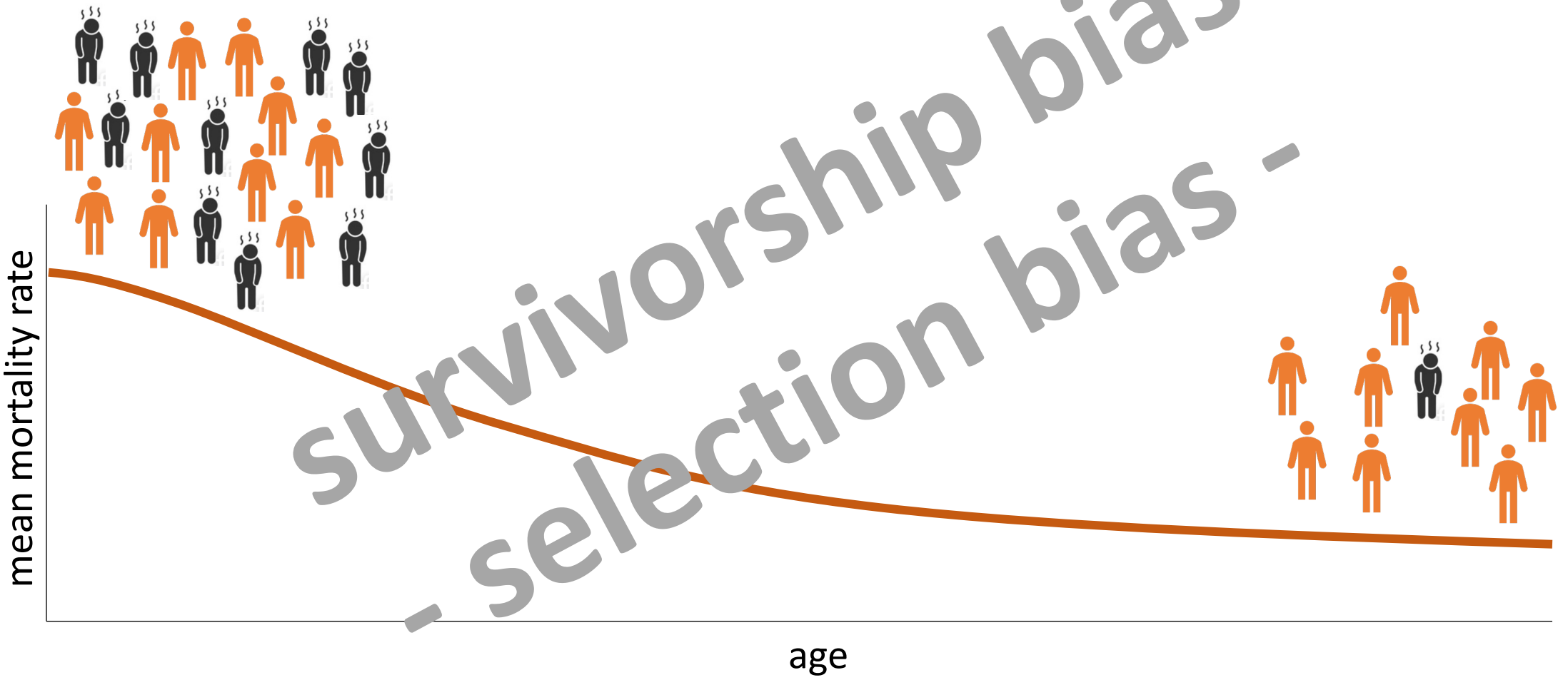
University of Strathclyde Science

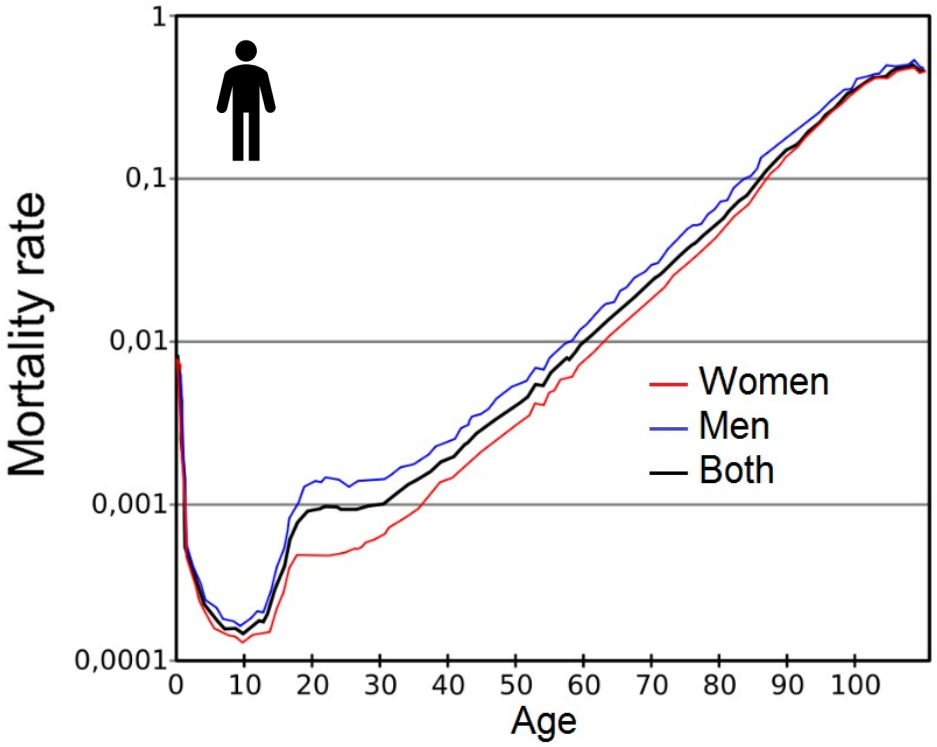
NOVAMATH

Individual variation in susceptibility or exposure to SARS-CoV-2 lowers the herd immunity threshold

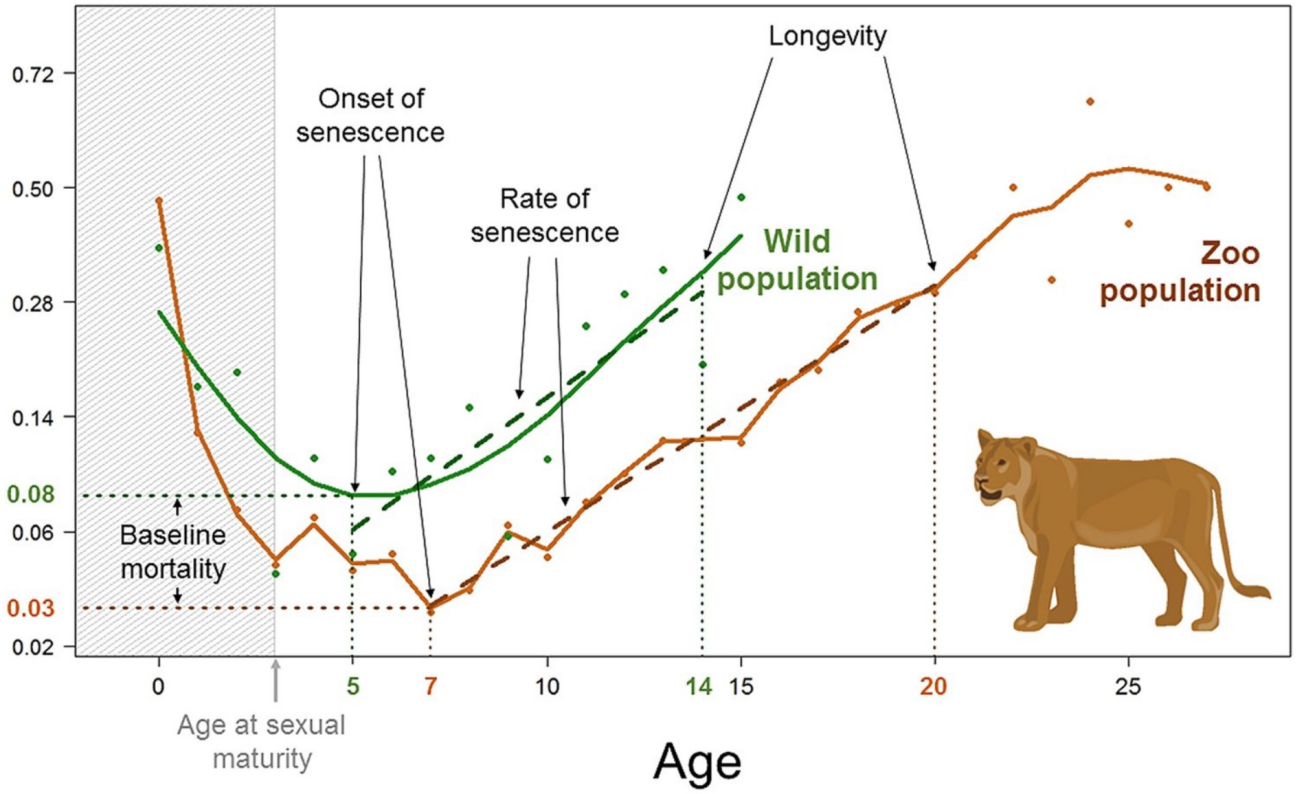
Gabriela Gomes | University of Strathclyde, Glasgow, and NOVA School of Science and Technology, Lisbon

Frailty variation subject to *selection* within cohorts





TG Goldsmith 2006 *The Evolution of Aging. Second Edition.* Azinet Press.



M Tidière *et al* 2016 Comparative analyses of longevity and senescence reveal variable survival benefits of living in zoos across mammals. *Sci Rep* 6:36361.

References (1970s):

- N Keyfitz, G Littman G 1979 Mortality in a heterogeneous population. *Popul Stud* 33:333-342.
- JW Vaupel, KG Manton, E Stallard 1979 The impact of heterogeneity in individual frailty on the dynamics of mortality. *Demography* 16:439-454.

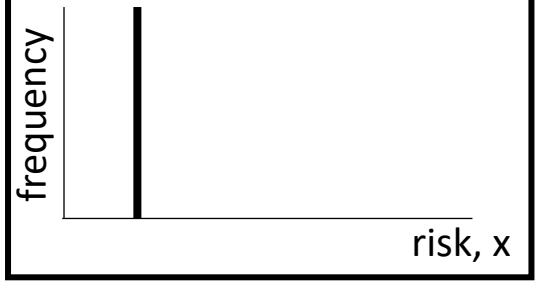
Endemic infections (e.g., HIV)

Homogeneous risk
(susceptibility x connectivity):

$$\frac{dS}{dt} = \mu - \beta IS - \mu S$$

$$\frac{dI}{dt} = \beta IS - \mu I$$

$$\mathcal{R}_0 = \frac{\beta}{\mu}$$

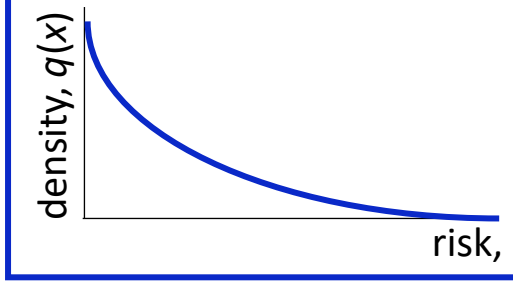


Heterogeneous susceptibility:

$$\frac{dS(x)}{dt} = q(x)\mu - \beta \int I(u)du\, xS(x) - \mu S(x)$$

$$\frac{dI(x)}{dt} = \beta \int I(u)du\, xS(x) - \mu I(x)$$

$$\mathcal{R}_0 = \frac{\beta}{\mu}$$

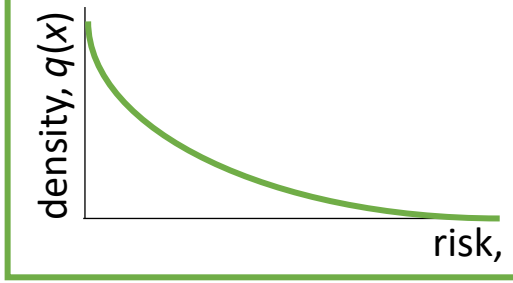


Heterogeneous connectivity:

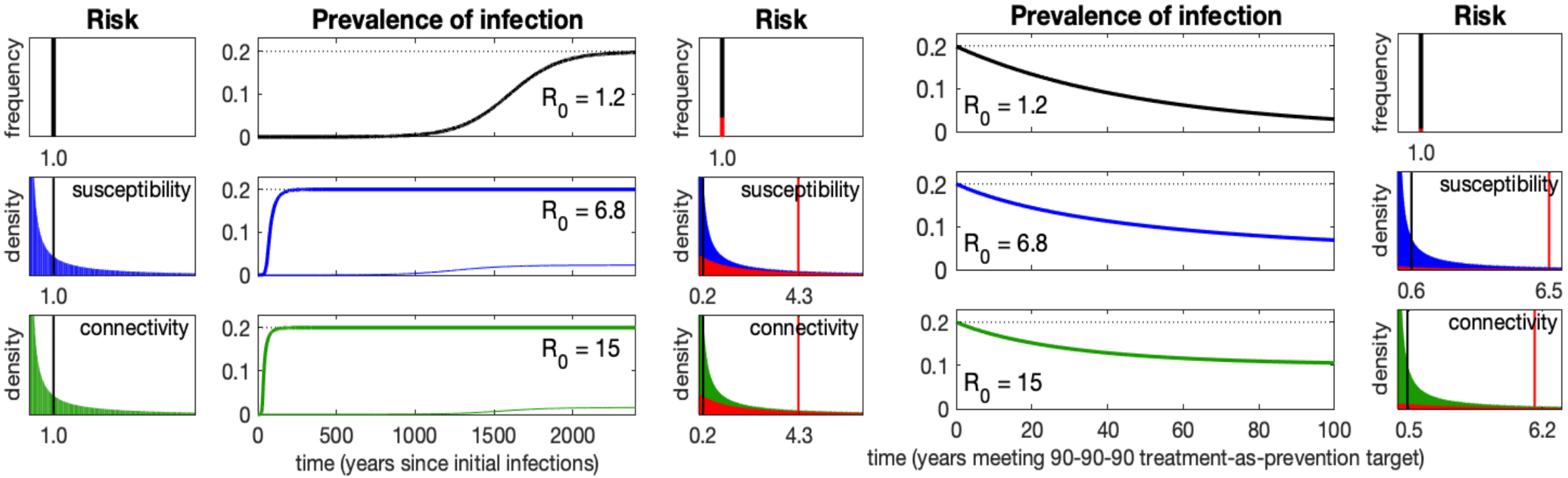
$$\frac{dS(x)}{dt} = q(x)\mu - \beta \int uI(u)du\, xS(x) - \mu S(x)$$

$$\frac{dI(x)}{dt} = \beta \int uI(u)du\, xS(x) - \mu I(x)$$

$$\mathcal{R}_0 = \frac{\beta}{\mu} \int x^2 q(x)dx$$



False homogeneity causes underestimation of reproduction numbers from endemic states and overoptimism about interventions



MGMG 2018 On the mathematics of populations. *CIM Bulletin* 40:21-27; MGMG *et al* 2020 A pragmatic approach to infer individual risk heterogeneity for optimising disease forecasts and policy development. Preprint, https://arxiv.org/abs/2009.01354

References (1980s):

- RM Anderson, GF Medley, RM May, AM Johnson 1986 A preliminary study of the transmission dynamics of the human immunodeficiency virus (HIV), the causative agent of AIDS. *IMA J Math Appl Med Biol* 3:229-263.
- SA Colgate, AE Stanley, JM Hyman, SP Layne, C Qualls 1989 Risk behavior-based model of the cubic growth of acquired immunodeficiency syndrome in the United States. *Proc Natl Acad Sci USA* 86: 4793-4797.

Epidemic infections (e.g., COVID-19)

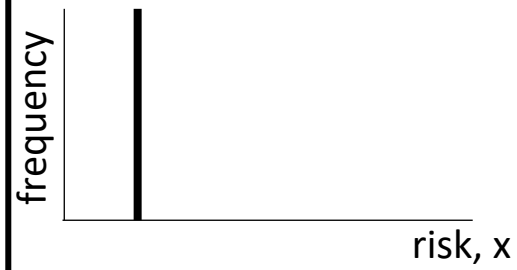
Homogeneous risk
(susceptibility x connectivity):

$$\frac{dS}{dt} = -\beta IS$$

$$\frac{dI}{dt} = \beta I(S + \sigma R) - \gamma I$$

$$\frac{dR}{dt} = \gamma I - \sigma\beta IR$$

$$\mathcal{R}_0 = \frac{\beta}{\gamma}$$



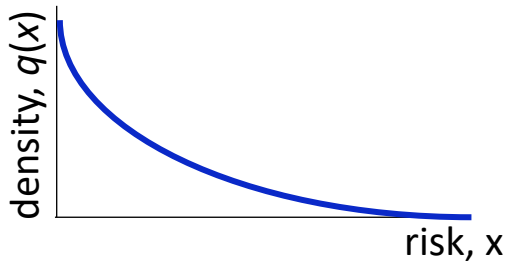
Heterogeneous susceptibility:

$$\frac{dS(x)}{dt} = -\beta \int I(u)du\, xS(x)$$

$$\frac{dI(x)}{dt} = \beta \int I(u)du\, x(S(x) + \sigma R(x)) - \gamma I(x)$$

$$\frac{dR(x)}{dt} = \gamma I(x) - \sigma\beta \int I(u)du\, xR(x)$$

$$\mathcal{R}_0 = \frac{\beta}{\gamma}$$



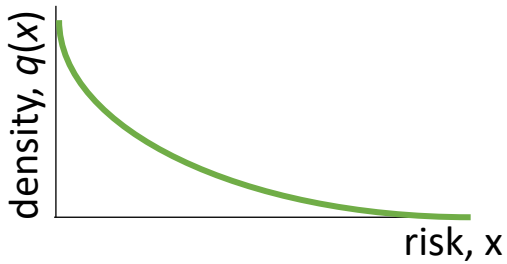
Heterogeneous connectivity:

$$\frac{dS(x)}{dt} = -\beta \int uI(u)du\, xS(x)$$

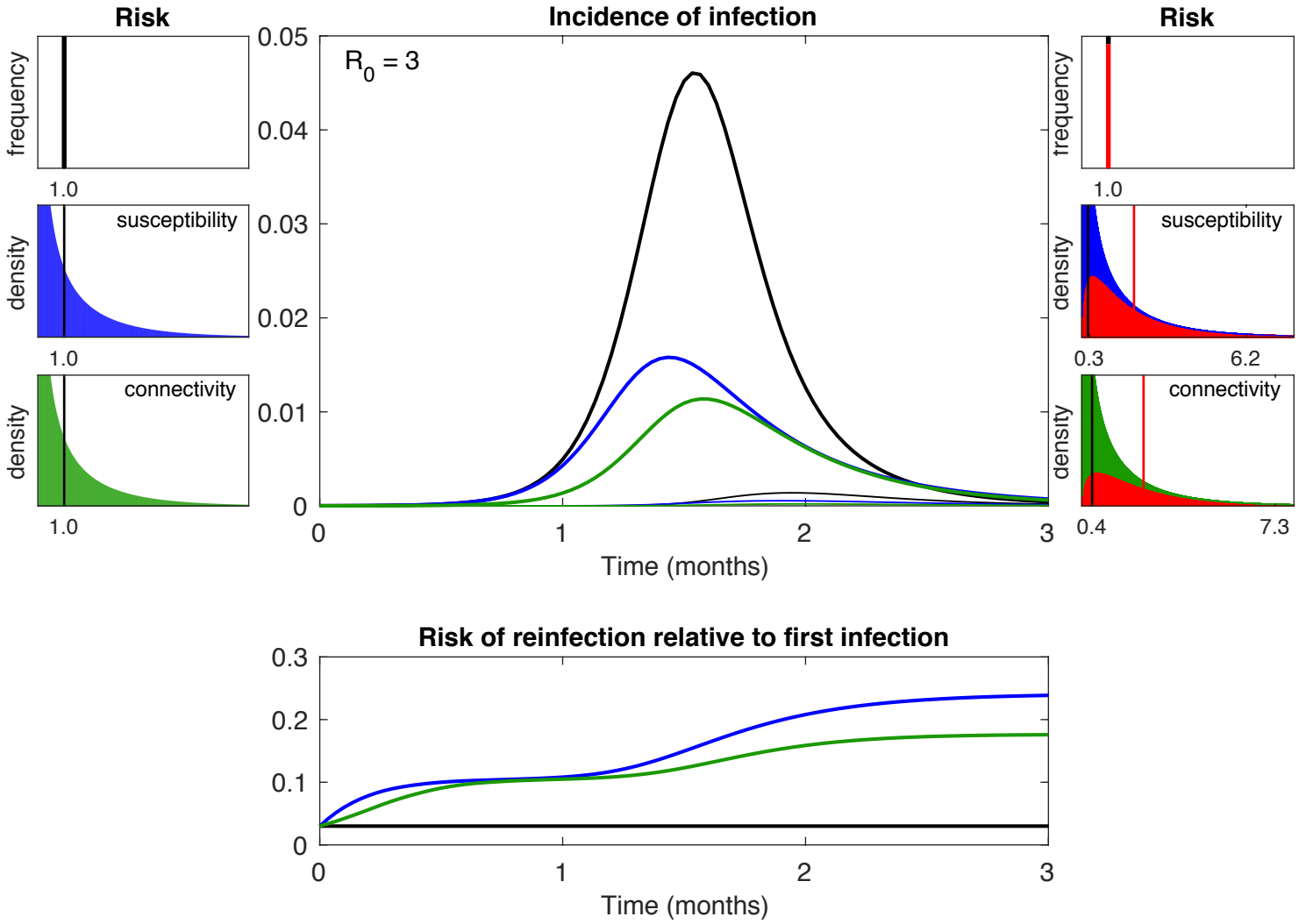
$$\frac{dI(x)}{dt} = \beta \int uI(u)du\, x(S(x) + \sigma R(x)) - \gamma I(x)$$

$$\frac{dR(x)}{dt} = \gamma I(x) - \sigma\beta \int uI(u)du\, xR(x)$$

$$\mathcal{R}_0 = \frac{\beta}{\gamma} \int x^2 q(x)dx$$



False homogeneity exaggerates epidemic final sizes and risk of reinfection



SEIR models

Heterogeneous susceptibility:

$$\frac{dS(x)}{dt} = -\beta \int I(u)du\, xS(x)$$

$$\frac{dE(x)}{dt} = \beta \int I(u)du\, x\big(S(x) + \sigma R(x)\big) - \delta E(x)$$

$$\frac{dI(x)}{dt} = \delta E(x) - \gamma I(x)$$

$$\frac{dR(x)}{dt} = (1-\phi)\gamma I(x) - \sigma\beta \int I(u)du\, xR(x)$$

$$\mathcal{H} = 1 - \left(\frac{1}{\mathcal{R}_0}\right)^{\frac{1}{1+\nu^2}}$$

$$\mathcal{R}_0 = \beta\left(\frac{\rho}{\delta} + \frac{1}{\gamma}\right)$$

Heterogeneous connectivity:

$$\frac{dS(x)}{dt} = -\beta \int uI(u)du\, xS(x)$$

$$\frac{dE(x)}{dt} = \beta \int uI(u)du\, x\big(S(x) + \sigma R(x)\big) - \delta E(x)$$

$$\frac{dI(x)}{dt} = \delta E(x) - \gamma I(x)$$

$$\frac{dR(x)}{dt} = (1-\phi)\gamma I(x) - \sigma\beta \int uI(u)du\, xR(x)$$

$$\mathcal{H} = 1 - \left(\frac{1}{\mathcal{R}_0}\right)^{\frac{1}{1+2\nu^2}}$$

$$\mathcal{R}_0 = (1+\nu^2)\beta\left(\frac{\rho}{\delta} + \frac{1}{\gamma}\right)$$

where ν is the coefficient of variation of the risk distribution.

MGMG *et al* 2022 Individual variation in susceptibility or exposure to SARS-CoV-2 lowers herd immunity thresholds. *J Theor Biol* 540:111063; A Montalban, RM Corder, MGMG 2022 Herd immunity under individual variation and reinfection. *J Math Biol*, accepted.

Reduced SEIR models with gamma distributed susceptibility or exposure to infection ($\sigma = 0$)

Heterogeneous susceptibility:

$$\frac{d\mathrm{S}}{dt} = -\beta(\rho\mathrm{E} + \mathrm{I})\left(\frac{\mathrm{S}}{\mathrm{N}}\right)^{1+\nu^2}$$

$$\frac{d\mathrm{E}}{dt} = \beta(\rho\mathrm{E} + \mathrm{I})\left(\frac{\mathrm{S}}{\mathrm{N}}\right)^{1+\nu^2} - \delta\mathrm{E}$$

$$\frac{d\mathrm{I}}{dt} = \delta\mathrm{E} - \gamma\mathrm{I}$$

$$\frac{d\mathrm{R}}{dt} = (1-\phi)\gamma\mathrm{I}$$

$$\mathcal{R}_0 = \beta\left(\frac{\rho}{\delta} + \frac{1}{\gamma}\right)$$

Heterogeneous connectivity:

$$\frac{d\mathrm{S}}{dt} = -(1+\nu^2)\beta(\rho\mathrm{E} + \mathrm{I})\left(\frac{\mathrm{S}}{\mathrm{N}}\right)^{1+2\nu^2}$$

$$\frac{d\mathrm{E}}{dt} = (1+\nu^2)\beta(\rho\mathrm{E} + \mathrm{I})\left(\frac{\mathrm{S}}{\mathrm{N}}\right)^{1+2\nu^2} - \delta\mathrm{E}$$

$$\frac{d\mathrm{I}}{dt} = \delta\mathrm{E} - \gamma\mathrm{I}$$

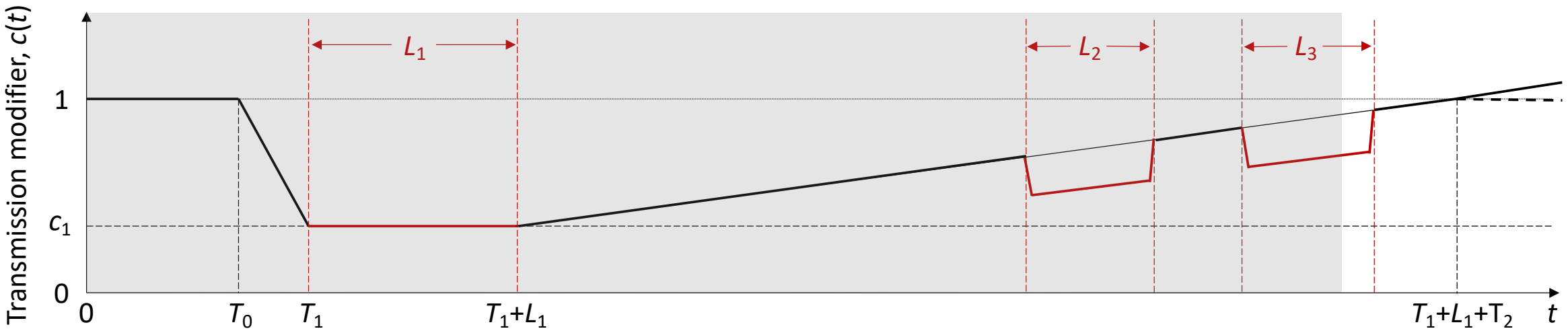
$$\frac{d\mathrm{R}}{dt} = (1-\phi)\gamma\mathrm{I}$$

$$\mathcal{R}_0 = (1+\nu^2)\beta\left(\frac{\rho}{\delta} + \frac{1}{\gamma}\right)$$

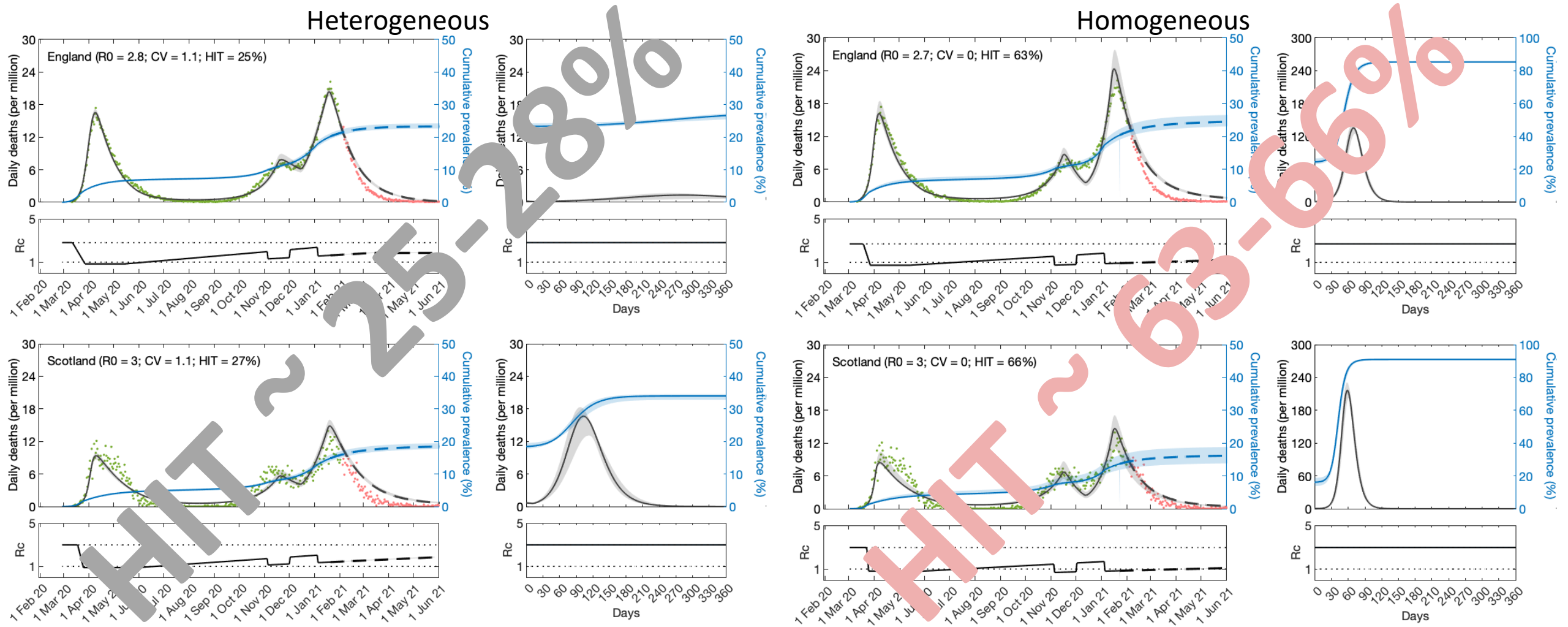
where $\mathrm{S} = \int_0^\infty S(x)\,dx$, $\mathrm{E} = \int_0^\infty E(x)\,dx$, $\mathrm{I} = \int_0^\infty I(x)\,dx$ and $\mathrm{R} = \int_0^\infty R(x)\,dx$.

A Montalban, RM Corder, MGMG 2022 Herd immunity under individual variation and reinfection. *J Math Biol*, accepted.

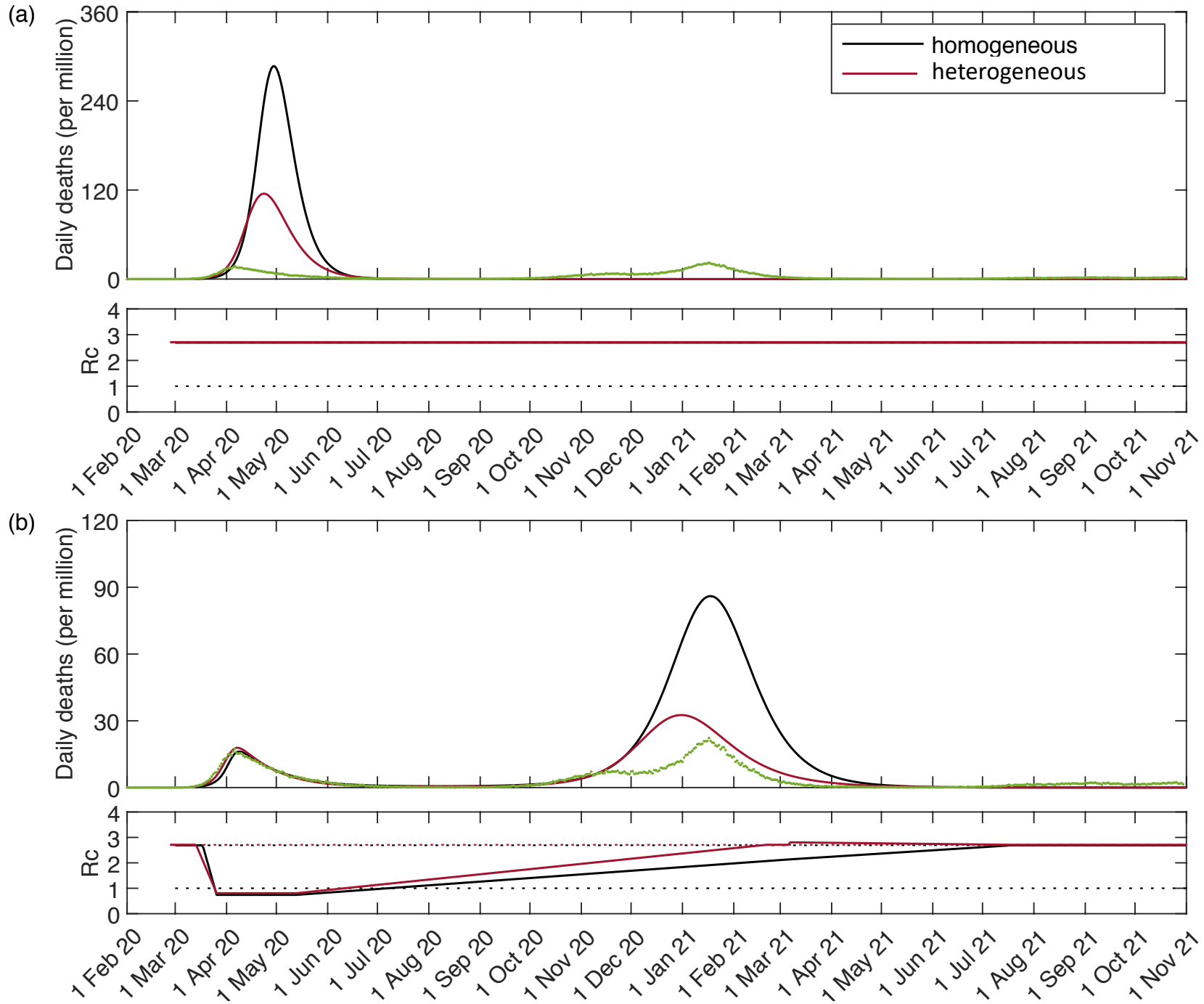
Two-wave fits

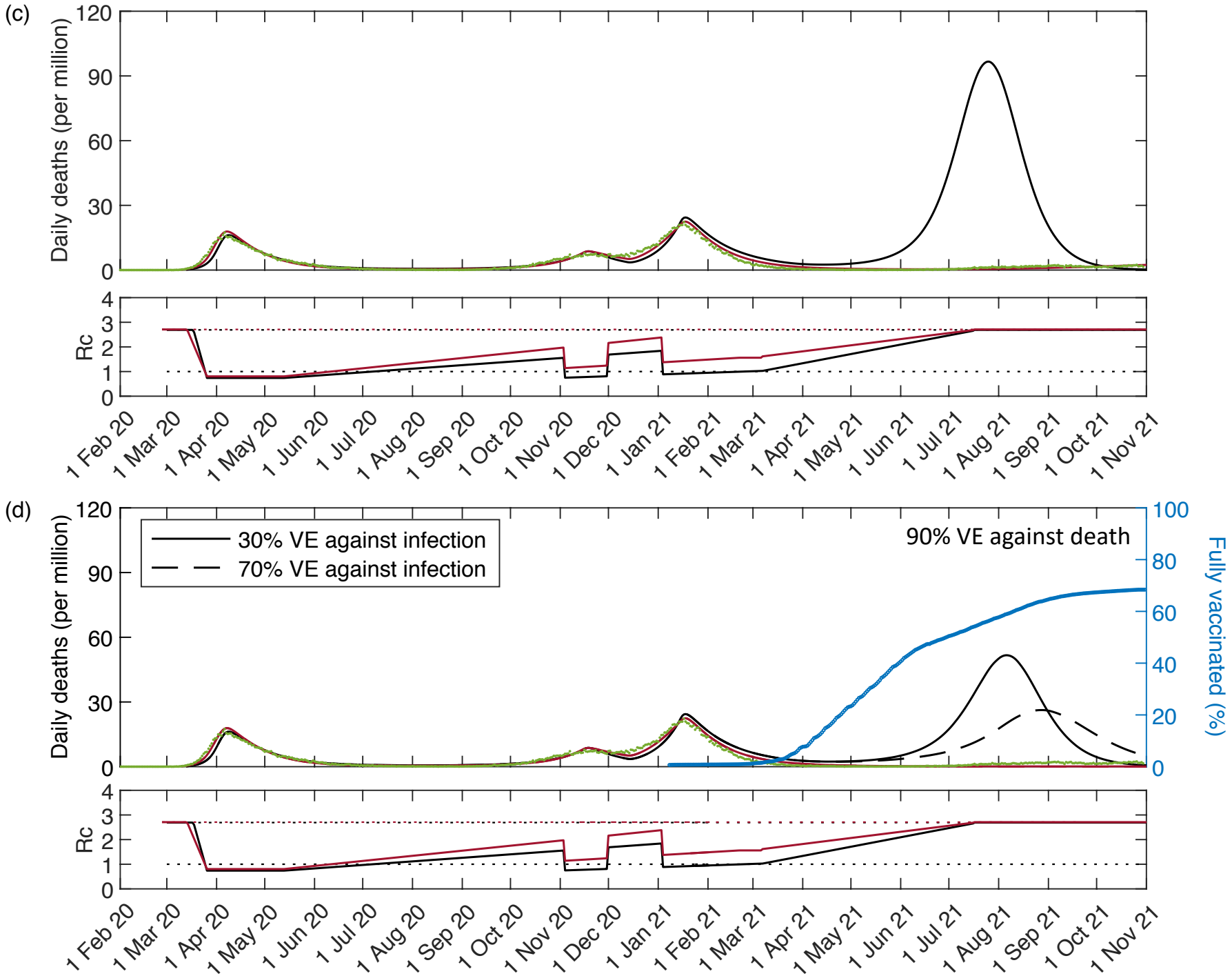


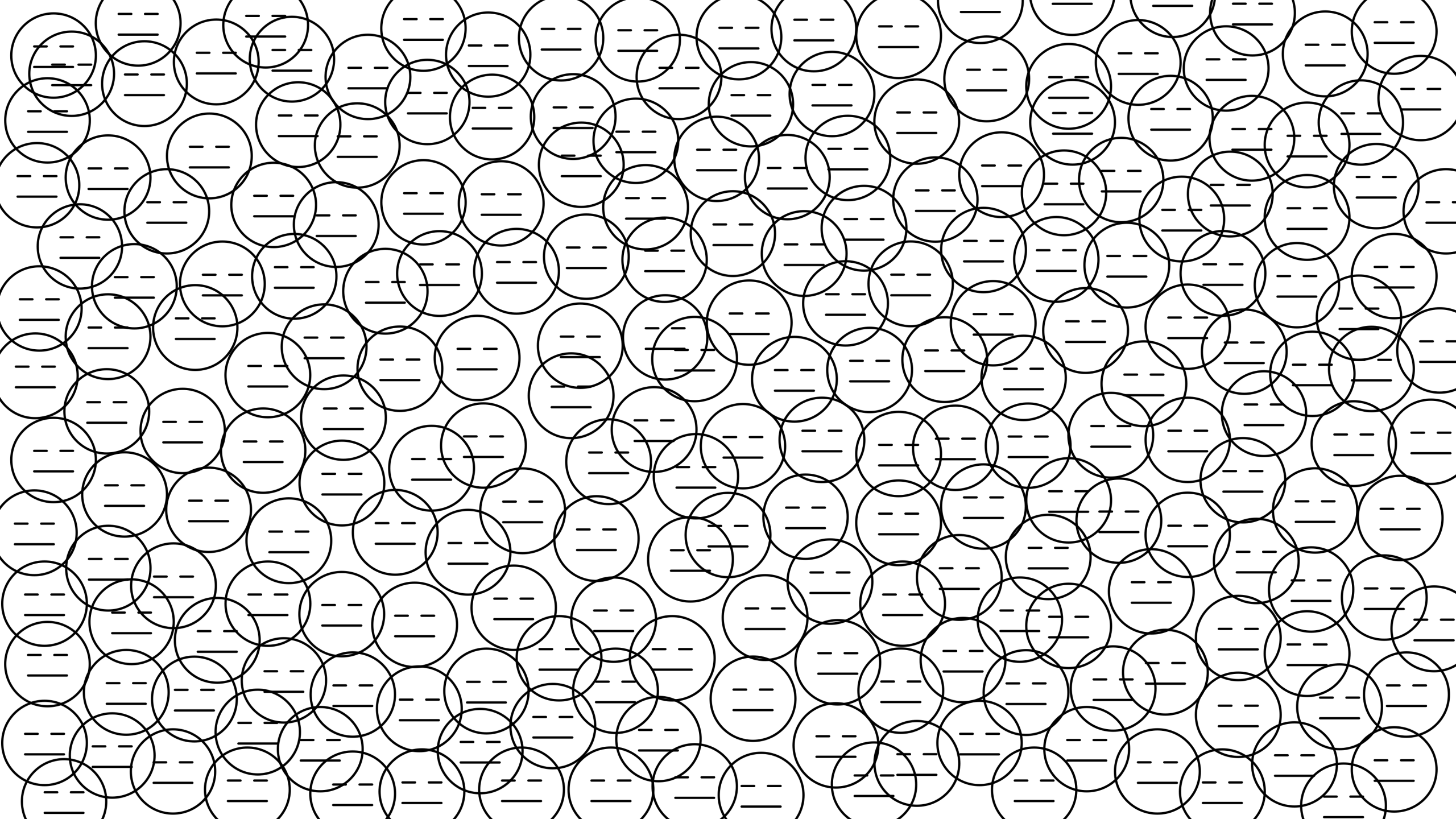
False homogeneity exaggerates herd immunity thresholds

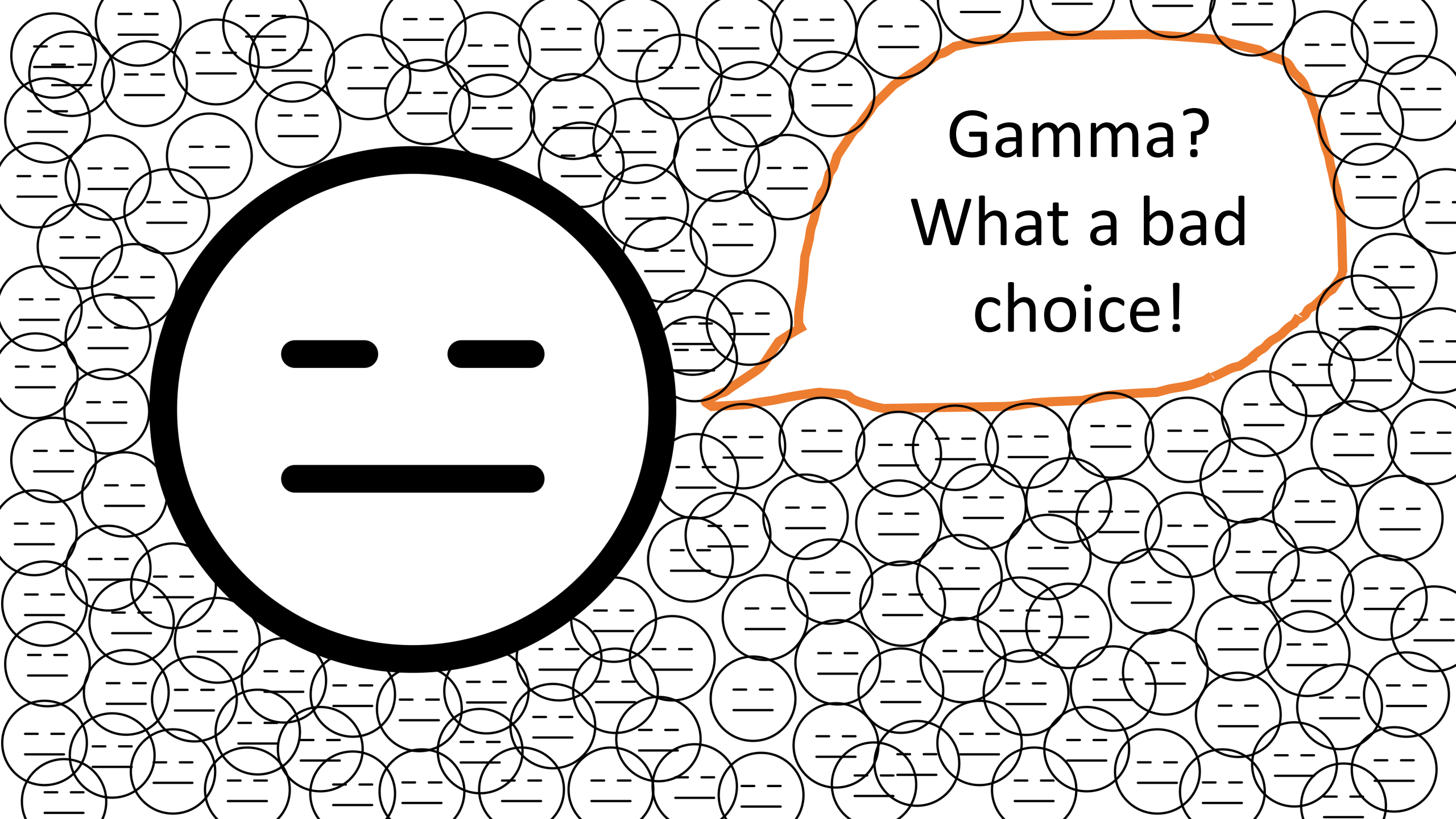


MGMG *et al* 2022 Individual variation in susceptibility or exposure to SARS-CoV-2 lowers herd immunity thresholds. *J Theor Biol* 540:111063.

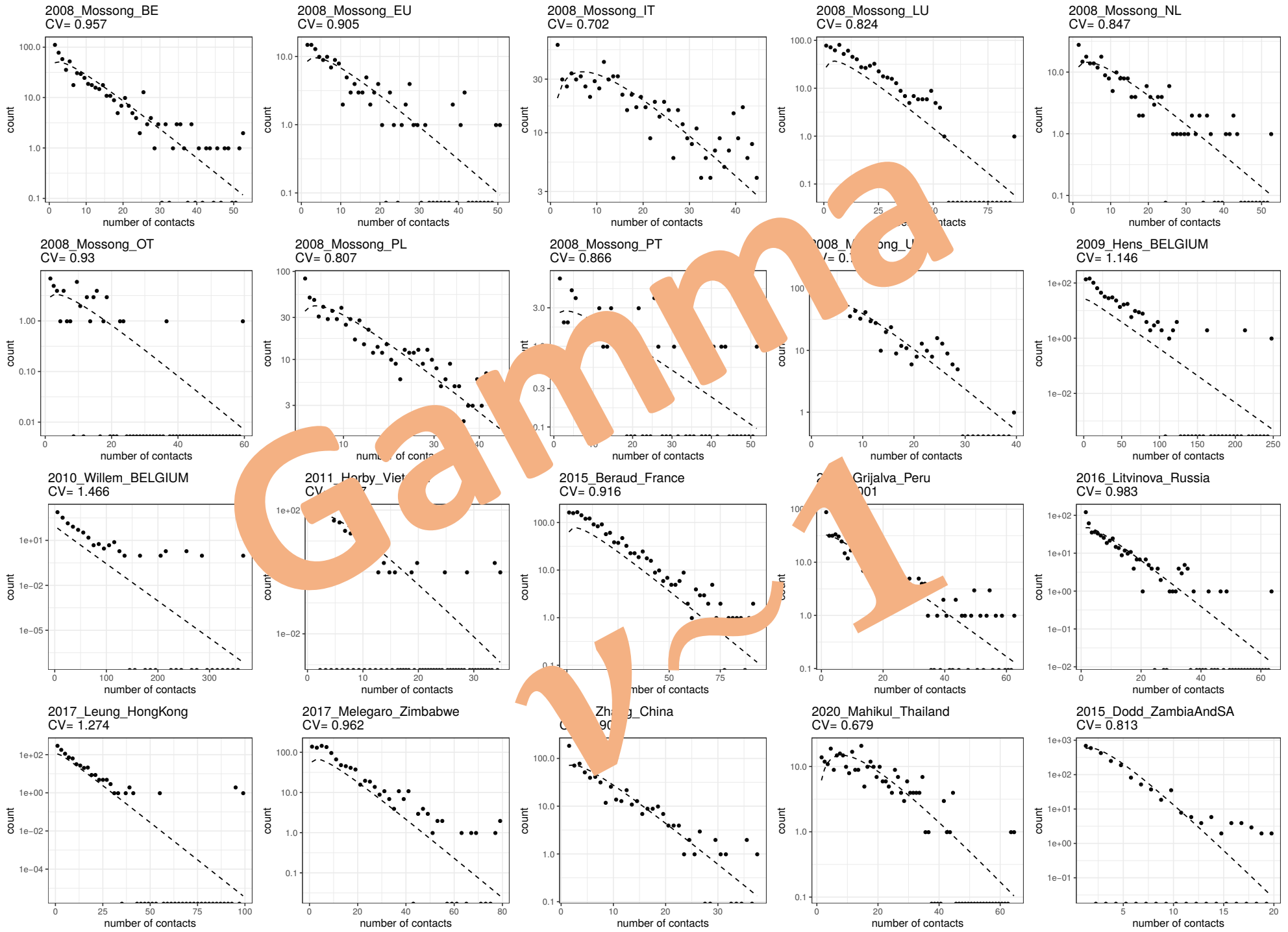

(a)
Daily deaths (per million)
360
240
120
0
homogeneous
heterogeneous
Rc
4
3
2
1
0
1 Feb 20
1 Mar 20
1 Apr 20
1 May 20
1 Jun 20
1 Jul 20
1 Aug 20
1 Sep 20
1 Oct 20
1 Nov 20
1 Dec 20
1 Jan 21
1 Feb 21
1 Mar 21
1 Apr 21
1 May 21
1 Jun 21
1 Jul 21
1 Aug 21
1 Sep 21
1 Oct 21
1 Nov 21
(b)
Daily deaths (per million)
120
90
60
30
0
Rc
4
3
2
1
0
1 Feb 20
1 Mar 20
1 Apr 20
1 May 20
1 Jun 20
1 Jul 20
1 Aug 20
1 Sep 20
1 Oct 20
1 Nov 20
1 Dec 20
1 Jan 21
1 Feb 21
1 Mar 21
1 Apr 21
1 May 21
1 Jun 21
1 Jul 21
1 Aug 21
1 Sep 21
1 Oct 21
1 Nov 21

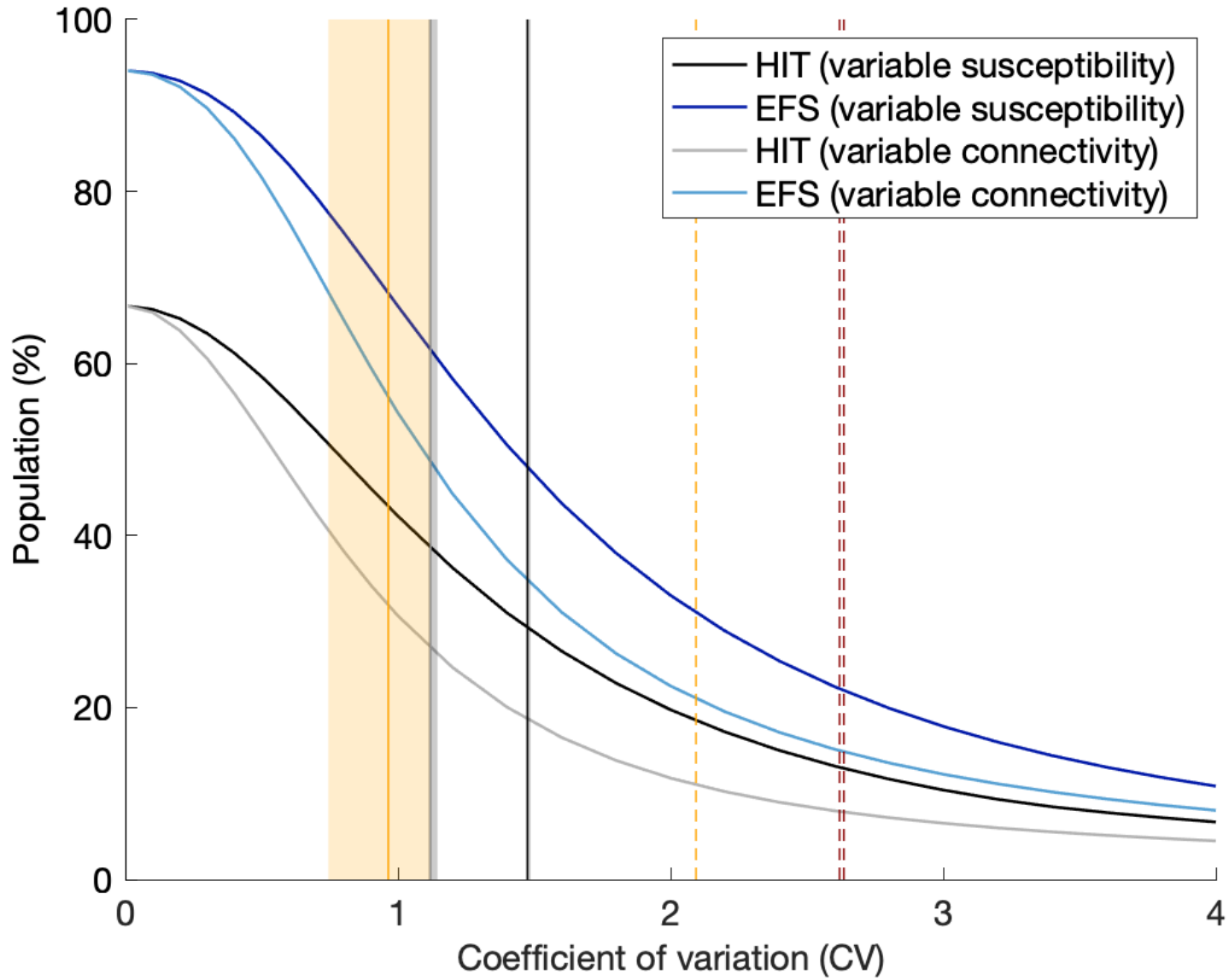

(c)
Daily deaths (per million)
120
90
60
30
0
Rc
4
3
2
1
0
1 Feb 20
1 Mar 20
1 Apr 20
1 May 20
1 Jun 20
1 Jul 20
1 Aug 20
1 Sep 20
1 Oct 20
1 Nov 20
1 Dec 20
1 Jan 21
1 Feb 21
1 Mar 21
1 Apr 21
1 May 21
1 Jun 21
1 Jul 21
1 Aug 21
1 Sep 21
1 Oct 21
1 Nov 21
(d)
30% VE against infection
70% VE against infection
90% VE against death
Fully vaccinated (%)
100
80
60
40
20
0

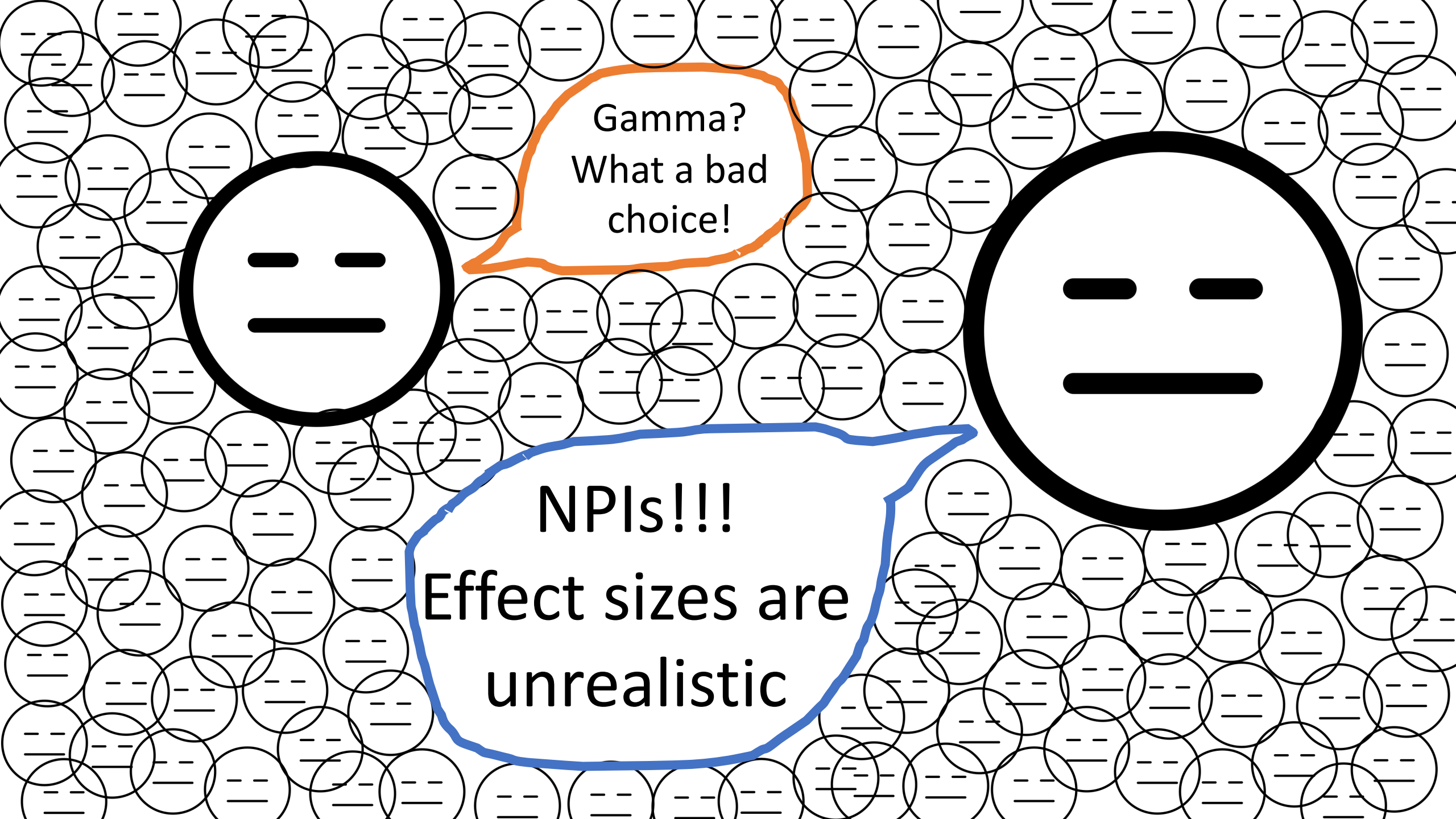



Gamma?
What a bad
choice!

POLYMOD




HIT (variable susceptibility)
EFS (variable susceptibility)
HIT (variable connectivity)
EFS (variable connectivity)
Population (%)
100
80
60
40
20
0
0
1
2
3
4
Coefficient of variation (CV)

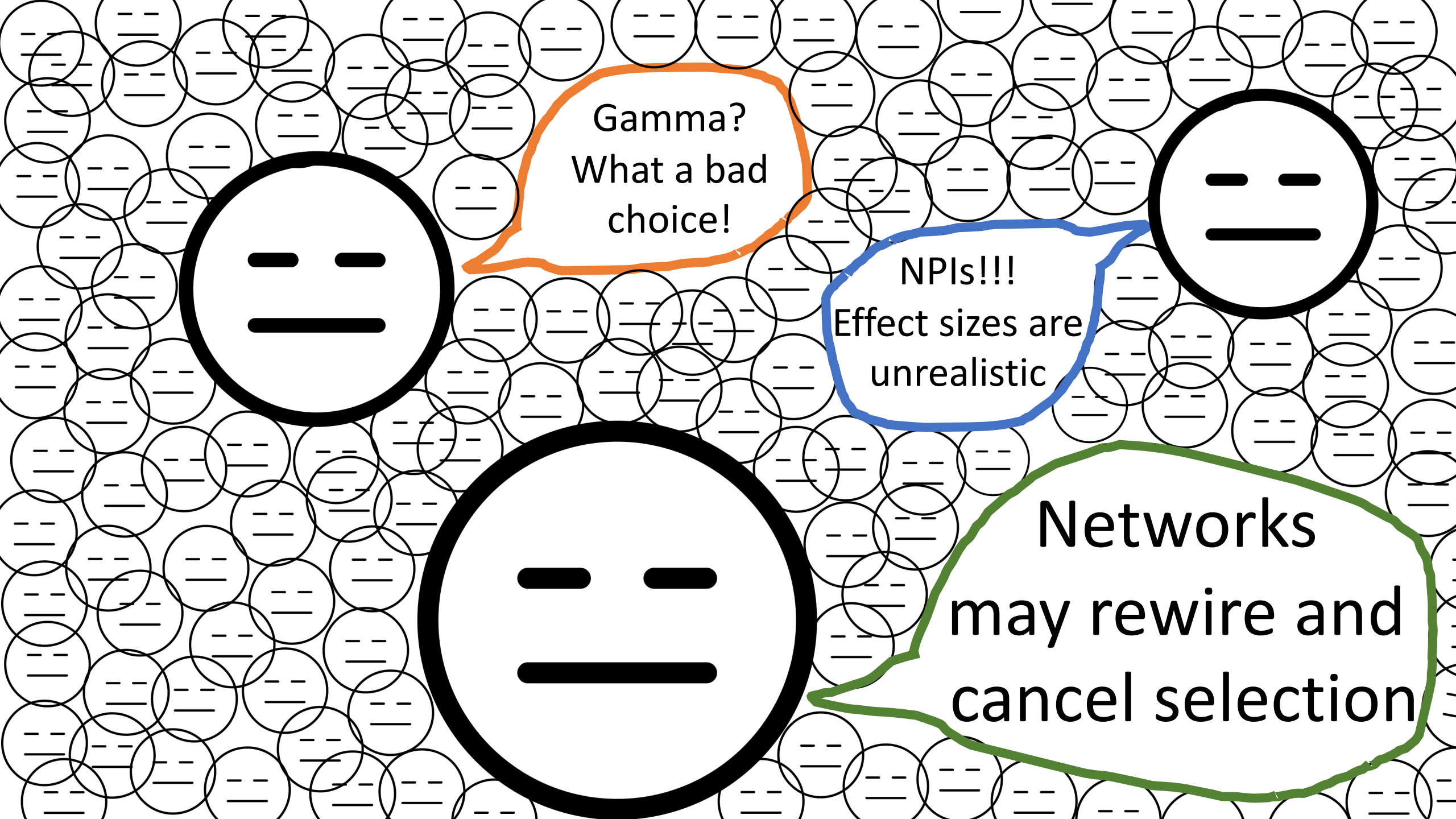

Gamma?
What a bad
choice!
NPIs!!!
Effect sizes are
unrealistic

CoMix survey

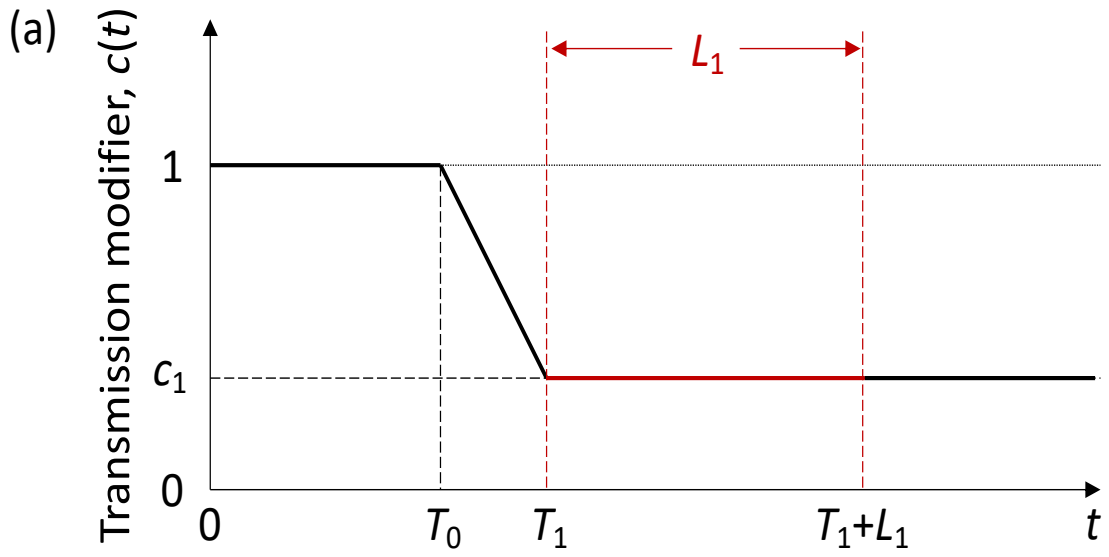
CoMix found a **74%** reduction in the average daily number of contacts observed per participant.

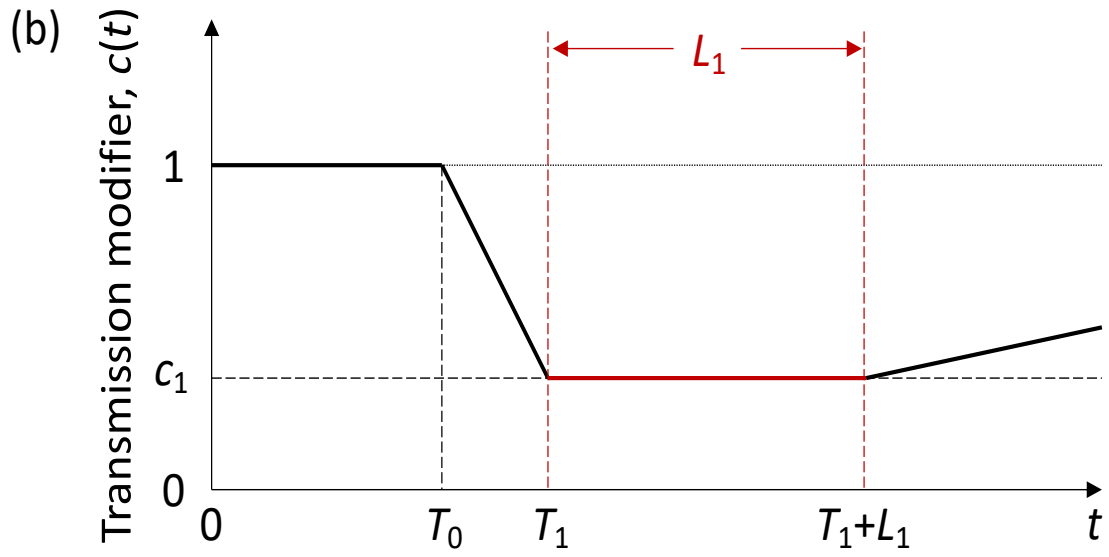
We estimate **70-77%**.

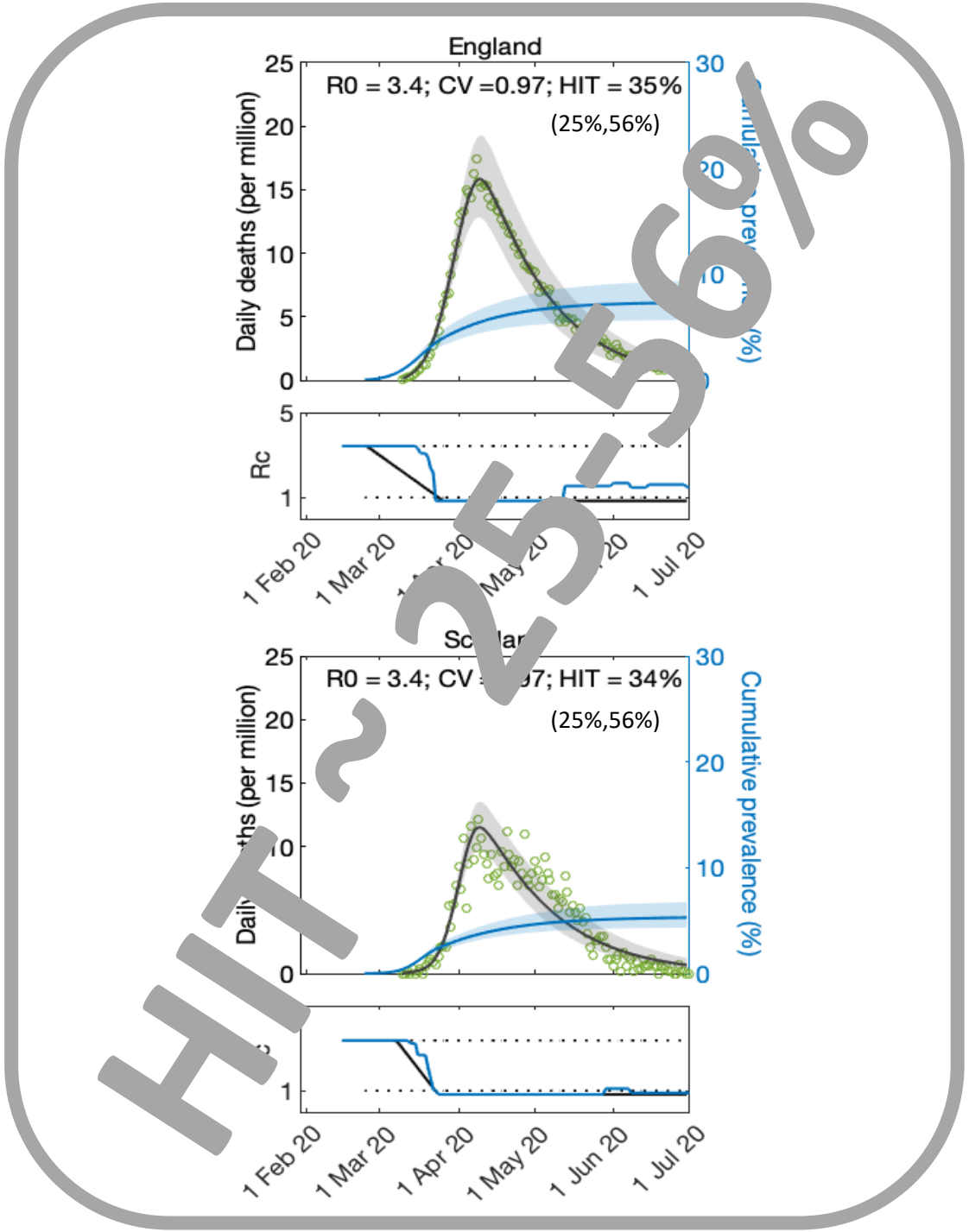
CL Jarvis *et al* 2020 Quantifying the impact of physical distance measures on the transmission of COVID-19 in the UK *BMC Med* 18:124.

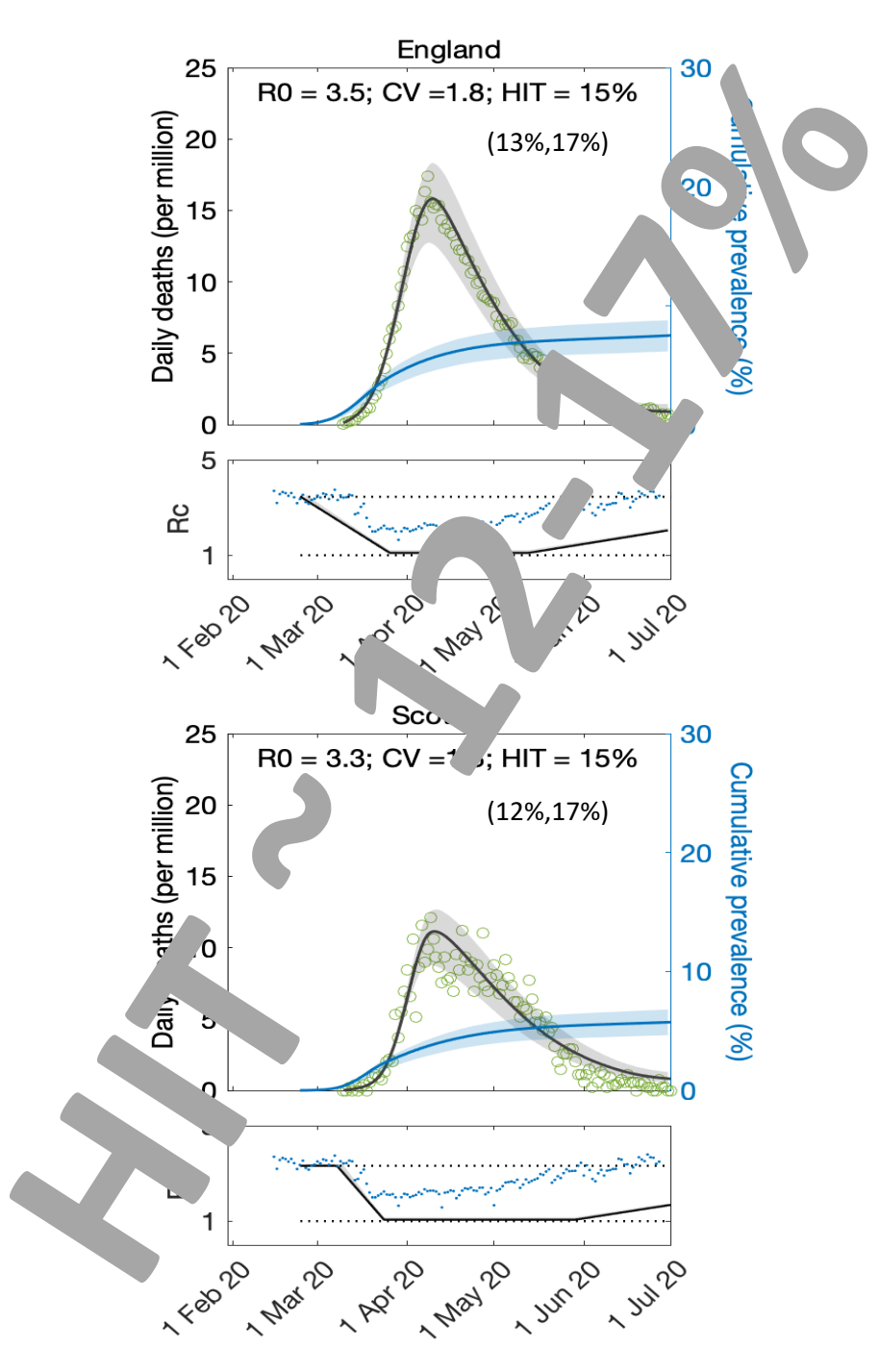

Gamma?
What a bad
choice!
NPIs!!!
Effect sizes are
unrealistic
Networks
may rewire and
cancel selection

One-wave fits





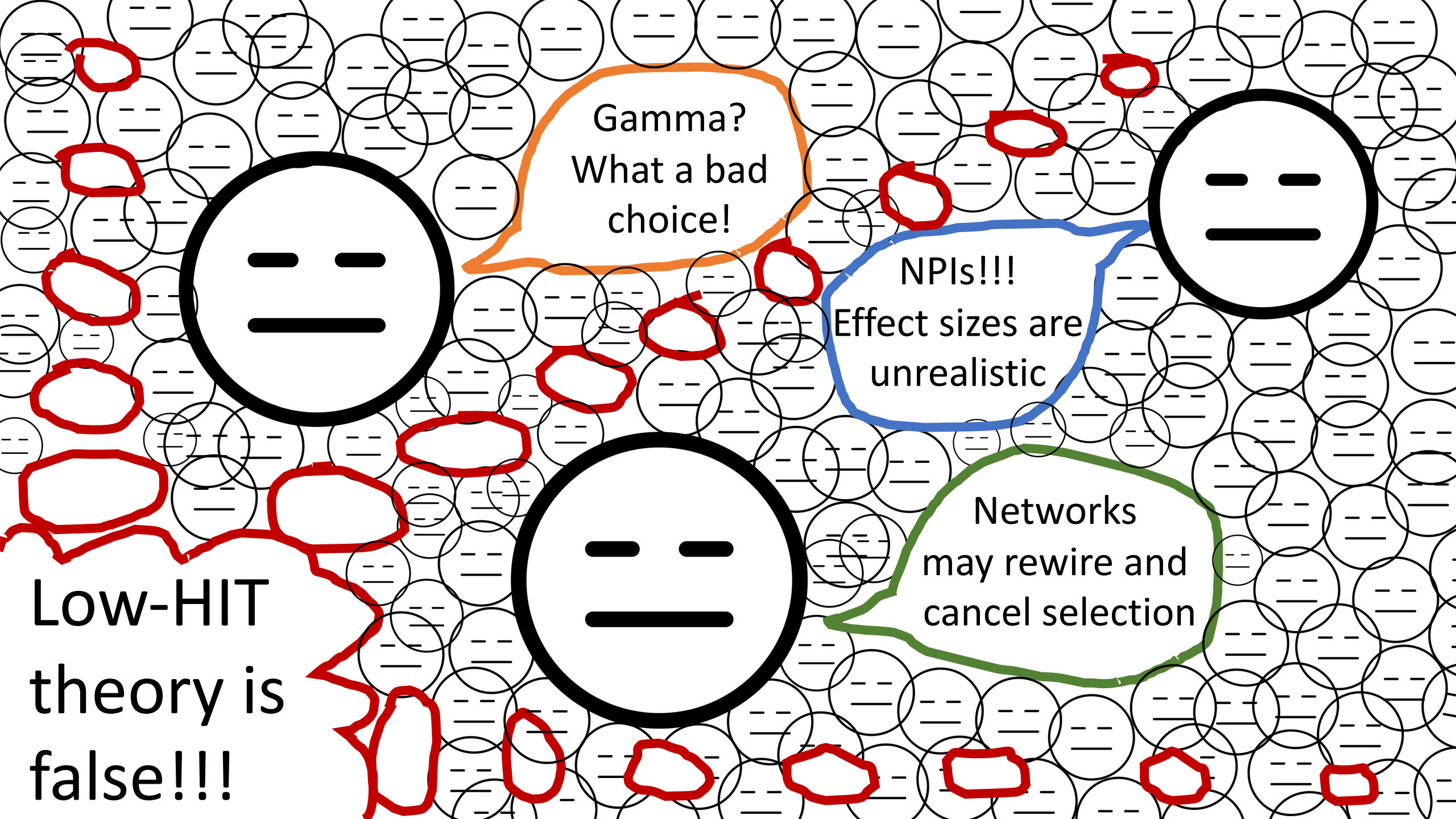

England
R0 = 3.4; CV =0.97; HIT = 35%
(25%,56%)
Daily deaths (per million)
Cumulative prevalence (%)
Rc
1 Feb 20
1 Mar 20
1 Apr 20
1 May 20
1 Jun 20
1 Jul 20
R0 = 3.4; CV = 97; HIT = 34%
(25%,56%)
HIT ~ 25-56%


England
R0 = 3.5; CV =1.8; HIT = 15%
(13%,17%)
Daily deaths (per million)
Cumulative prevalence (%)
Rc
1 Feb 20
1 Mar 20
1 Apr 20
1 May 20
1 Jun 20
1 Jul 20
R0 = 3.3; CV =1.5; HIT = 15%
(12%,17%)
HIT ~ 12-17%

If rewiring cancelled selection, then…

we should get higher HIT estimates by fitting two waves than by fitting one wave only.

Not what we see in England and Scotland!


Gamma?
What a bad
choice!
NPIs!!!
Effect sizes are
unrealistic
Networks
may rewire and
cancel selection
Low-HIT
theory is
false!!!

For the next pandemic let us:

1) remove selection biases from predictive models

and

2) be professional

Low-HIT theory lives!