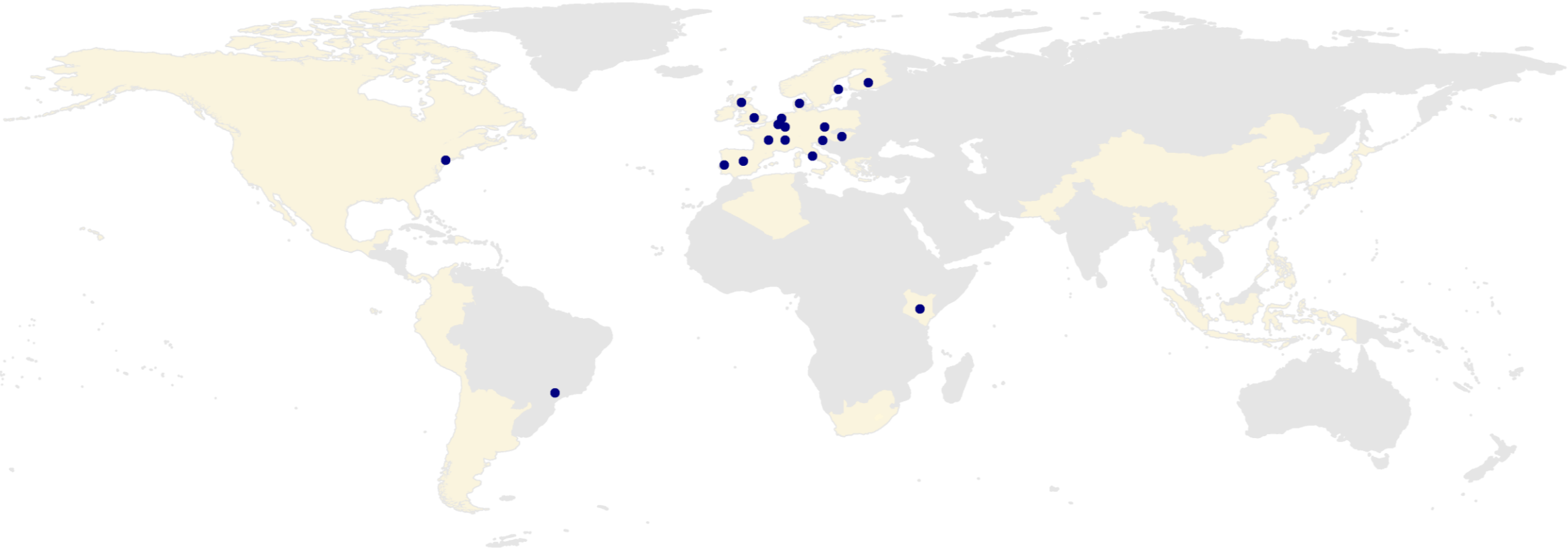
- Other factors to consider when assessing the IFR:
    - Accurate reporting of deaths
    - Prevalence of comorbidities
    - Access to healthcare
    - Quality of healthcare

Key Questions

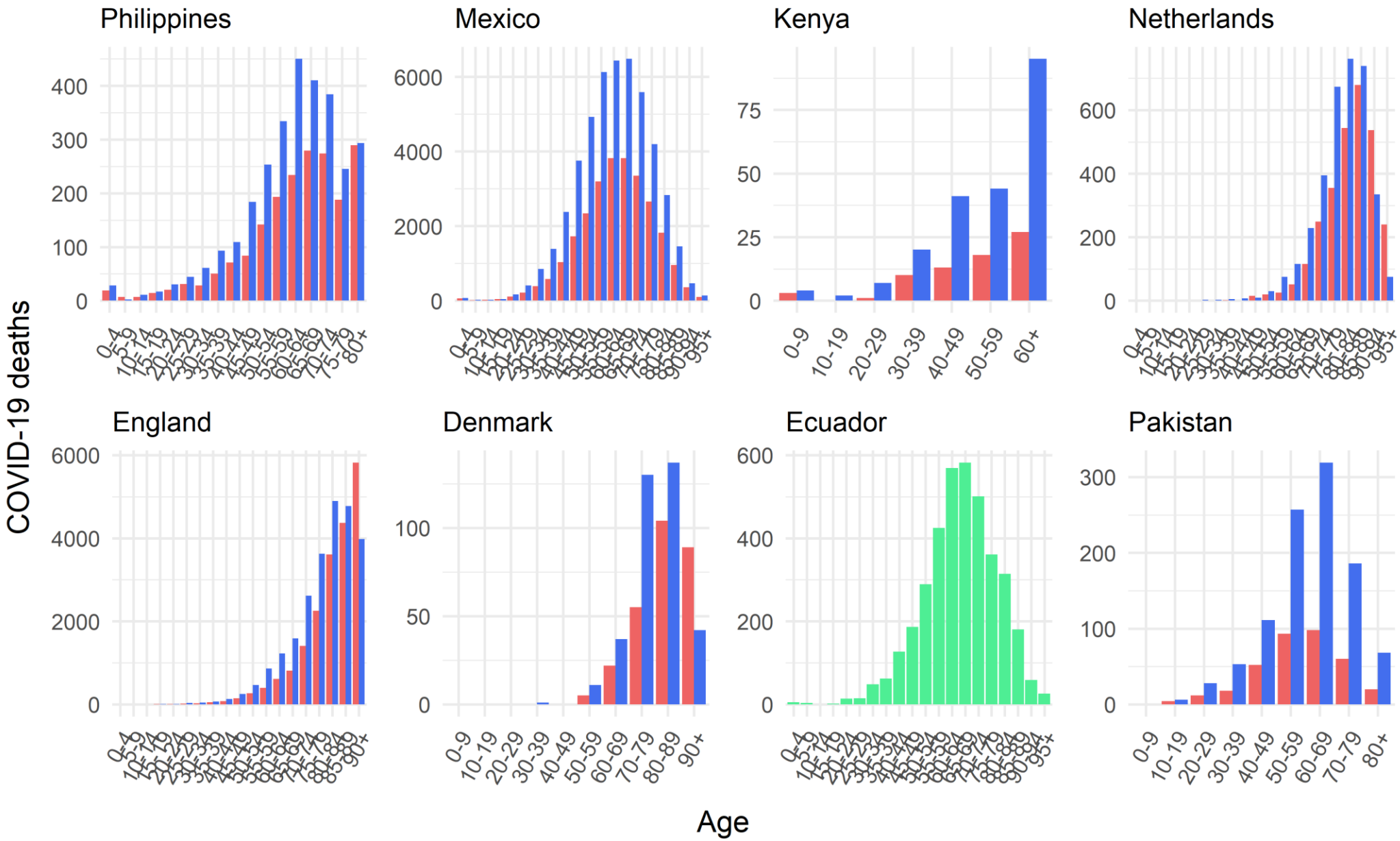
- How consistent is the age-distribution of COVID-19 deaths across countries?
- What does seroprevalence data suggest about the IFR of SARS-CoV-2?
  - Is this consistent across different studies or settings?
- How many people are likely to have been infected?

Data

- Age-specific COVID-19 death data from 45 countries
- 22 national-level seroprevalence surveys from 16 countries



Age Distributions



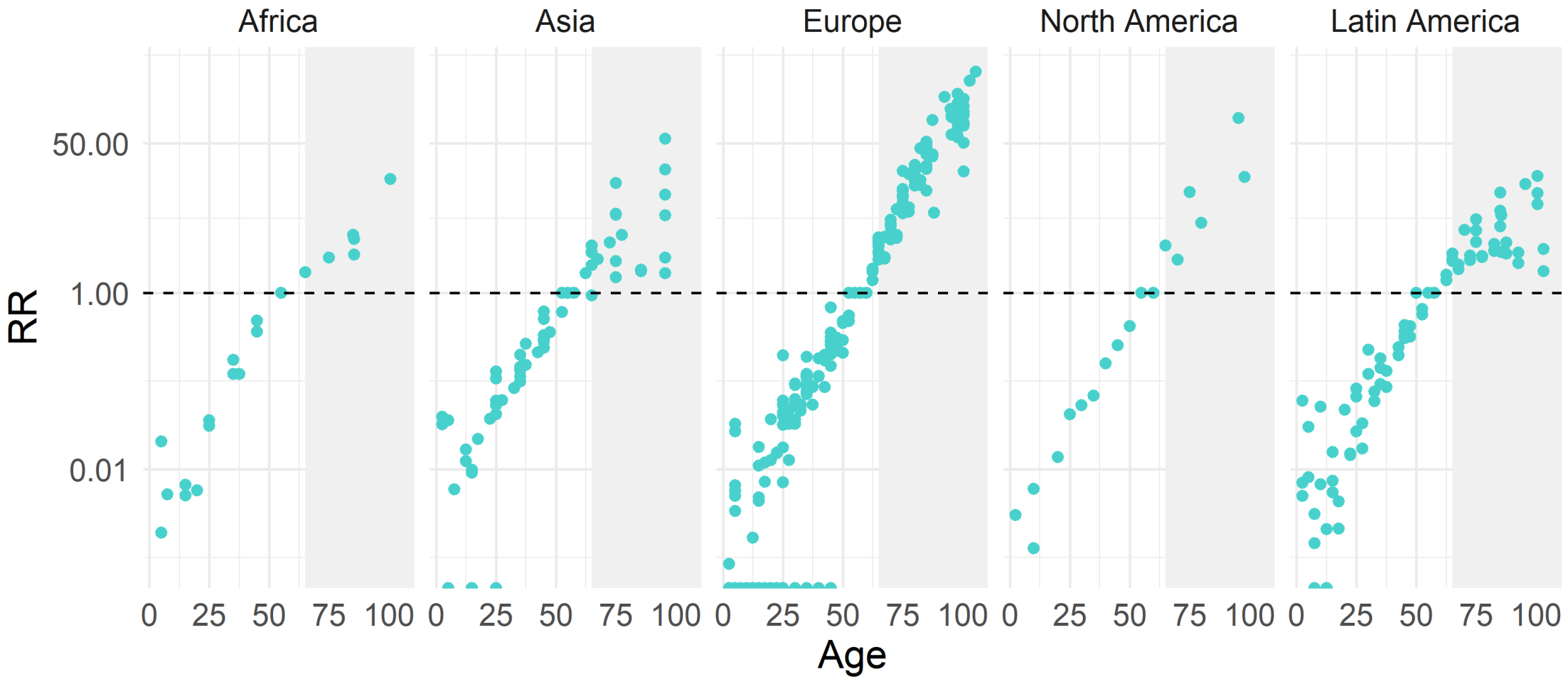
Relative Risks of death by age

To compare the age distribution of deaths across countries accounting for different population demographics we calculate a relative risk (RR) of death by age:

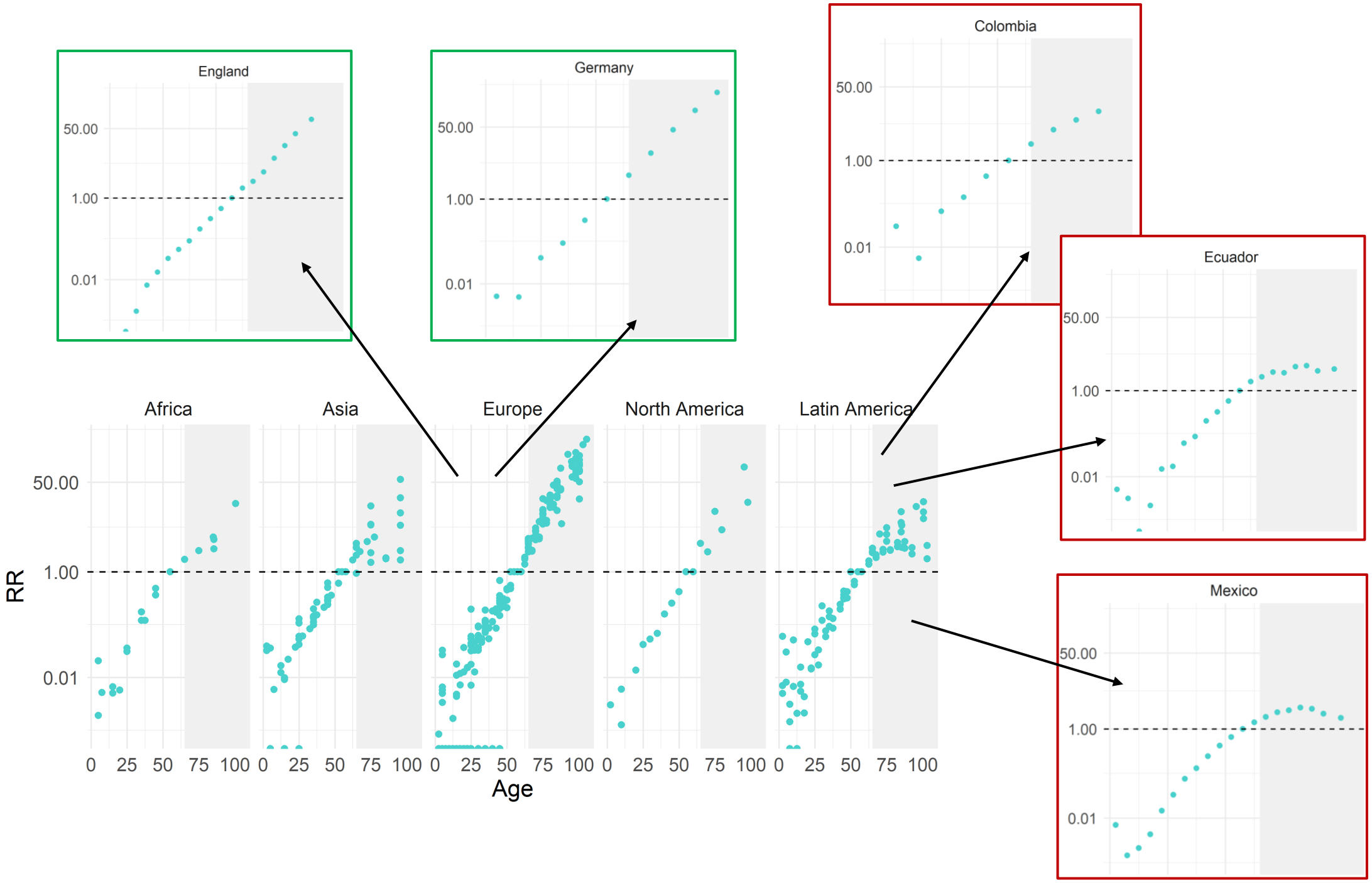
- Risk of death in age group *a,* relative to the risk of death in a reference age group

$$RR = \frac{deaths_a / population_a}{deaths_{ref} / population_{ref}}$$

Relative Risks of death by age



*note the log scale


England
Germany
Colombia
Ecuador
Mexico
Africa
Asia
Europe
North America
Latin America
RR
50.00
1.00
0.01
0
25
50
75
100
Age

Modelling methods

We developed a modelling framework to combine all the results of the available seroprevalence studies and the age-specific death data from all countries

- Fit exclusively to deaths <65 years
- Derived IFRs >65 using non-nursing home data from England
- Bayesian framework

Modelling methods

Inputs:

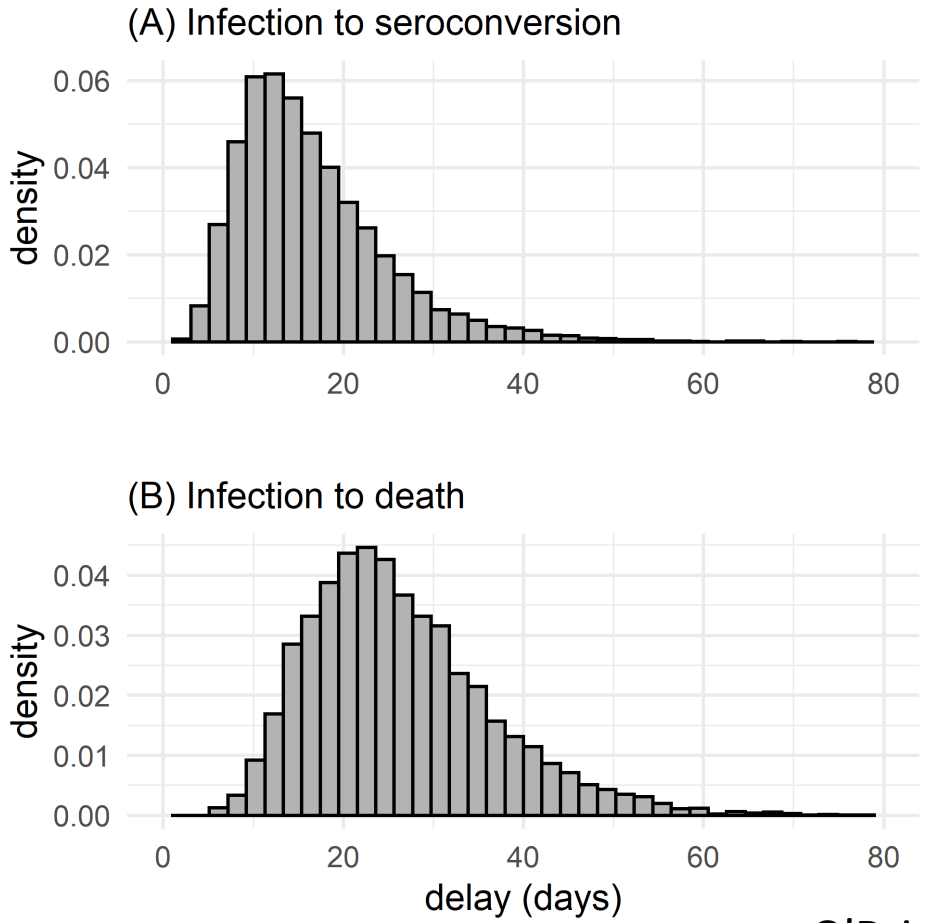
- 22 Seroprevalence studies
- Age-specific death data from 45 countries
- Time series of COVID-19 deaths from 45 countries

Outputs:

- Age-specific IFR estimates (global)
- Population IFR estimates for each country
- Estimates of the proportion infected in each country

Modelling methods

Used delay distributions to link the timing of death data and seroprevalence data



$$D_{c,a,s} = N_{c,a,s} \cdot \Lambda_c \cdot \delta_a \cdot IFR_{a,s}$$

$$\lambda_{c,t} = \Lambda_c \cdot \sum_{i=1}^{t} S_{c,i} \,/\, \sum_{i=1}^{T_c} D_{c,i}$$

O'Driscoll et al., *Nature* https://www.nature.com/articles/s41586-020-2918-0

Modelling methods

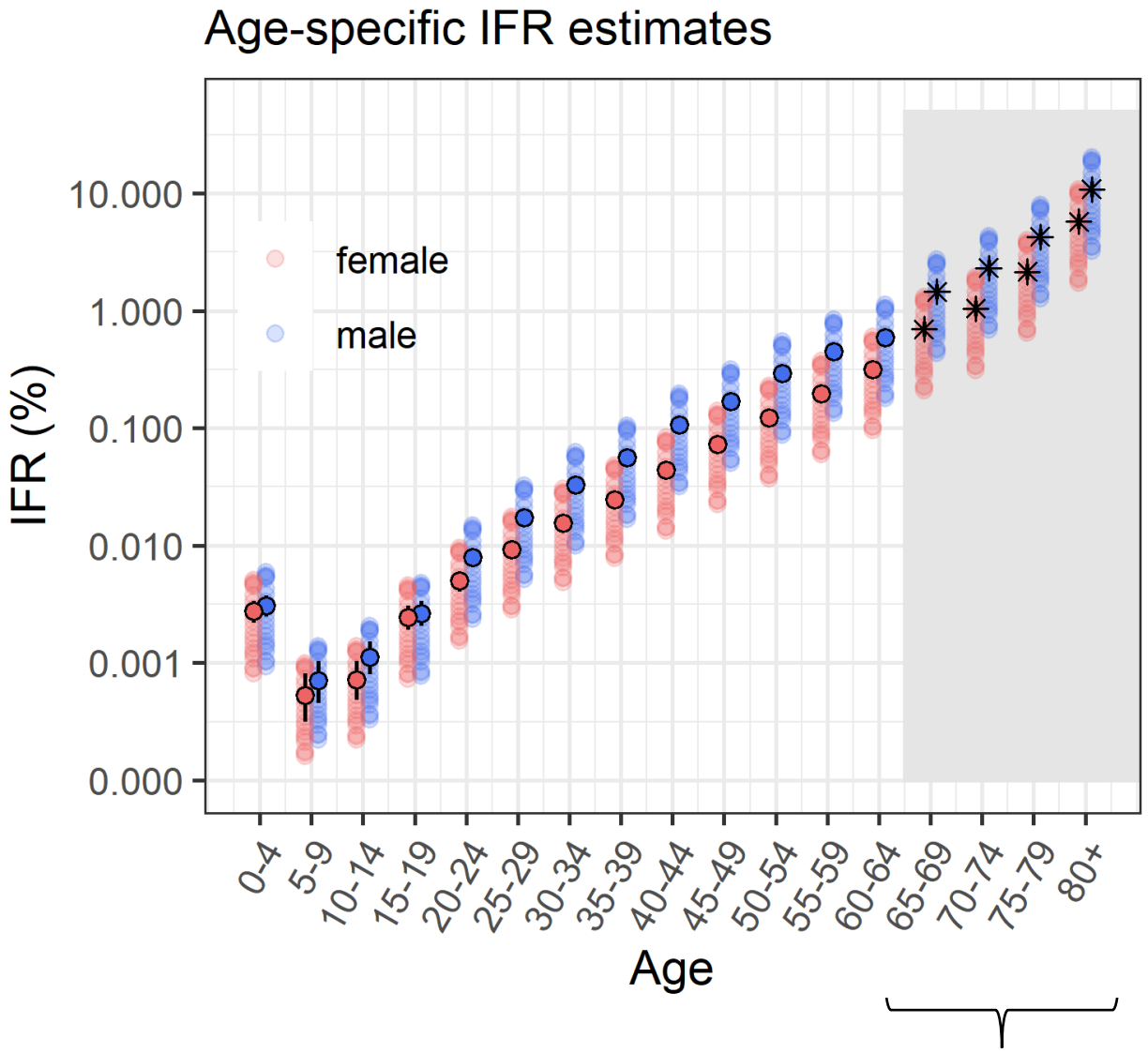
Additional Assumptions:

- Equal infection attack rates by age <65 years
- Relative infection attack rate of 0.7 in those >65 years
- Age distribution of deaths is constant in time

Modelling methods

- **Ensemble Model:**
  - Included all national-level death data & seroprevalence studies

- Individual country/seroprevalence study models

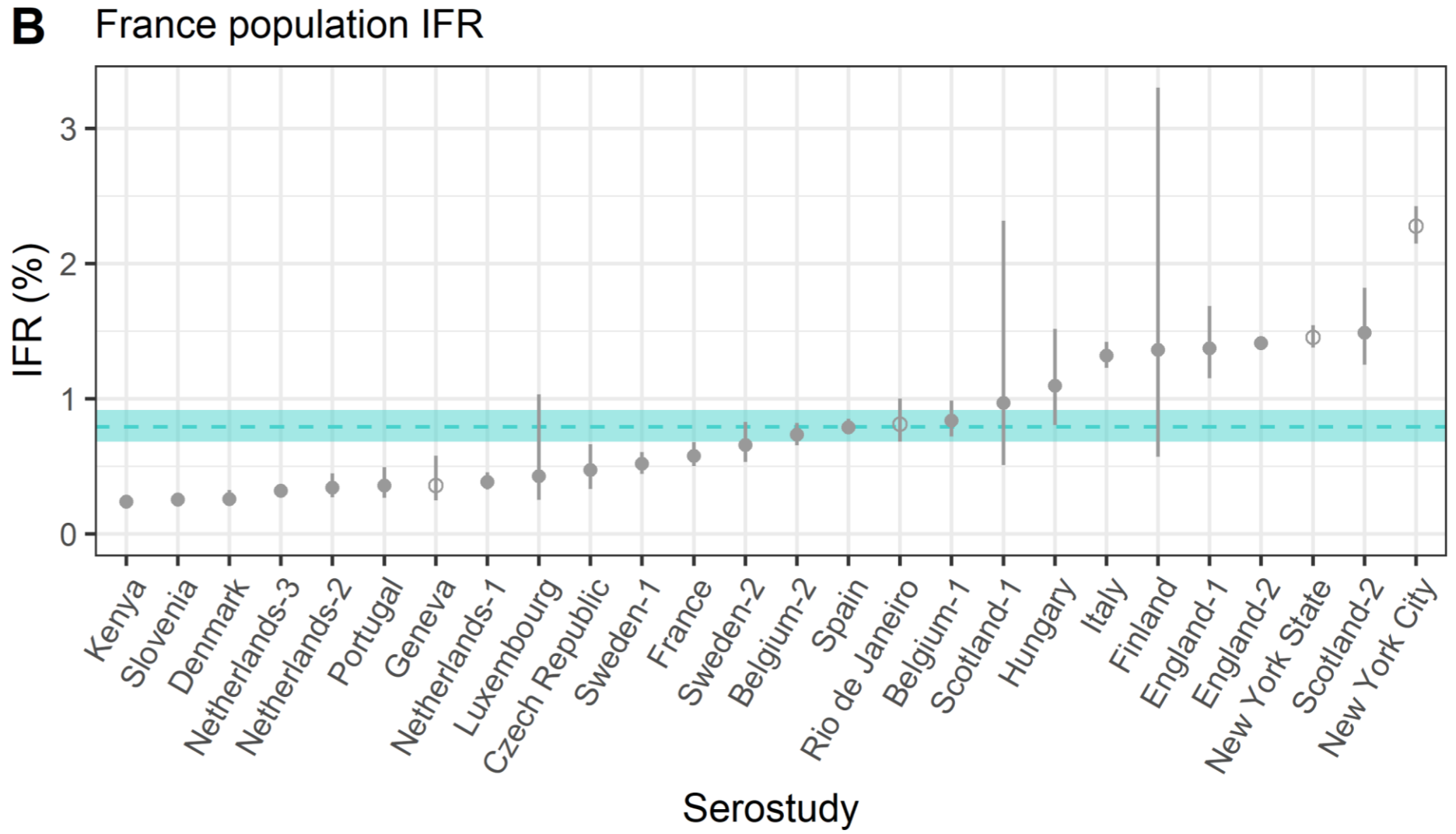


- Lowest IFR in 5-9 year olds:
  - 0.001% (0.000-0.001%)
- Highest IFR in 80+:
  - 8.29% (7.11-9.59%)
- Differences by sex increase with age

Excluded from model fitting

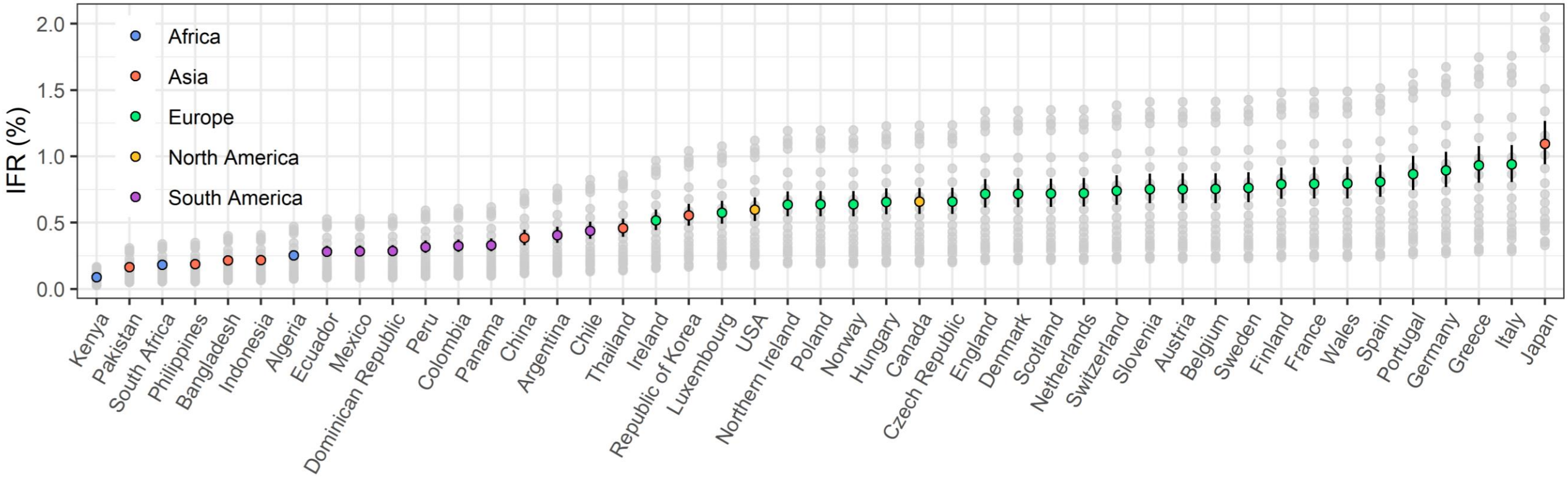
IFRs derived from the relative risk of non-nursing home COVID-19 deaths in England

Consistency of IFR across studies & countries



Demography and IFR

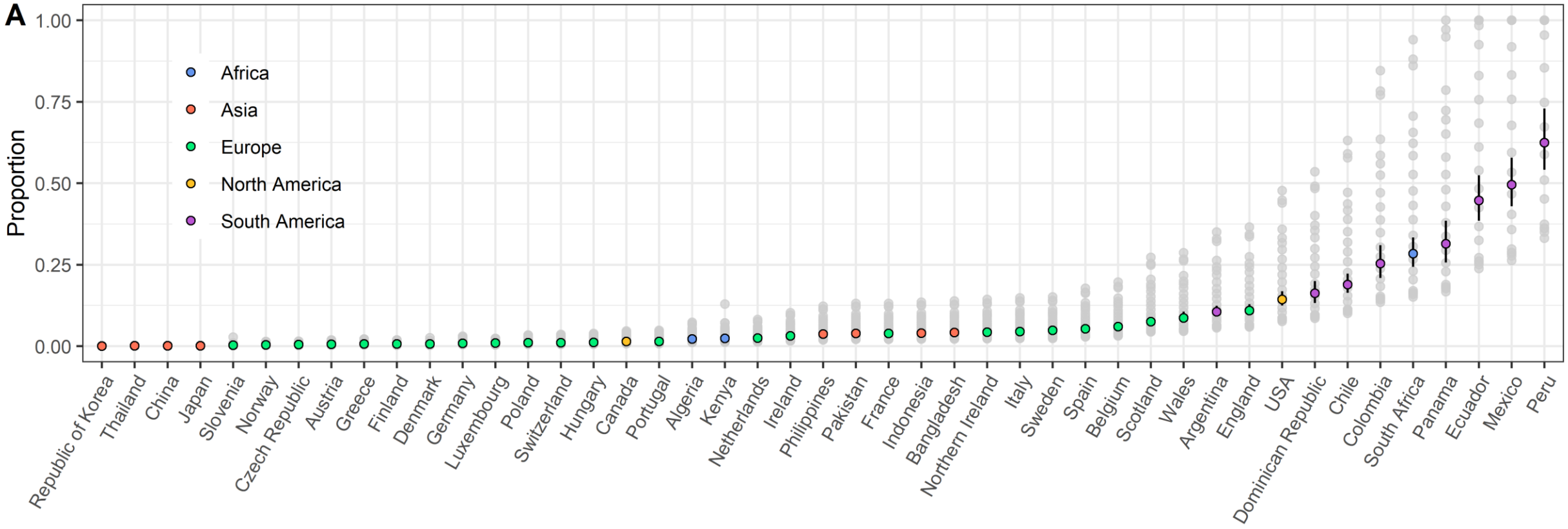
General population IFR



**Assumes that nursing home residents experience the same rates of infection and infection fatality as the general population*

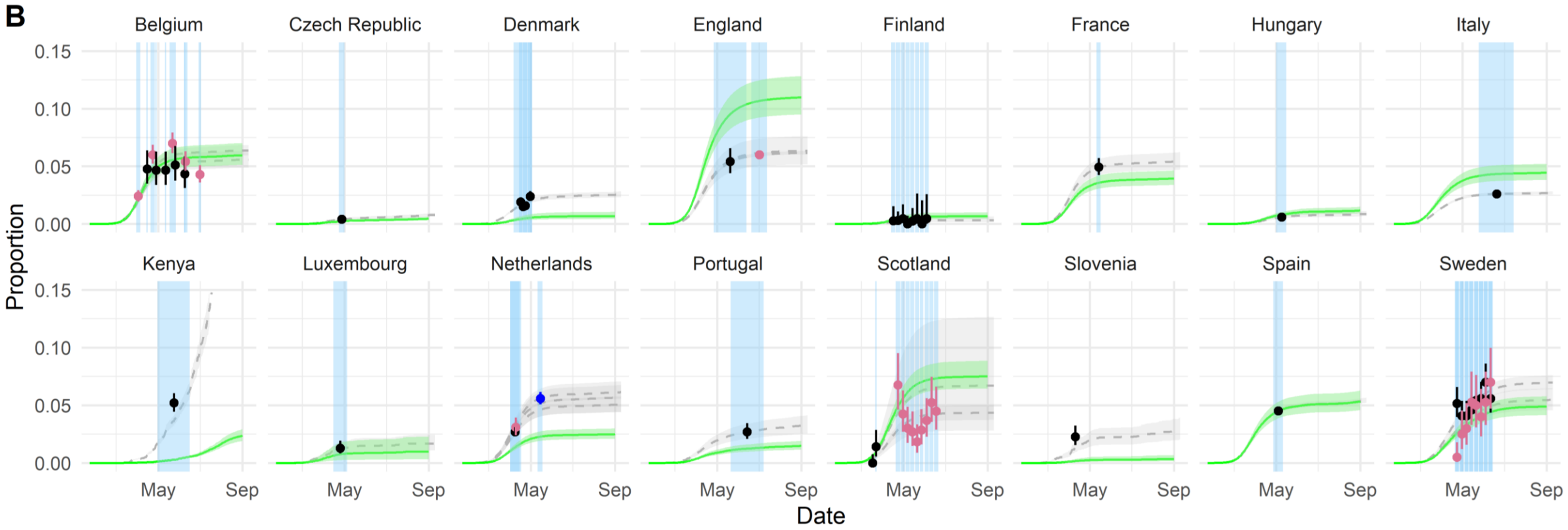
(Now very outdated!)

Proportion Infected by 1st September 2020

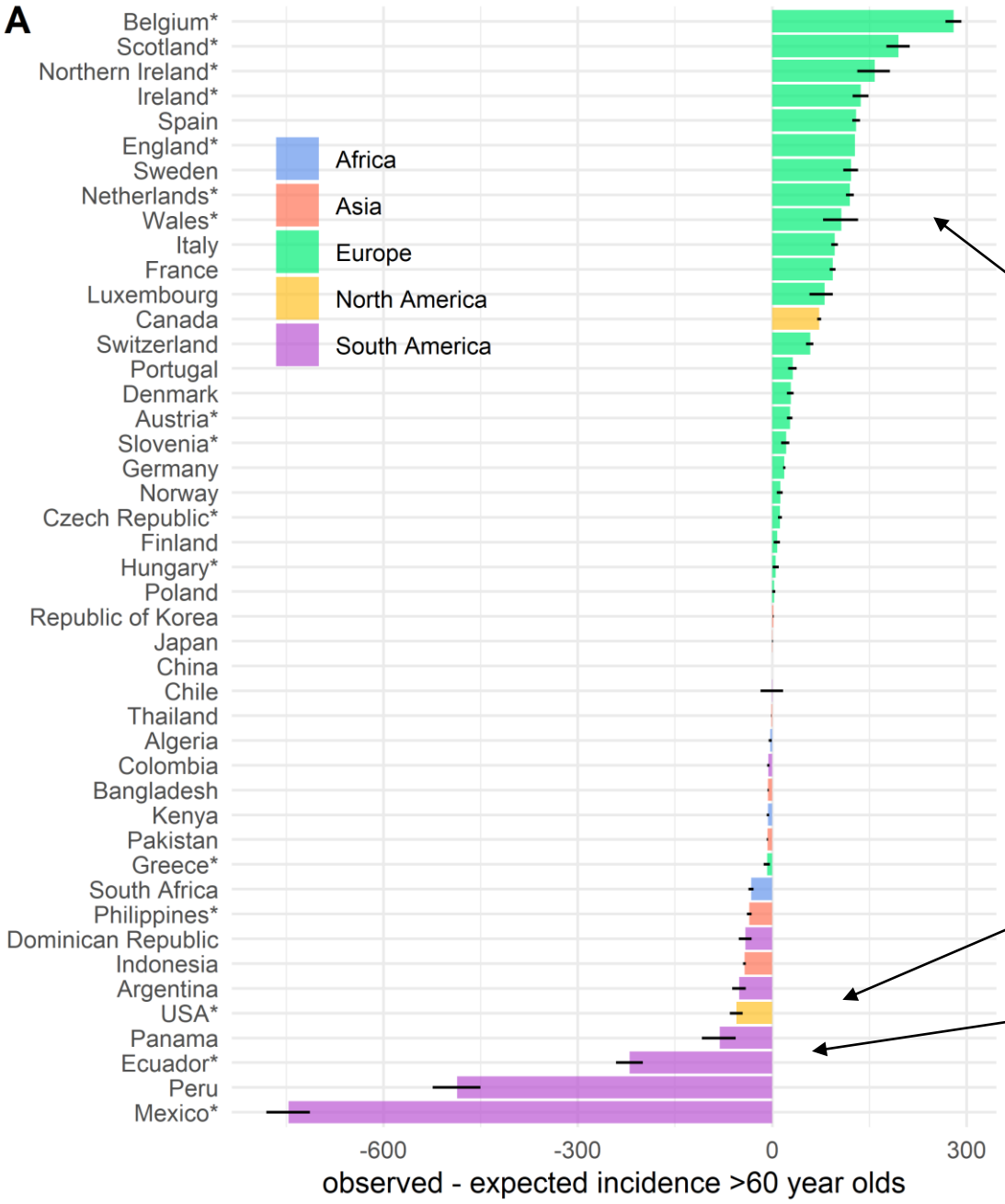


Important to consider full range of uncertainty in these estimates (grey dots)

Fits to seroprevalence data



Mortality rates in older individuals

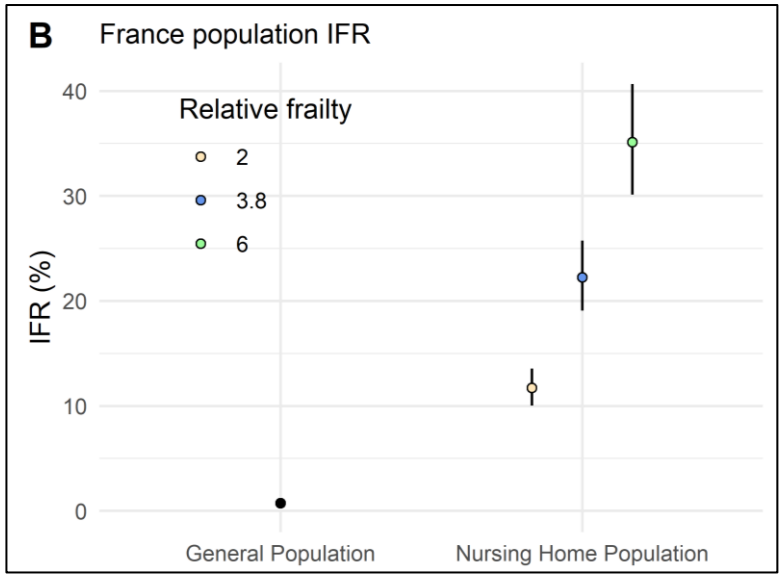


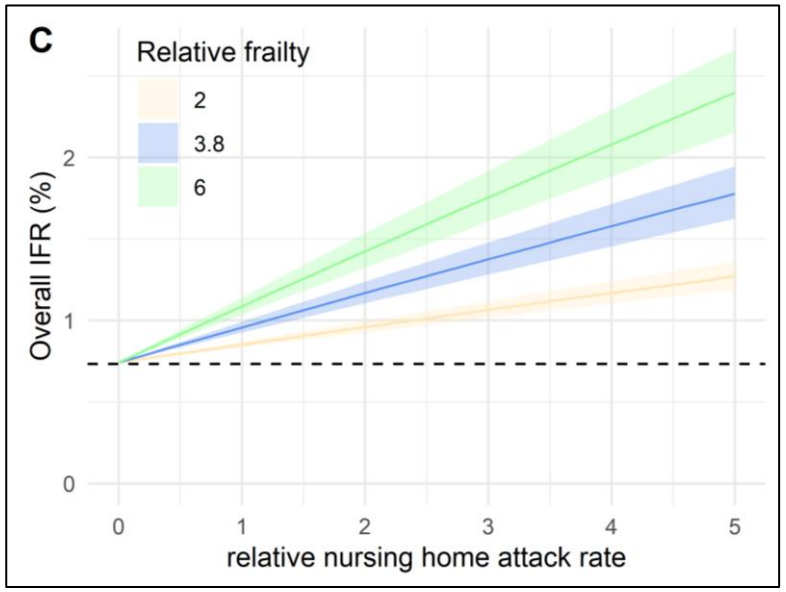
Nursing home outbreaks

Under-reporting of deaths?

Successful shielding programmes?

Nursing Homes and IFR



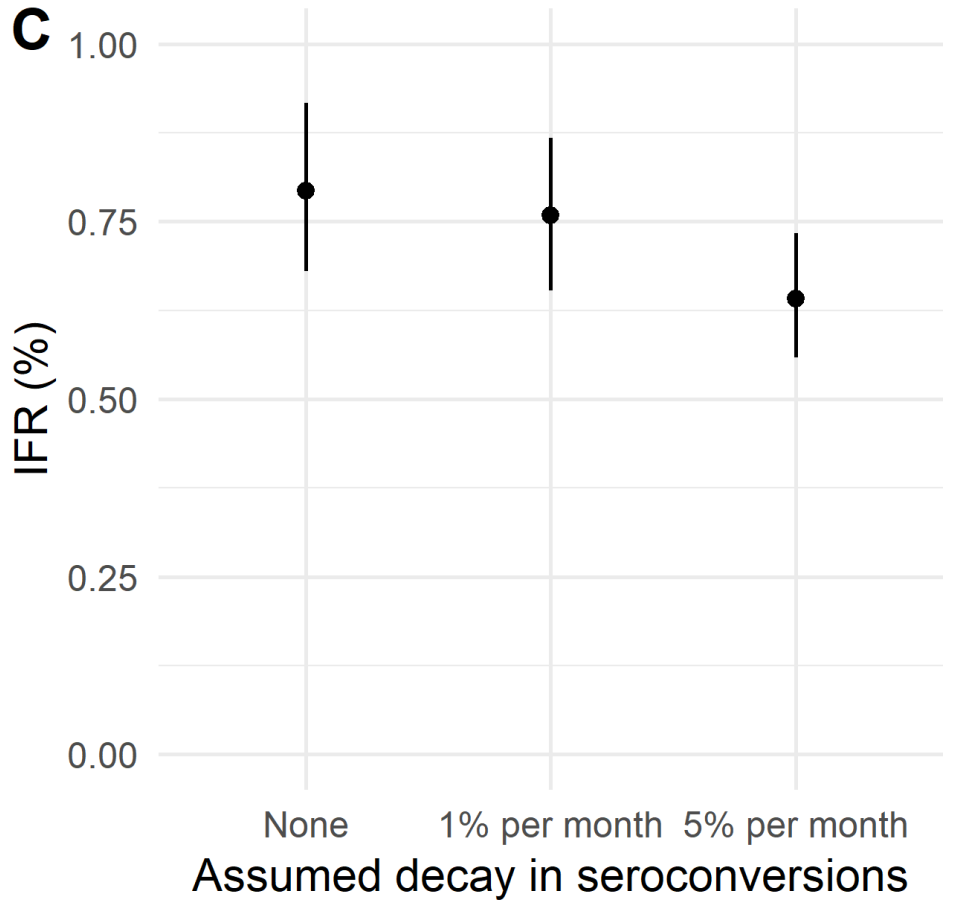


- General Population IFR:
  0.74% (0.64-0.86%)
- Nursing Home Population IFR:
  22.25% (19.06-25.74%)
- Overall IFR:
  1.10% (0.95-1.28%)

Molenberghs et al., *medrxiv*

Some things to consider

- Under-reporting of deaths
- Representativeness of seroprevalence data
- Improvements in severe outcomes over time
- Potential seroreversions
- Different mixing patterns



Acknowledgements

Henrik Salje, University of Cambridge

Simon Cauchemez, Institut Pasteur

Gabriel Ribeiro Dos Santos, University of Cambridge

Lin Wang, University of Cambridge

Derek Cummings, University of Florida

Andrew Azman, Johns Hopkins

Juliette Paireau, Institut Pasteur

Arnaud Fontanet, Institut Pasteur