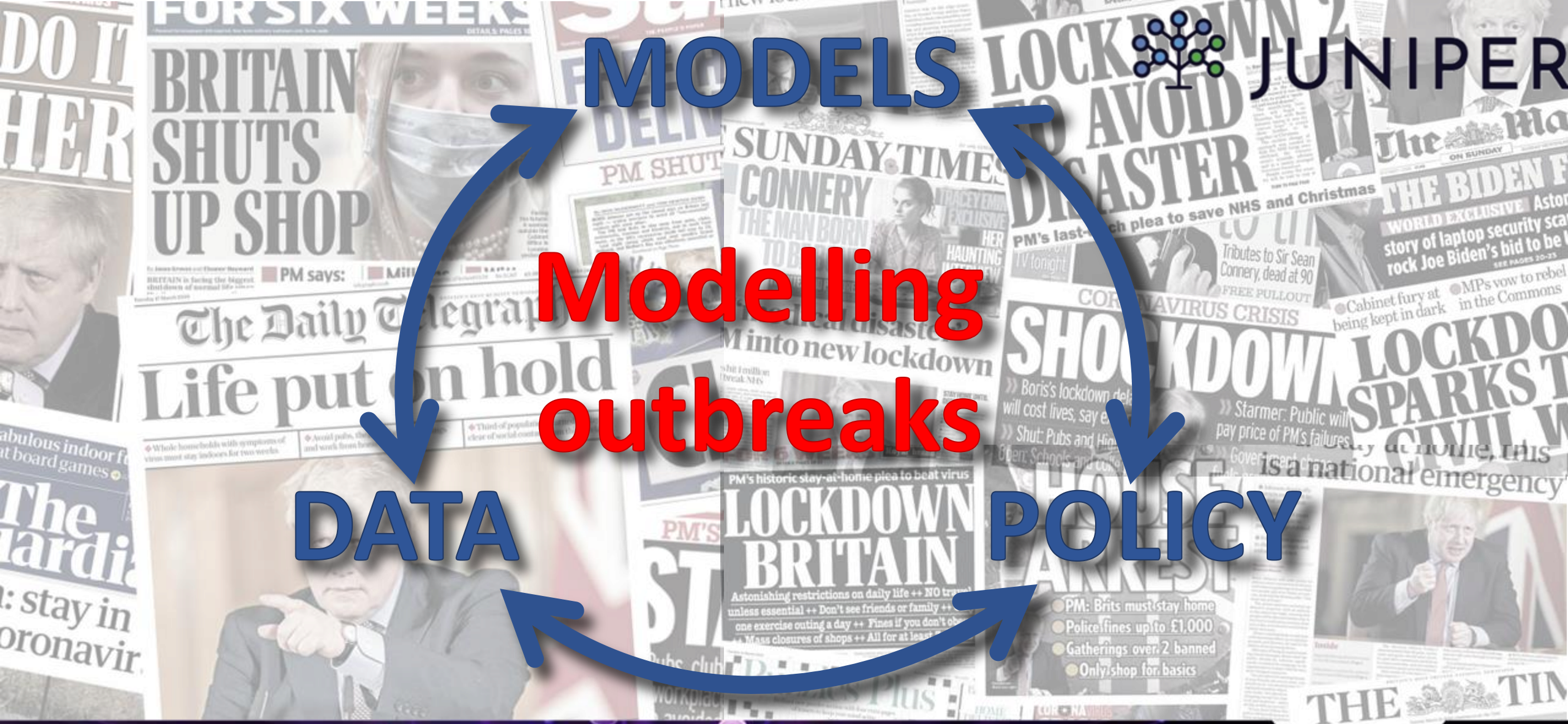
Modelling outbreaks



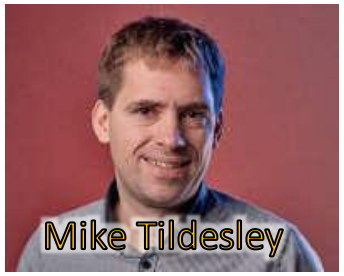
Matt Keeling

www.warwick.ac.uk/SBIDER

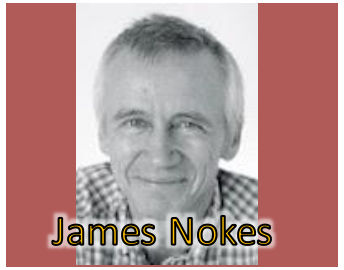
JUNIPER

WARWICK
THE UNIVERSITY OF WARWICK

The Team at Warwick



The Team at Kilifi, Kenya



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SPI-M-O

Funders

MRC Medical Research Council

UKRI UK Research and Innovation

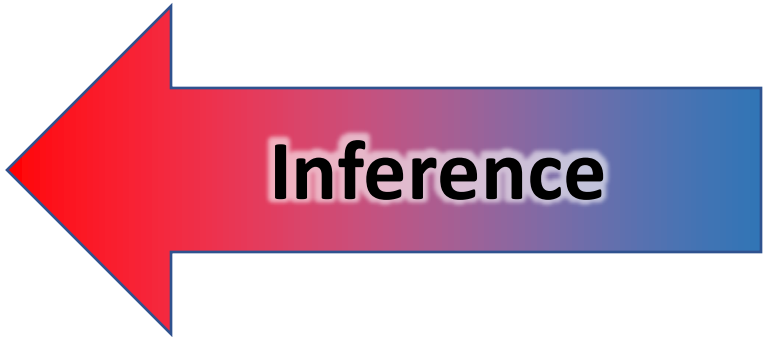
Starting point is (almost) always an SEIR-type framework.

This has proved hugely successful in the past, from Kermack & McKendrick's work in the 1920's to Anderson and May in the 1990's.

We may need to think about if the model needs to be deterministic or stochastic (will often depend on the size of the outbreak and quality of the data).

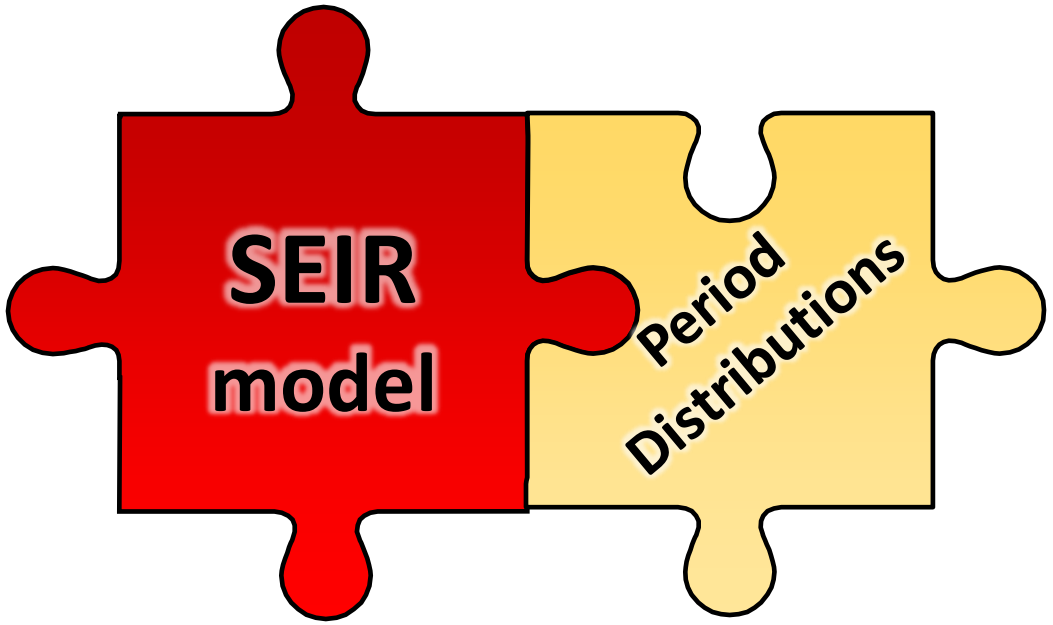
Starting point is (almost) always an SEIR-type framework.

To this we have to include high-quality statistical inference of parameters, and propagate any uncertainty through the modelling framework. Data always has to lead.



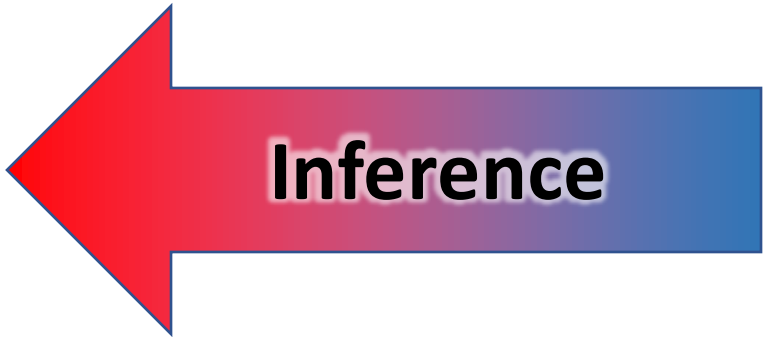
Starting point is (almost) always an SEIR-type framework.

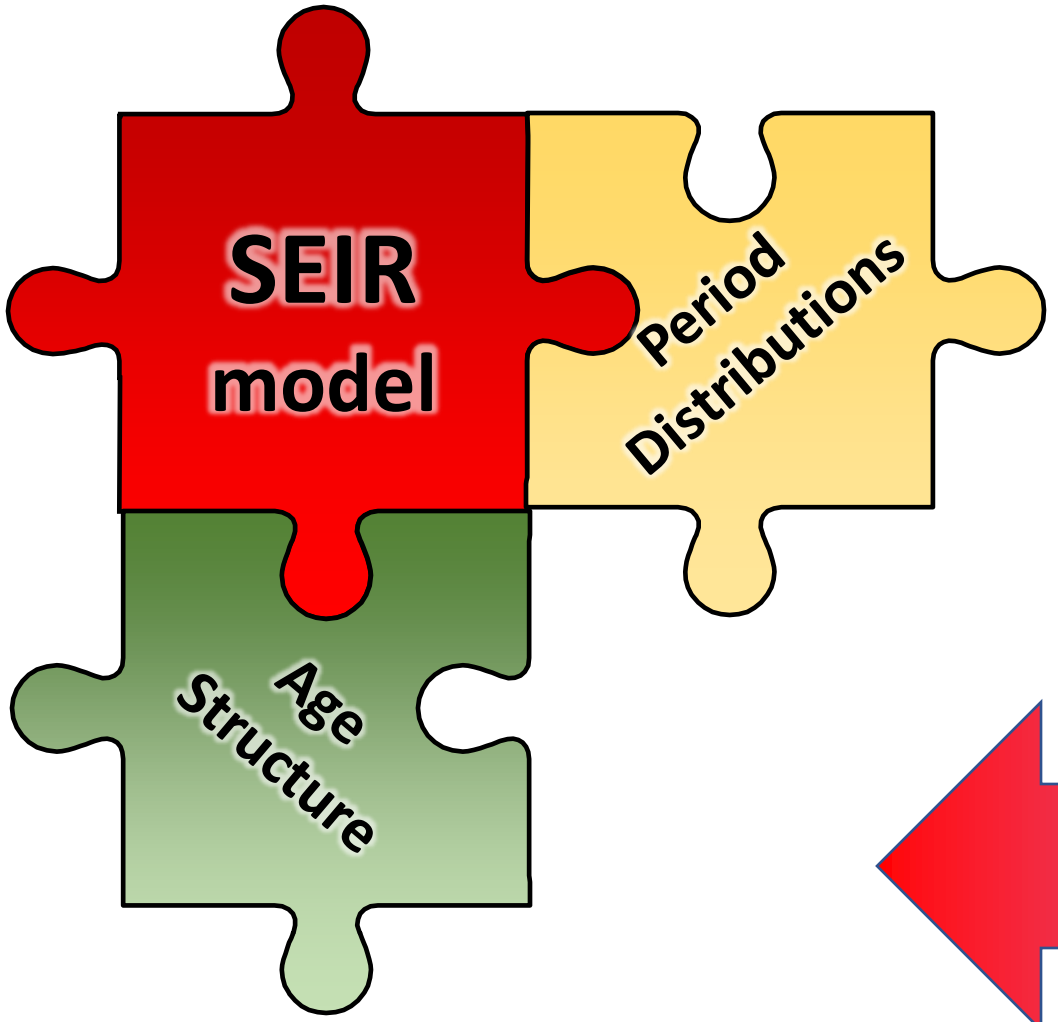
The next step is usually a characterization of the latent and infectious periods.



It is not simply enough to have reasonable estimates of the mean, but the distribution of times in each class can be equally important – we usually want to break the exponential distribution assumption.

Obtaining good estimates of these is key in translating growth rates to *R*-values.





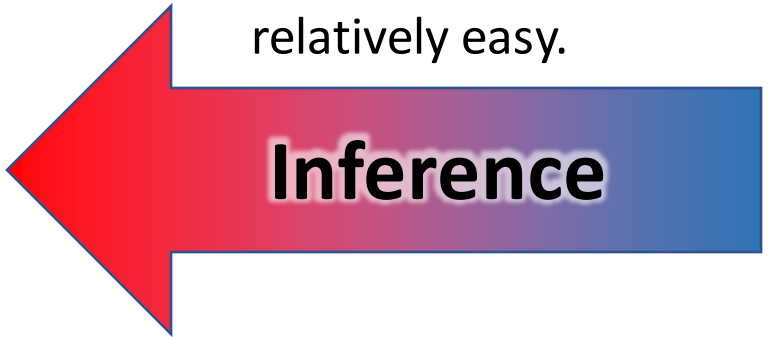
Starting point is (almost) always an SEIR-type framework.

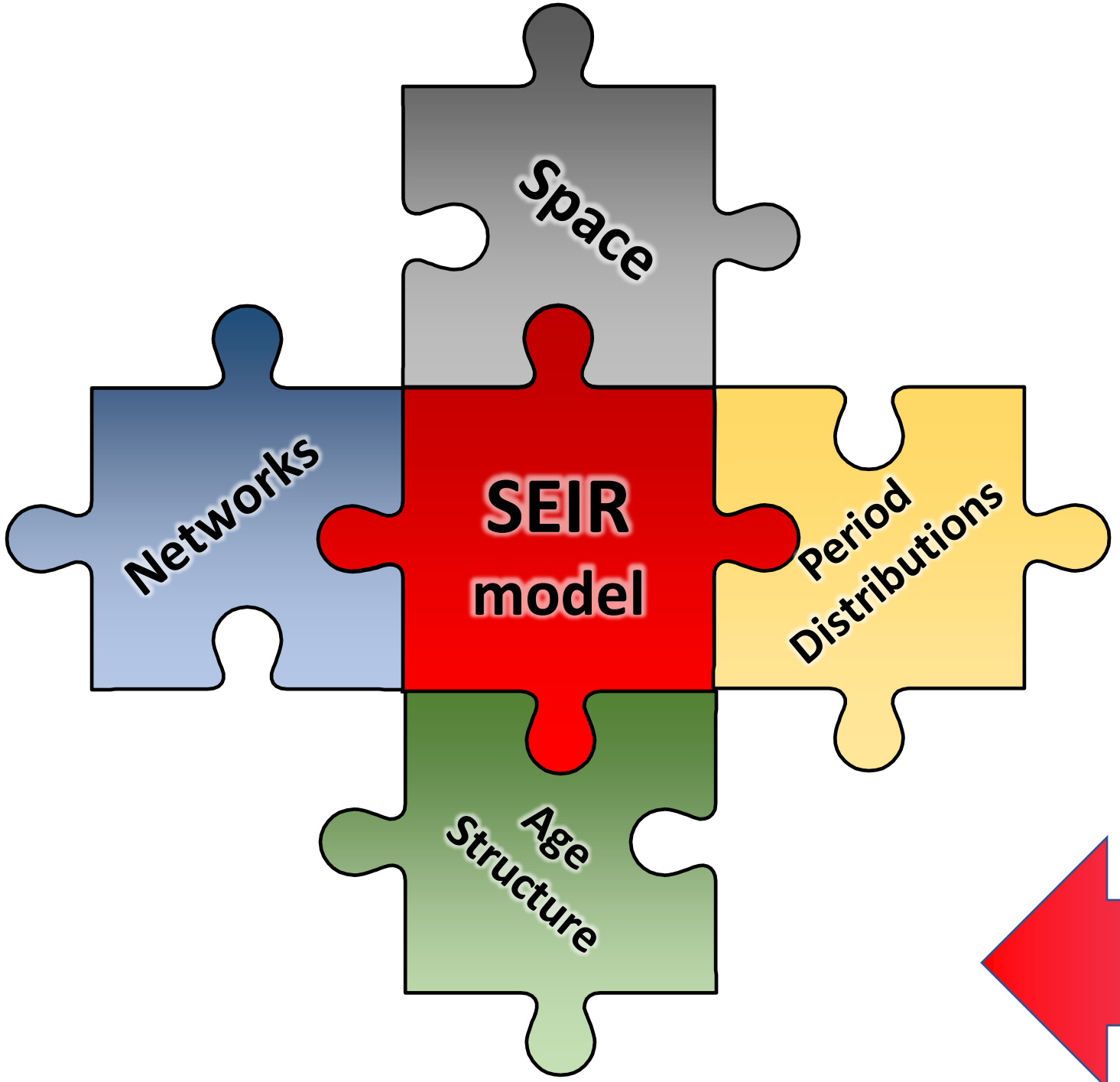
The next step is usually a characterization of the latent and infectious periods.

For most infections Age-structure is key and easily measured.

Patterns of social mixing, susceptibility to infection, hygiene practices, and severity of illness are frequently dependent on age.

Mixing matrices (such as POLYMOD) make the modelling of age-structure relatively easy.



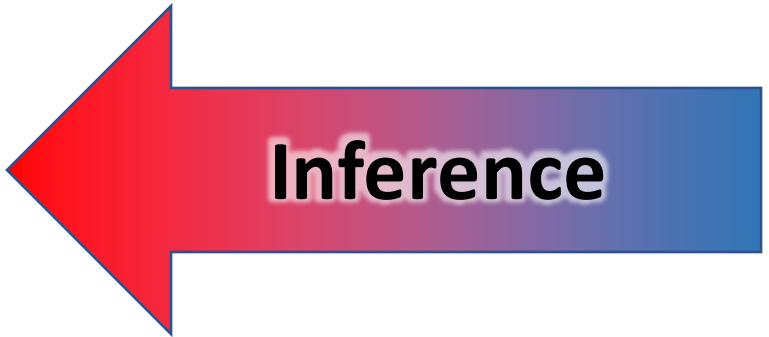


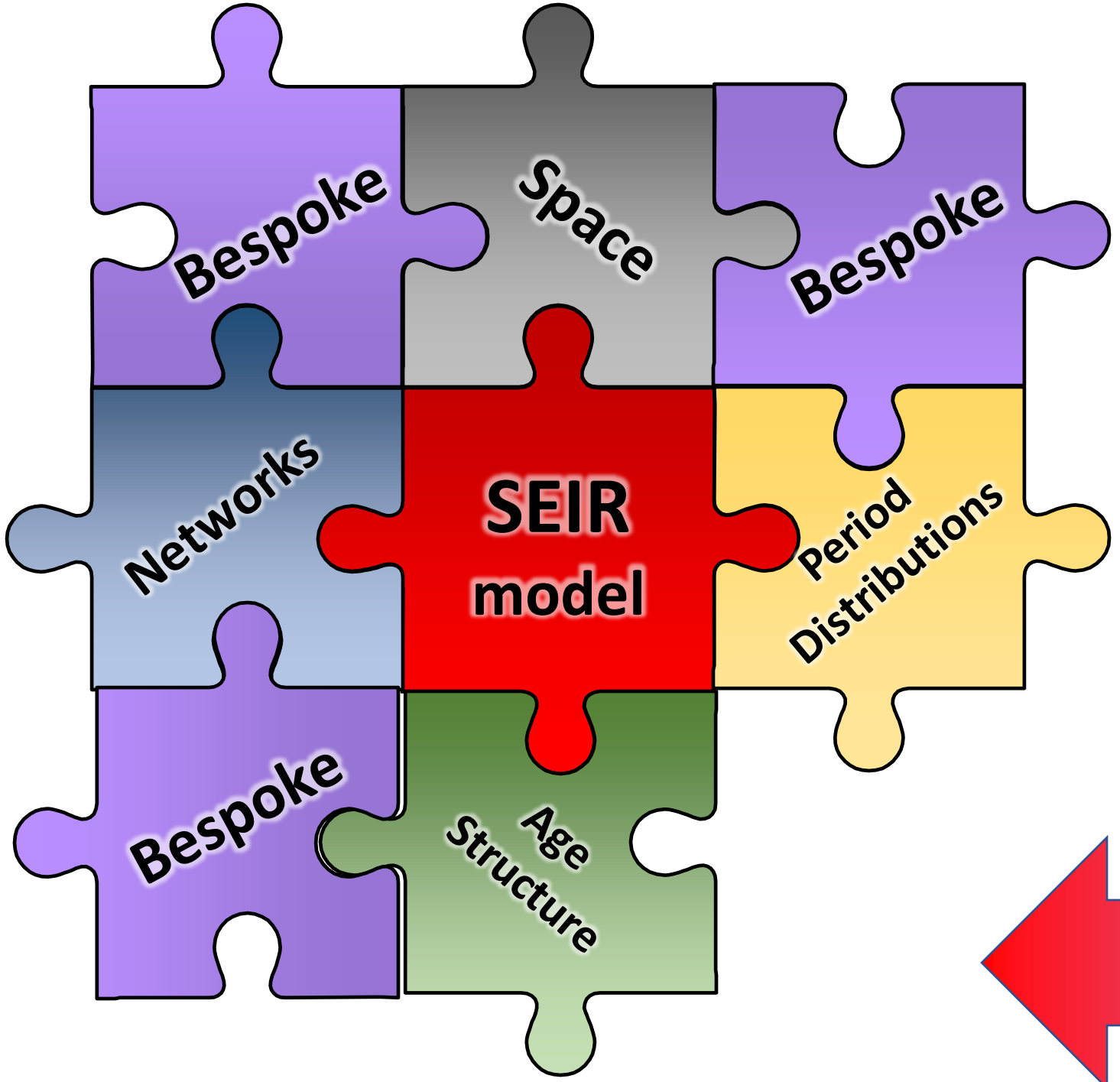
Starting point is (almost) always an SEIR-type framework.

The next step is usually a characterization of the latent and infectious periods.

For most infections Age-structure is key and easily measured.

Greater transmission structure in terms of space (regions or geographic locations) or network structure (sexual contacts or households).





Starting point is (almost) always an SEIR-type framework.

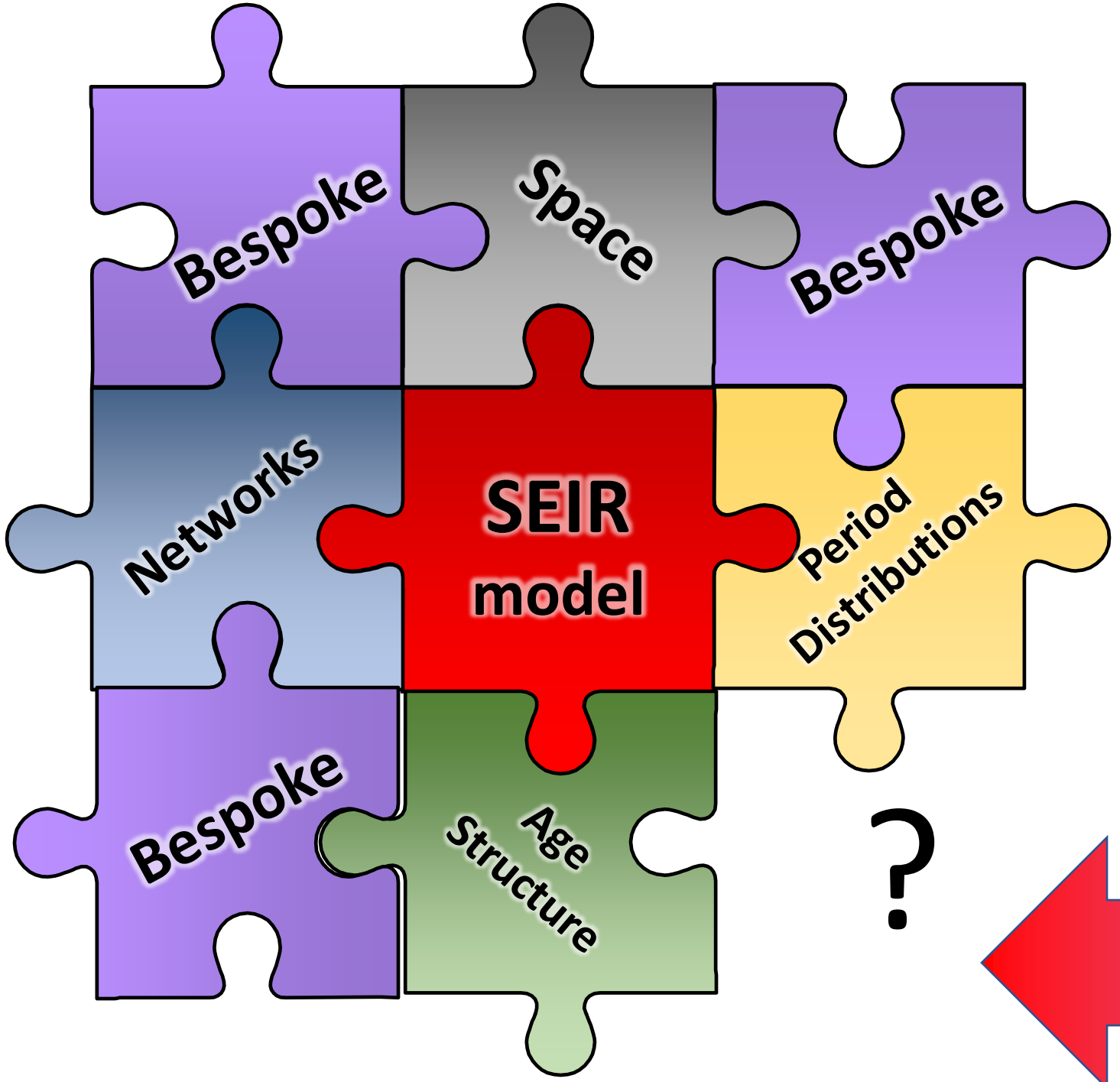
The next step is usually a characterization of the latent and infectious periods.

For most infections Age-structure is key and easily measured.

Greater transmission structure in terms of space or networks.

Bespoke infection specific elements (strain structure, deprivation, ethnicity, travel history).

Inference

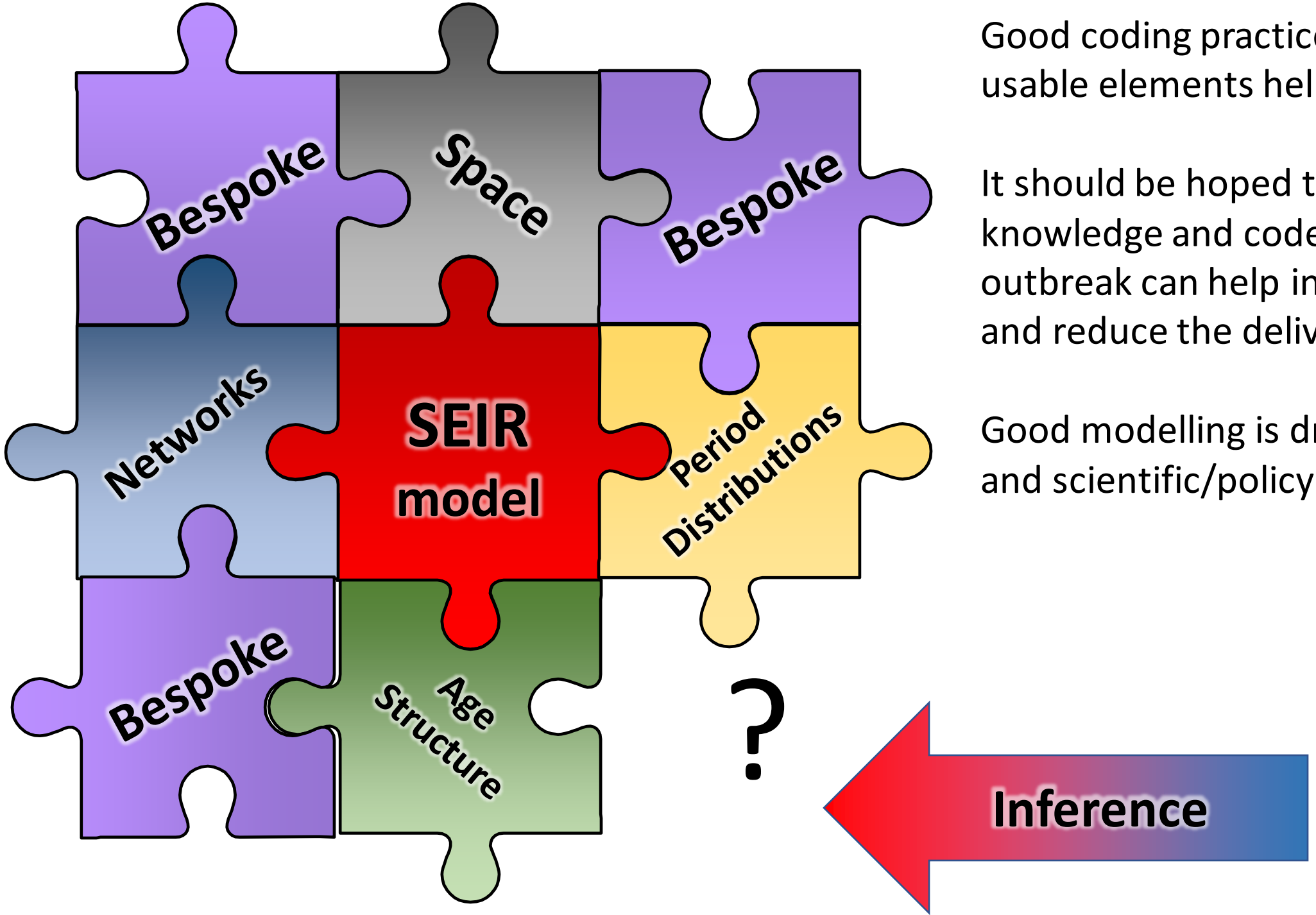


However, there will still be elements missing – models are caricatures of reality.

We have to trust that any missing elements are relatively minor compared to all the other factors that have been included.

And throughout this entire process we need to remain true to the data, with good inference across all model changes.

Inference



Good coding practice and re-usable elements helps.

It should be hoped that knowledge and code from one outbreak can help inform others and reduce the delivery time.

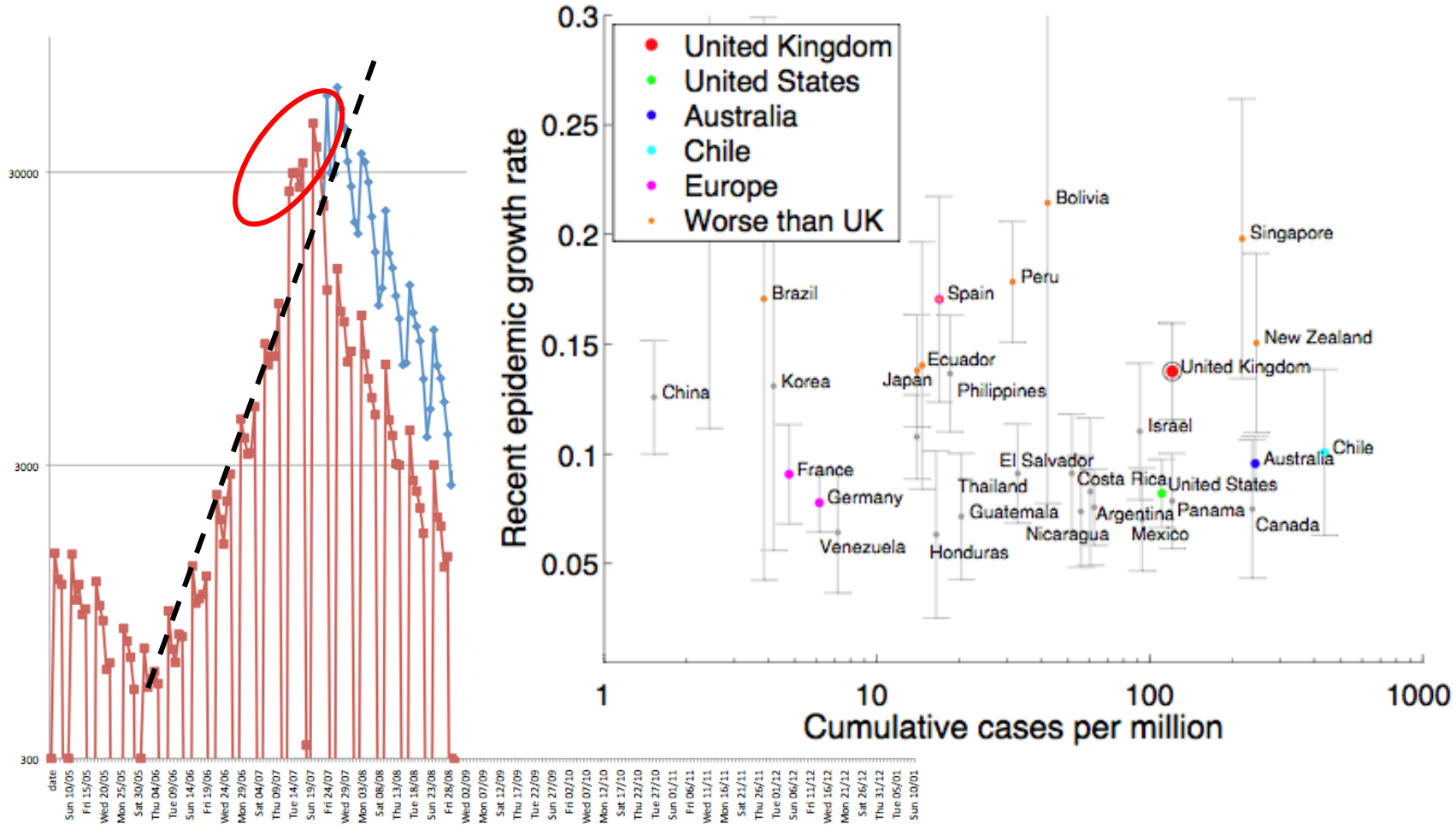
Good modelling is driven by data and scientific/policy questions.

"No battle plan ever survives contact with the enemy."

Helmuth von Moltke the Elder
Prussian general
born October 26, 1800

The same is undoubtedly true for modelling any pandemic.

Simple Statistics are powerful…. In particular growth rates from "log-linear" plots.



H1N1 pandemic (2009)

The early growth of H1N1 was well-captured by exponential growth (followed by exponential decay).

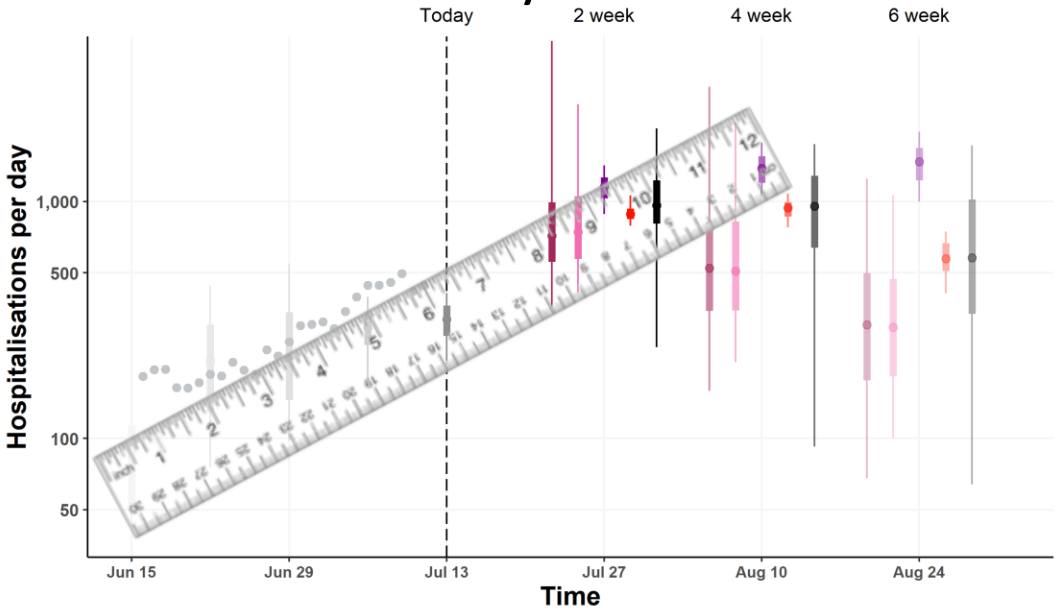
Different growth rates in different populations tell an important story.

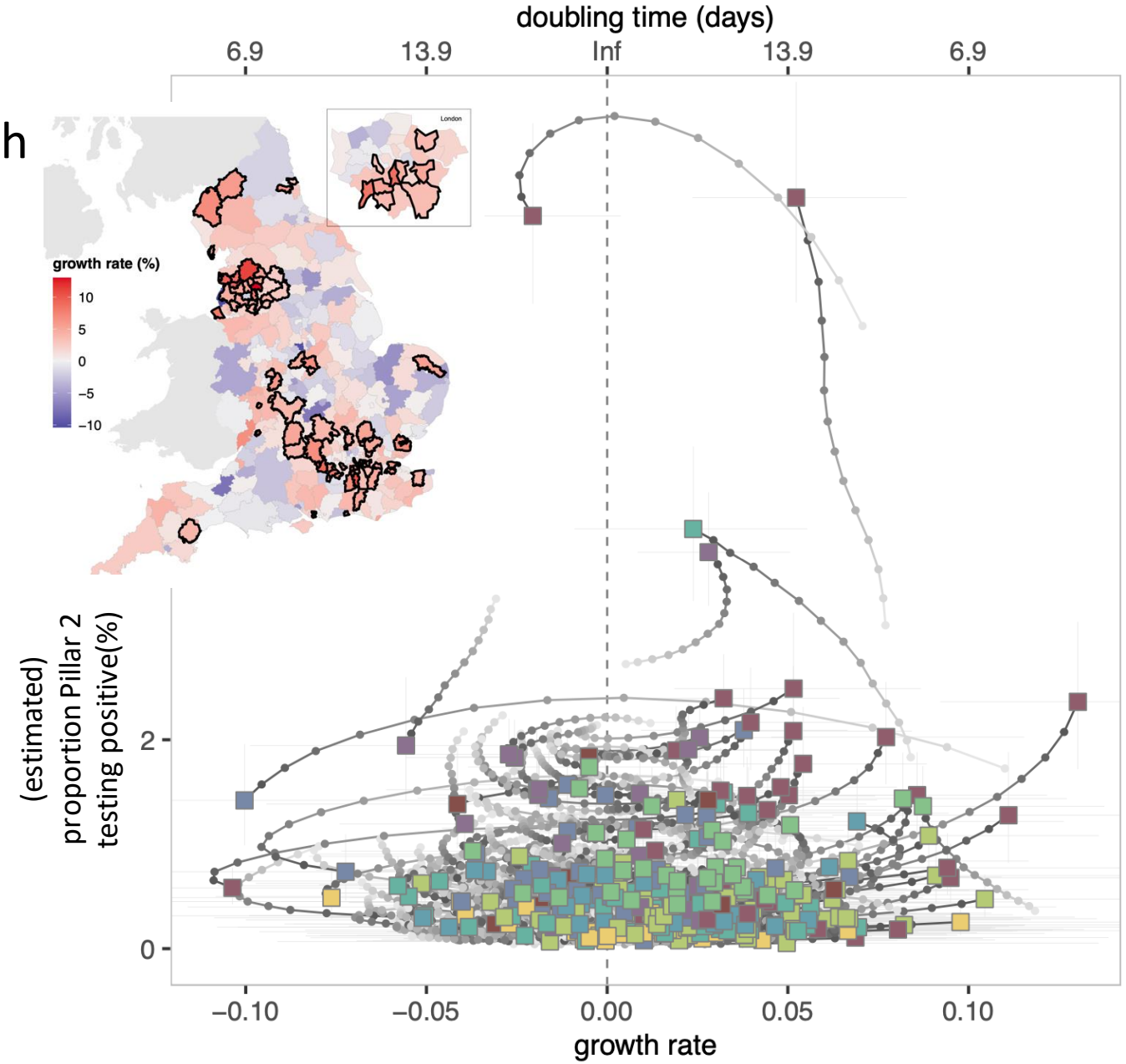
Simple Statistics are powerful…. In particular growth rates from “log-linear” plots.

COVID-19 (2020-22)

Early work fitting recent exponential growth has since been replaced by using Gaussian Processes

However, even when using complex projection models – we still apply a ‘ruler-test’ to check the dynamics.

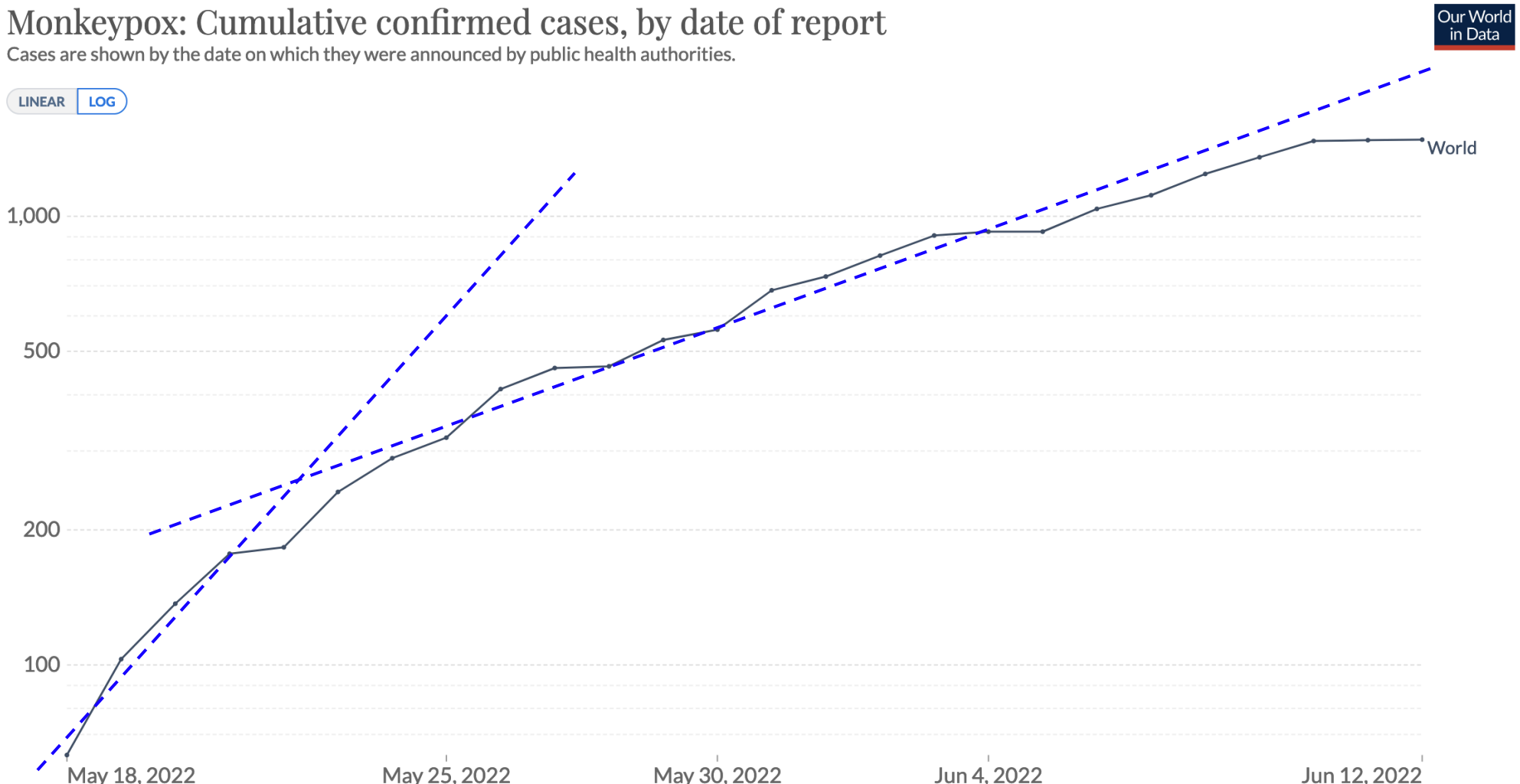




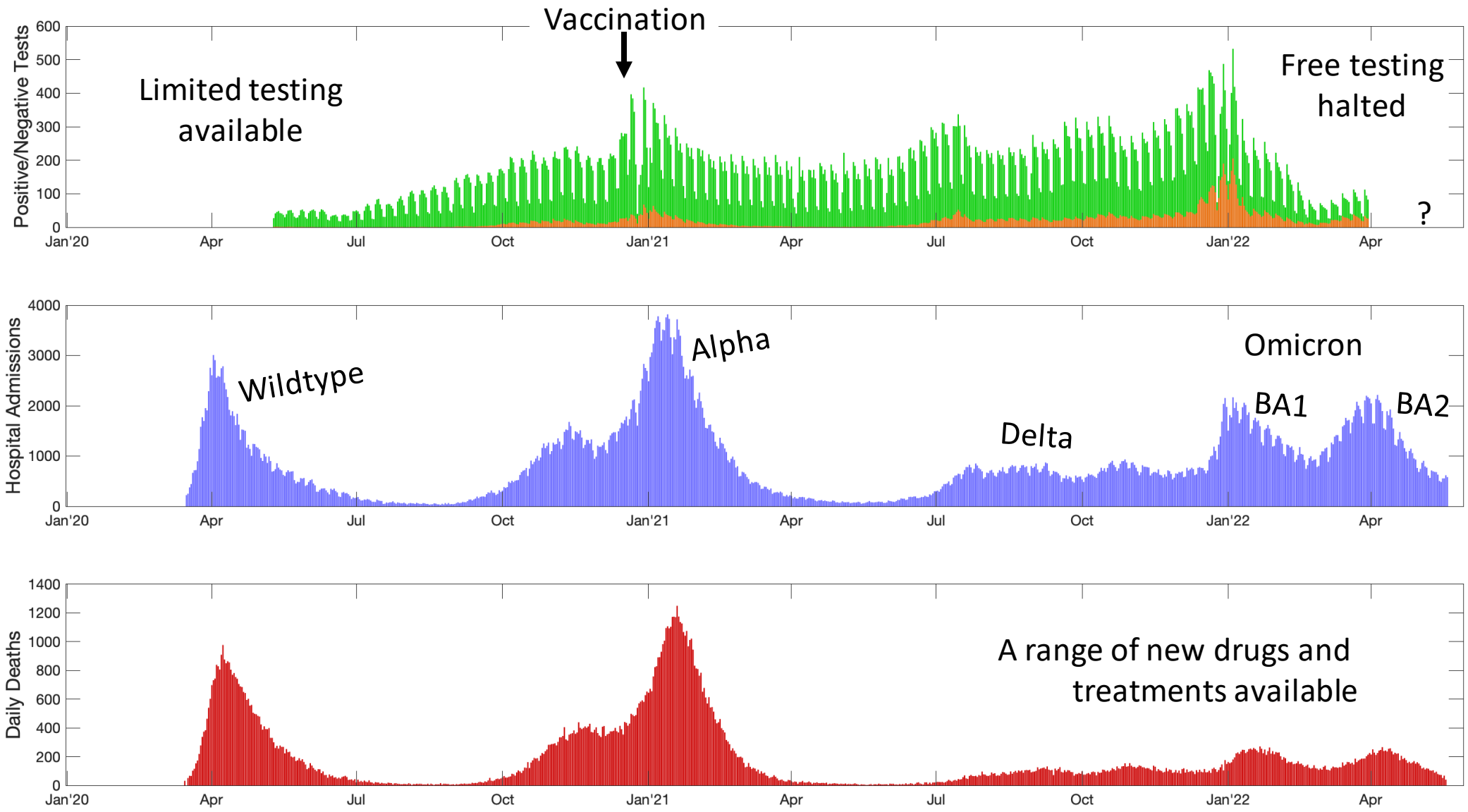
Simple Statistics are powerful…. In particular growth rates from “log-linear” plots.

Monkeypox (2022)

Must be careful about reading too much into early extrapolations, and eventually we need more complex approaches.



COVID: Data for England

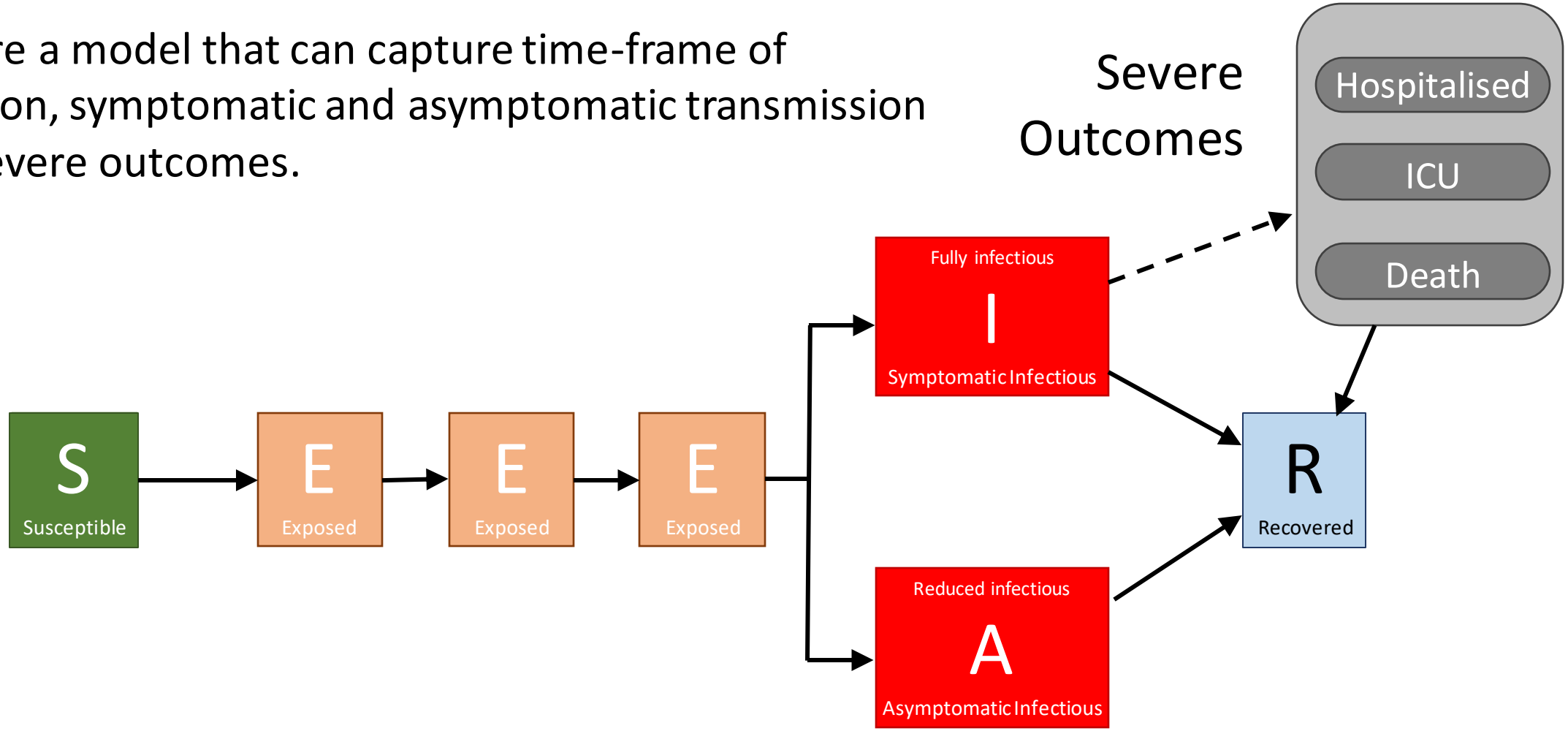


Wave 1 and Early Dynamics

Data:
Severe disease (hospital, ICU and Death)

Policy:
Lock-down and household isolation

Require a model that can capture time-frame of infection, symptomatic and asymptomatic transmission and severe outcomes.



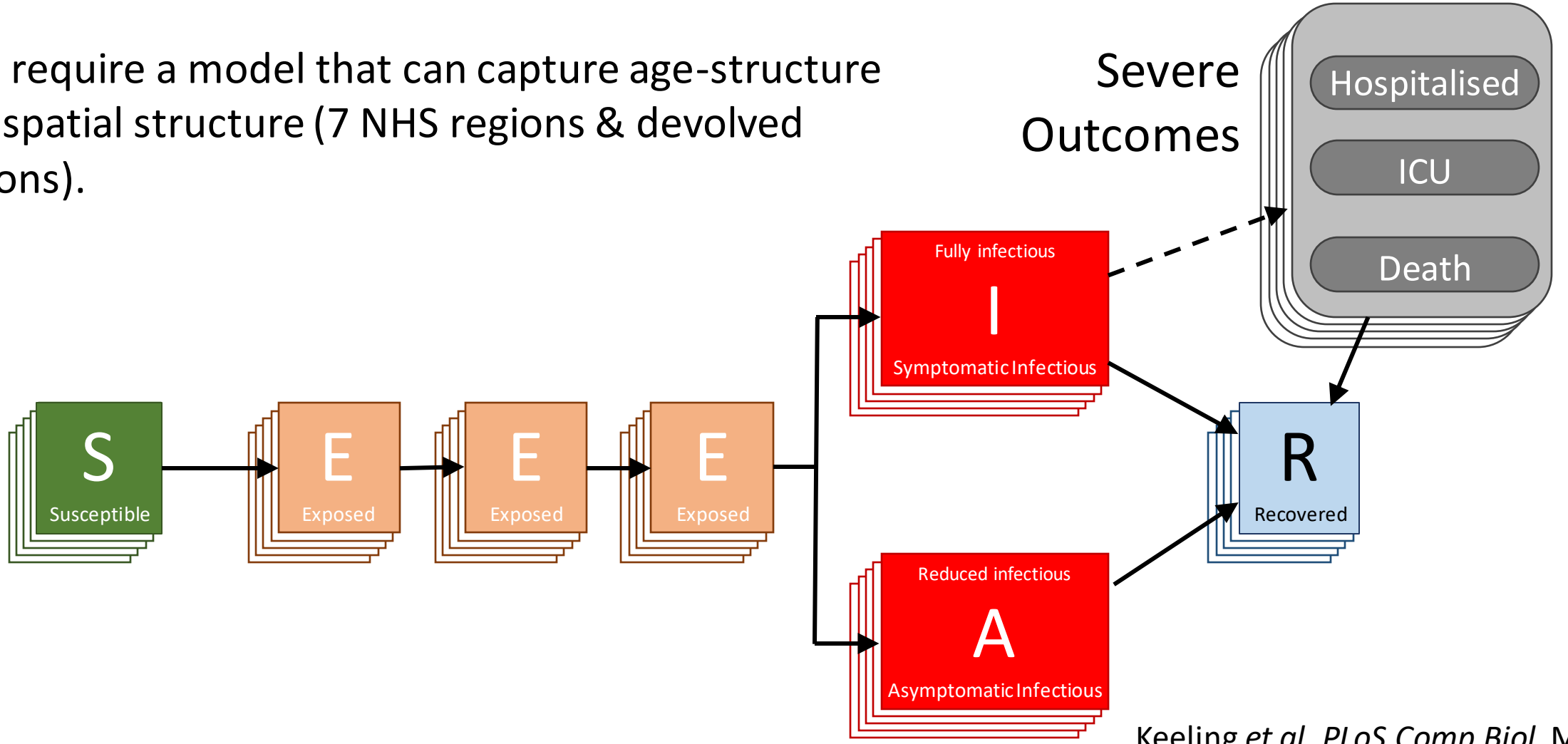
Keeling *et al*. *PLoS Comp Biol*. May 2020

Wave 1 and Early Dynamics

Data:
Severe disease (hospital, ICU and Death)

Policy:
Lock-down and household isolation

Also require a model that can capture age-structure and spatial structure (7 NHS regions & devolved nations).



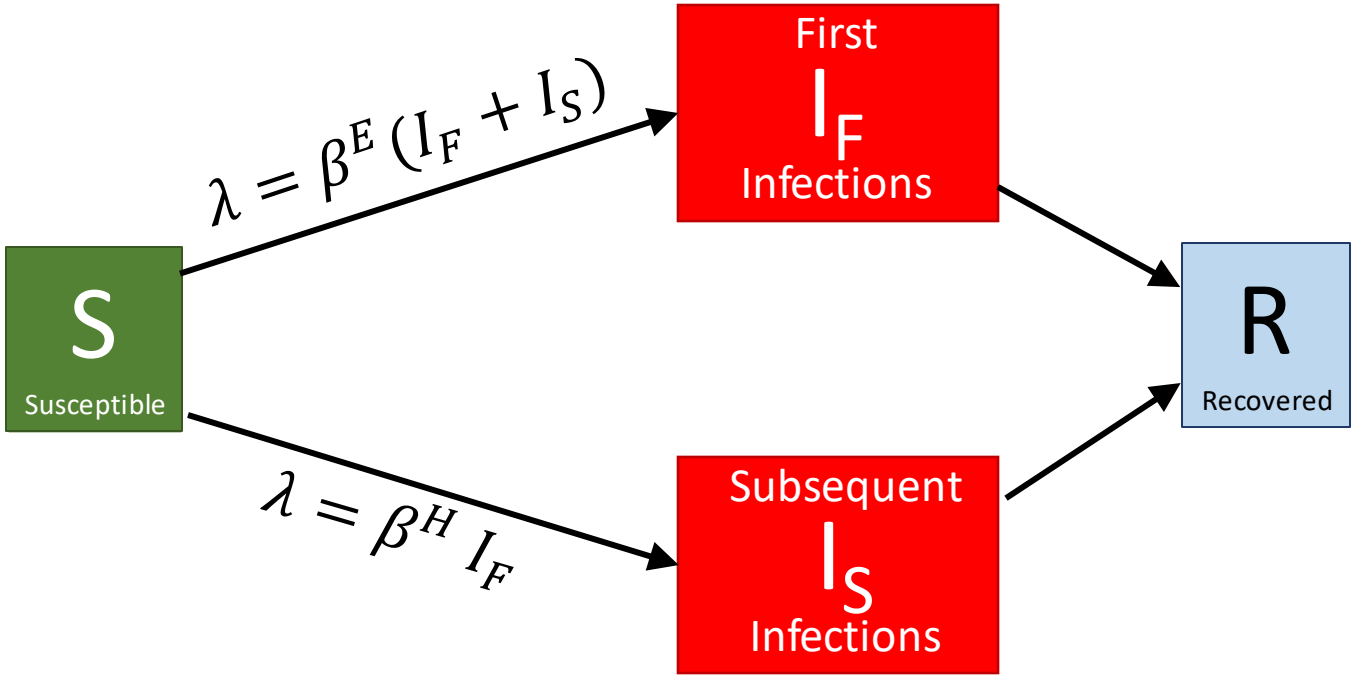
Keeling *et al*. *PLoS Comp Biol*. May 2020

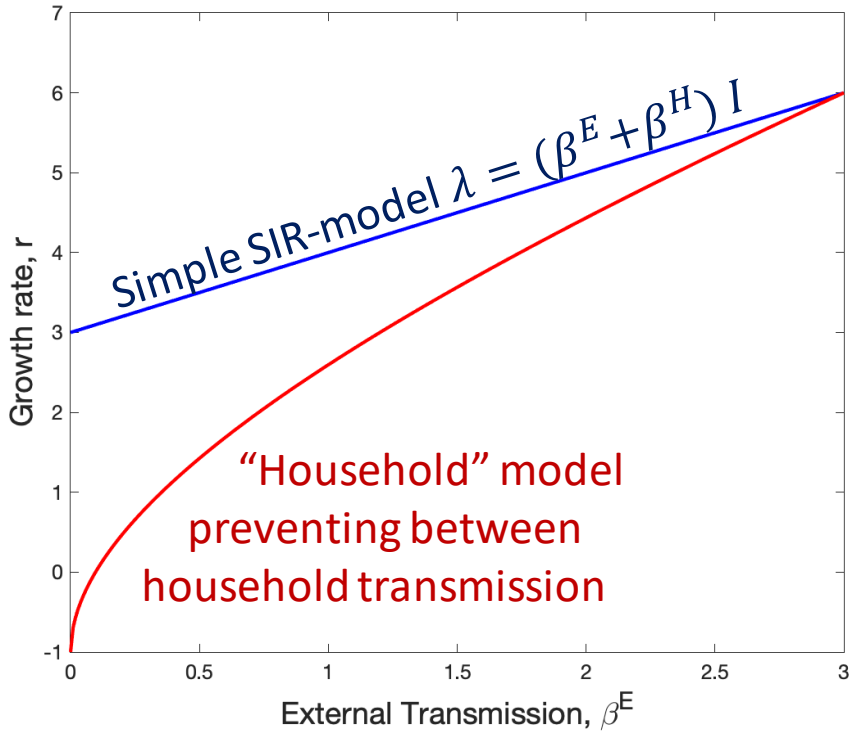
Wave 1 and Early Dynamics

Data:
Severe disease (hospital, ICU and Death)

Policy:
Lock-down and household isolation

Require a model that can capture household isolation.





Keeling *et al*. *PLoS Comp Biol*. May 2020

Wave 1 and Early Dynamics

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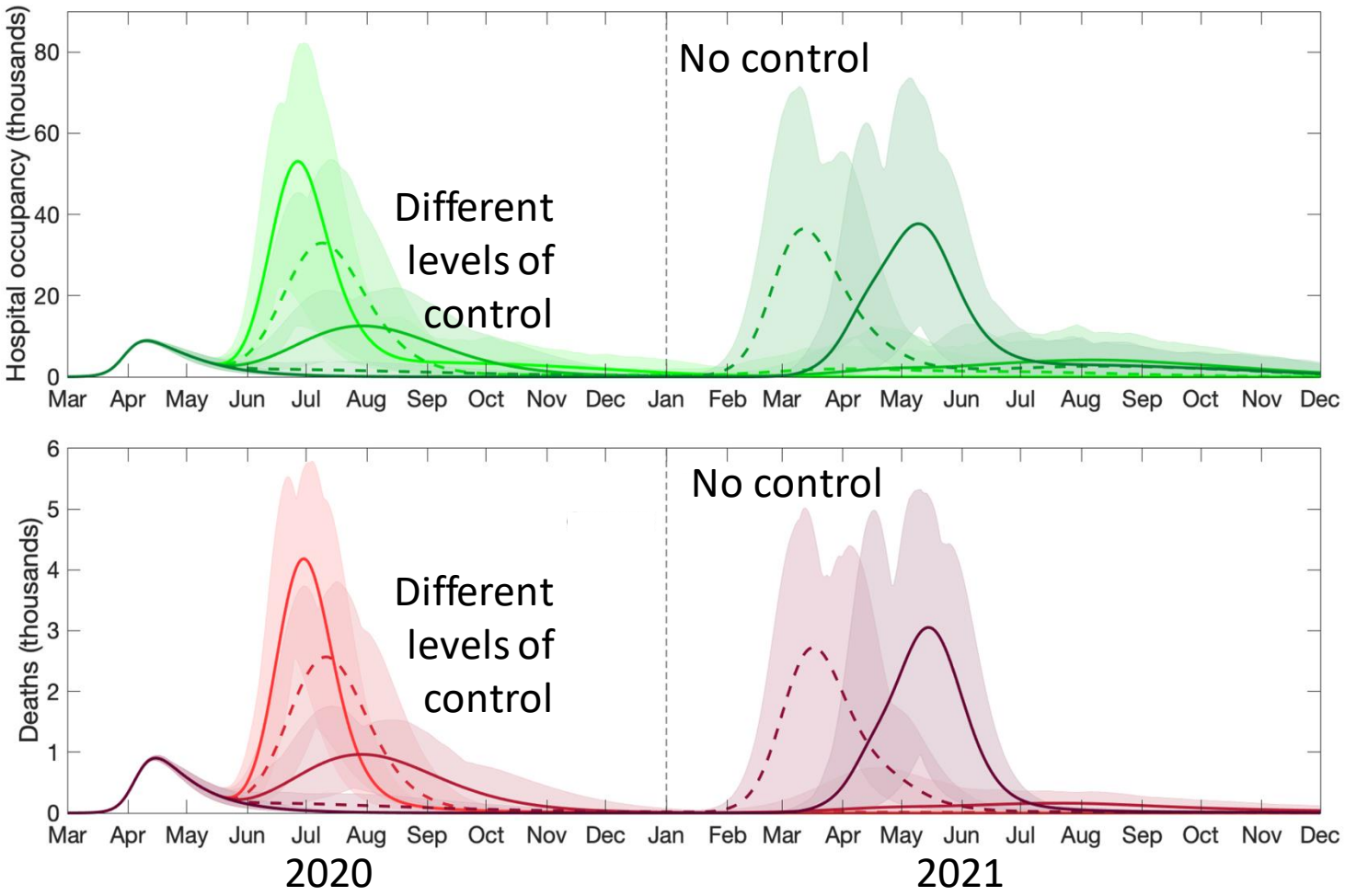


Even back in April/May 2020, our main concern was how to relax from lockdown.

We consider different levels of control in latter half of 2020, with no-control in 2021.

We found a moderate degree of NPI control in 2020, minimized the total epidemic size, but still lead to 152,000 deaths.

This was before vaccination and variants.

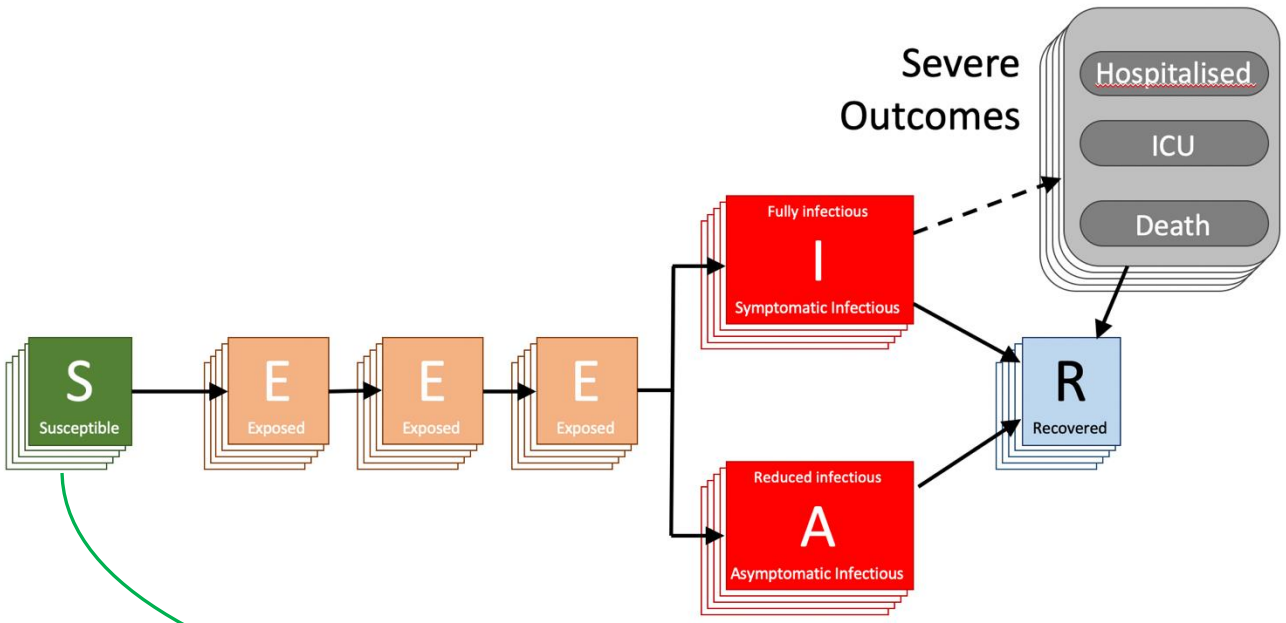
Keeling *et al*. *PLoS Comp Biol*. May 2020

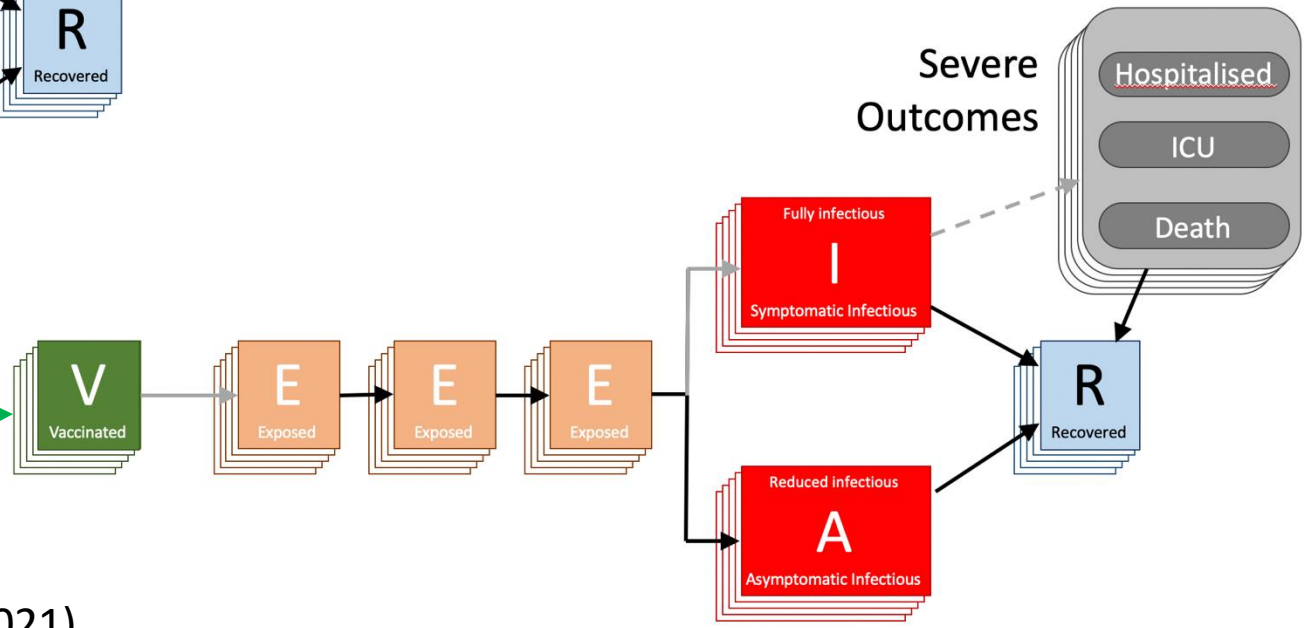
Wave 2, Variants and **Vaccines**

Data:
None !!

Policy:
How should vaccines be used

Adding vaccination effectively doubled the number of model states. As being vaccinated could affect risk of acquiring infection, risk of symptoms or risk of severe disease.





Moore *et al*. *PLoS Comp Biol*. Oct 2020 (published May 2021)

Wave 2, Variants and **Vaccines**

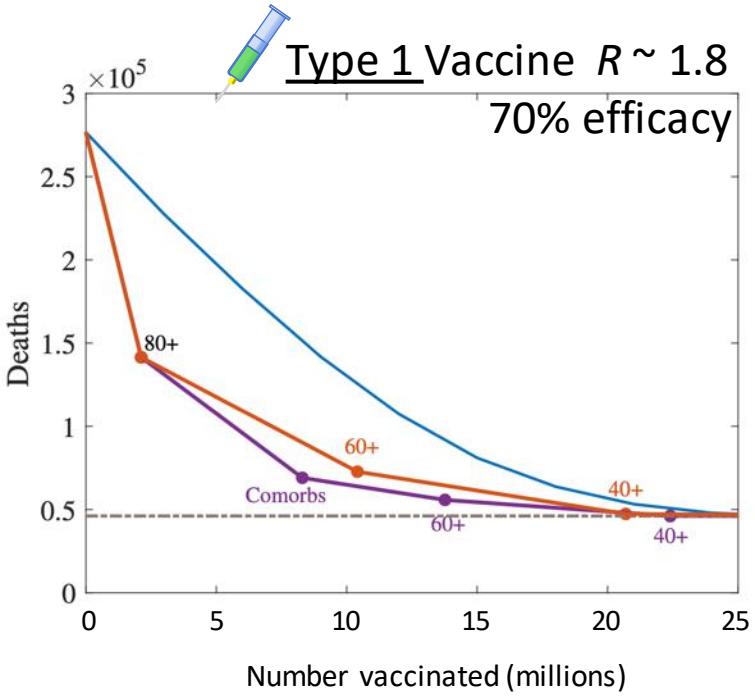
Data:
None !!

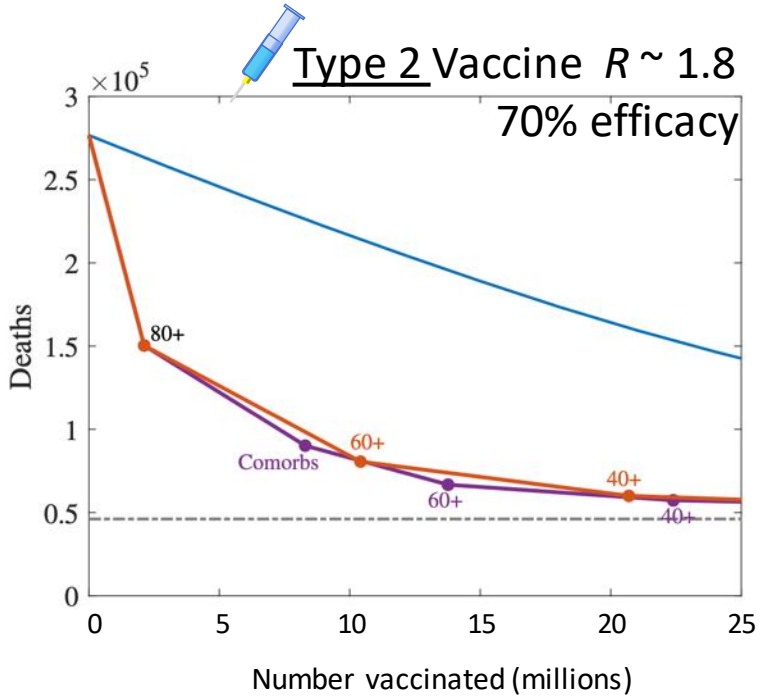
Policy:
How should vaccines be used?

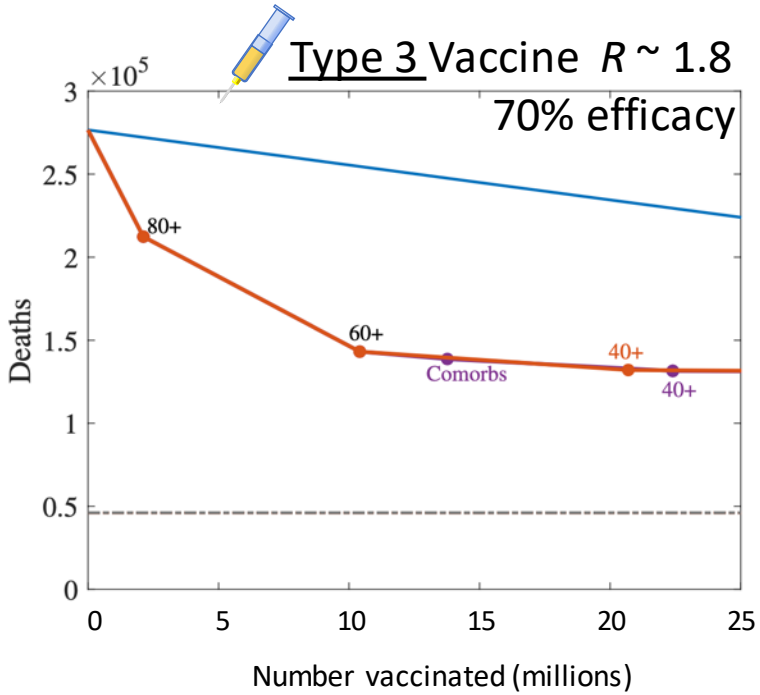
Type 1 vaccines reduce susceptibility to infection and therefore act to block transmission
65/80%

Type 2 vaccines reduce disease and therefore also reduce transmission (some asymptomatic transmission)
80/90%

Type 3 vaccines reduce severe disease, but have no impact on transmission.
> 90%







Wave 2, **Variants** and Vaccines

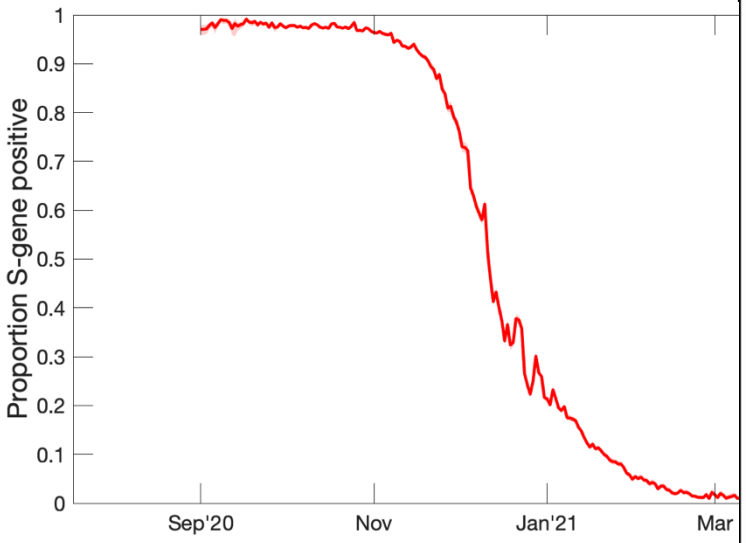
Data:
B.1.1.7 / Alpha variant is growing, data from S-gene failures.

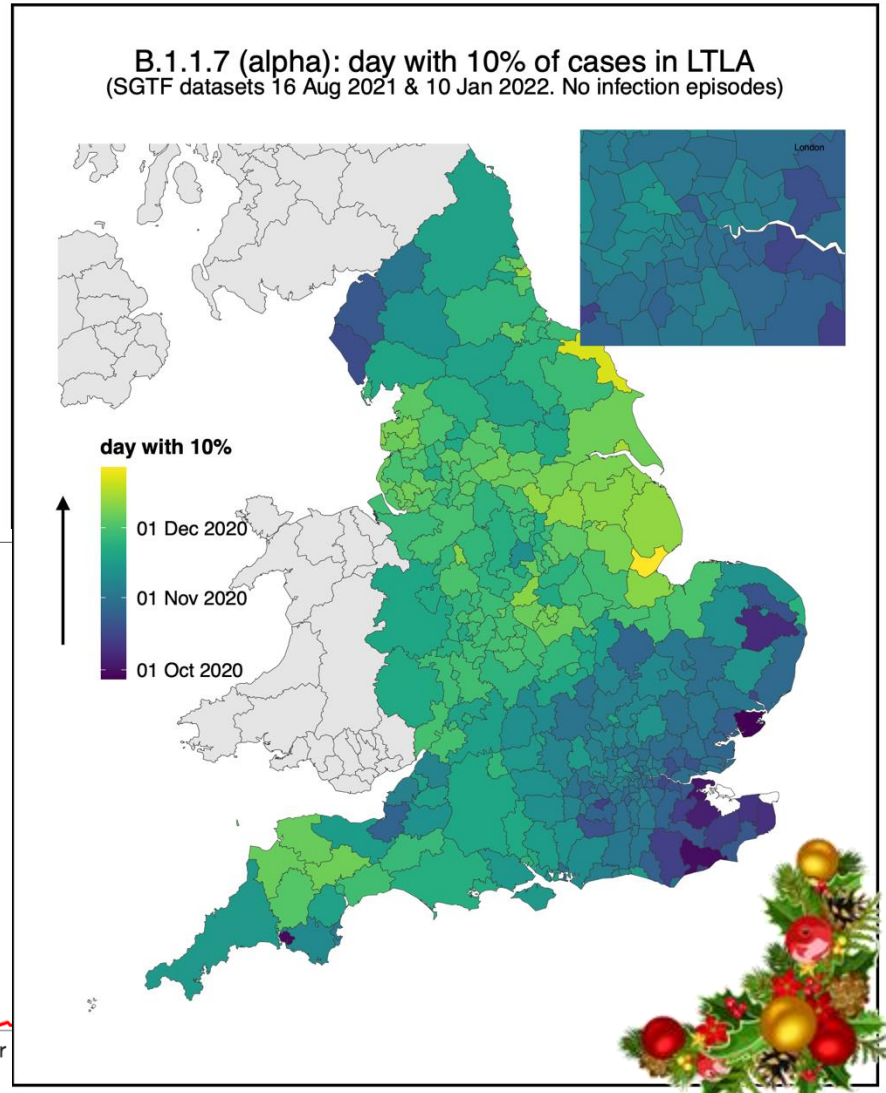
Policy:
What are the implications

Failure to detect the S-gene in TaqPath PCR tests, together with genomic confirmation, showed the rapid spread of a new variant from SE England.

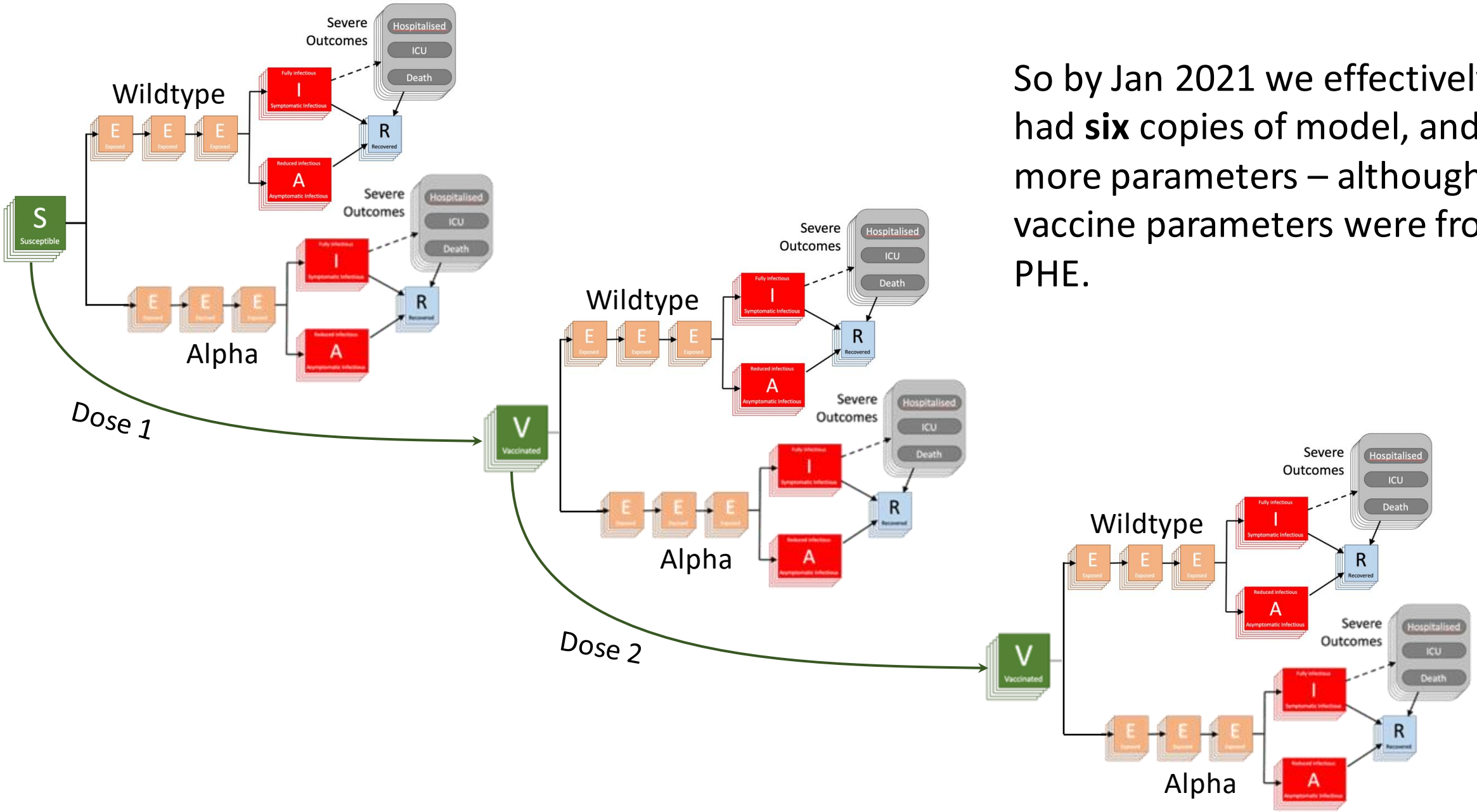
Initial work was largely statistical, Alpha was estimated to be 50% more transmissible than wildtype.

The new variant needed to be added to the model (effectively doubling the number of states).





Wave 2, **Variants** and Vaccines



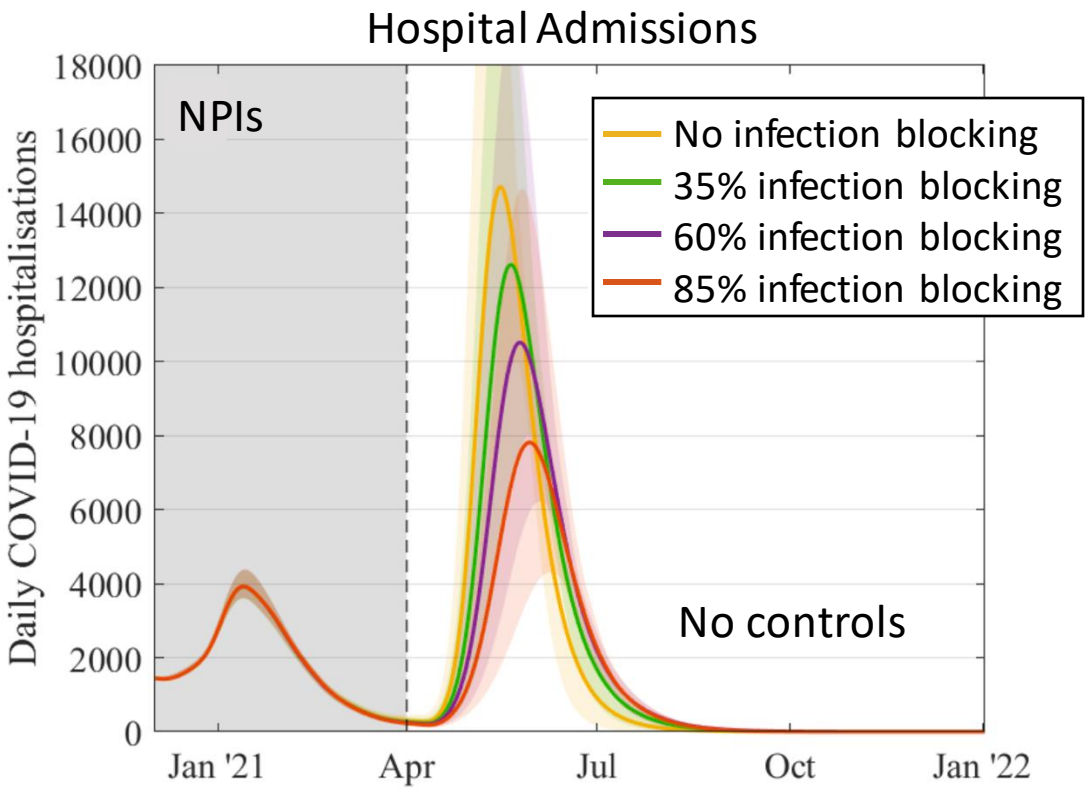
So by Jan 2021 we effectively had **six** copies of model, and more parameters – although vaccine parameters were from PHE.

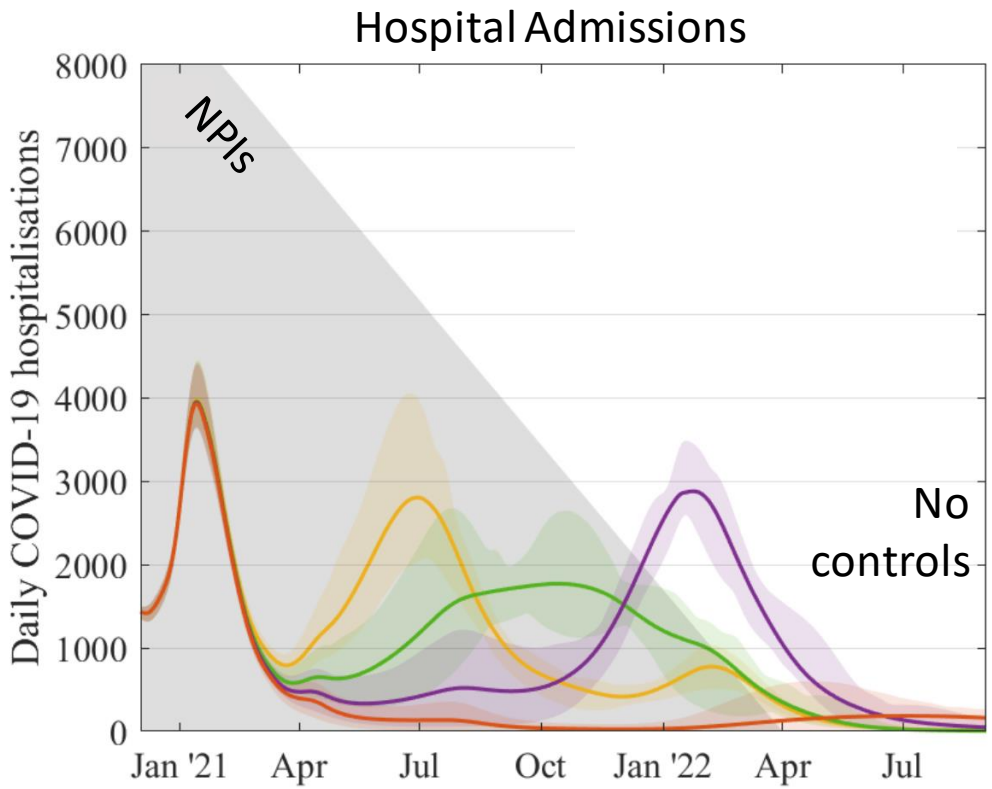
Wave 2, **Variants and Vaccines**

Data:
Clinical trial data – Type 1 vaccine.

Policy:
We have vaccines, can we relax now?

Even after 3-4 months of vaccination and ~30M doses, a sudden halt to controls is predicted to generate a massive resurgence of severe disease, slow relax of controls maintains control.



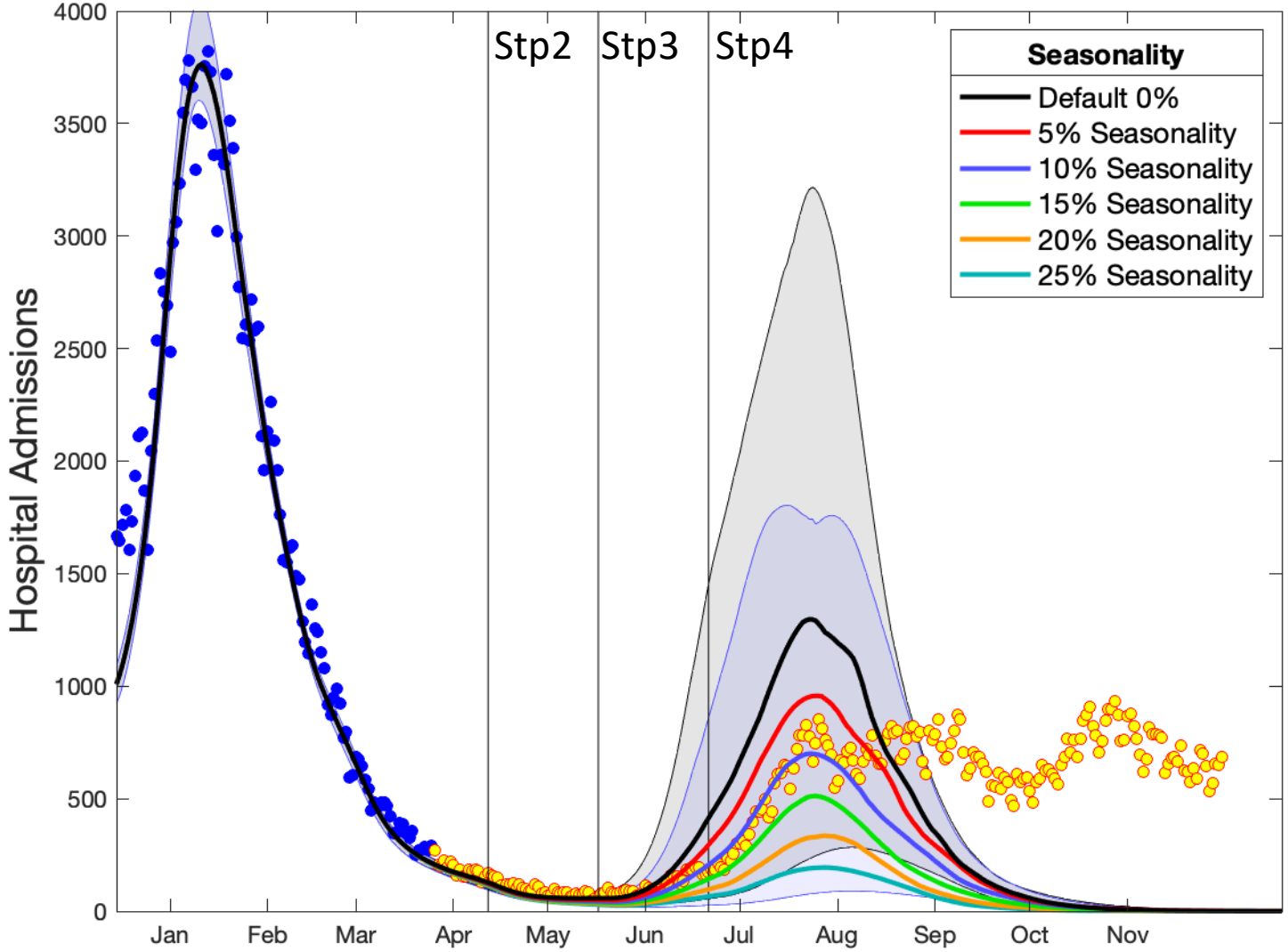


Moore *et al*. *Lancet ID*. Jan 2020 (published March 2021)

Roadmap for Relaxation

Data:
Still in rapid decline from lockdown.

Policy:
How do we 'safely' remove controls



Roadmap 2

Evaluation of Steps 2 to 4, with very limited information on how each would affect behaviour.

Over-estimated mixing, under-estimated vaccine efficacy, and didn't know about Delta.

10% seasonality, now the default.

Data used for inference

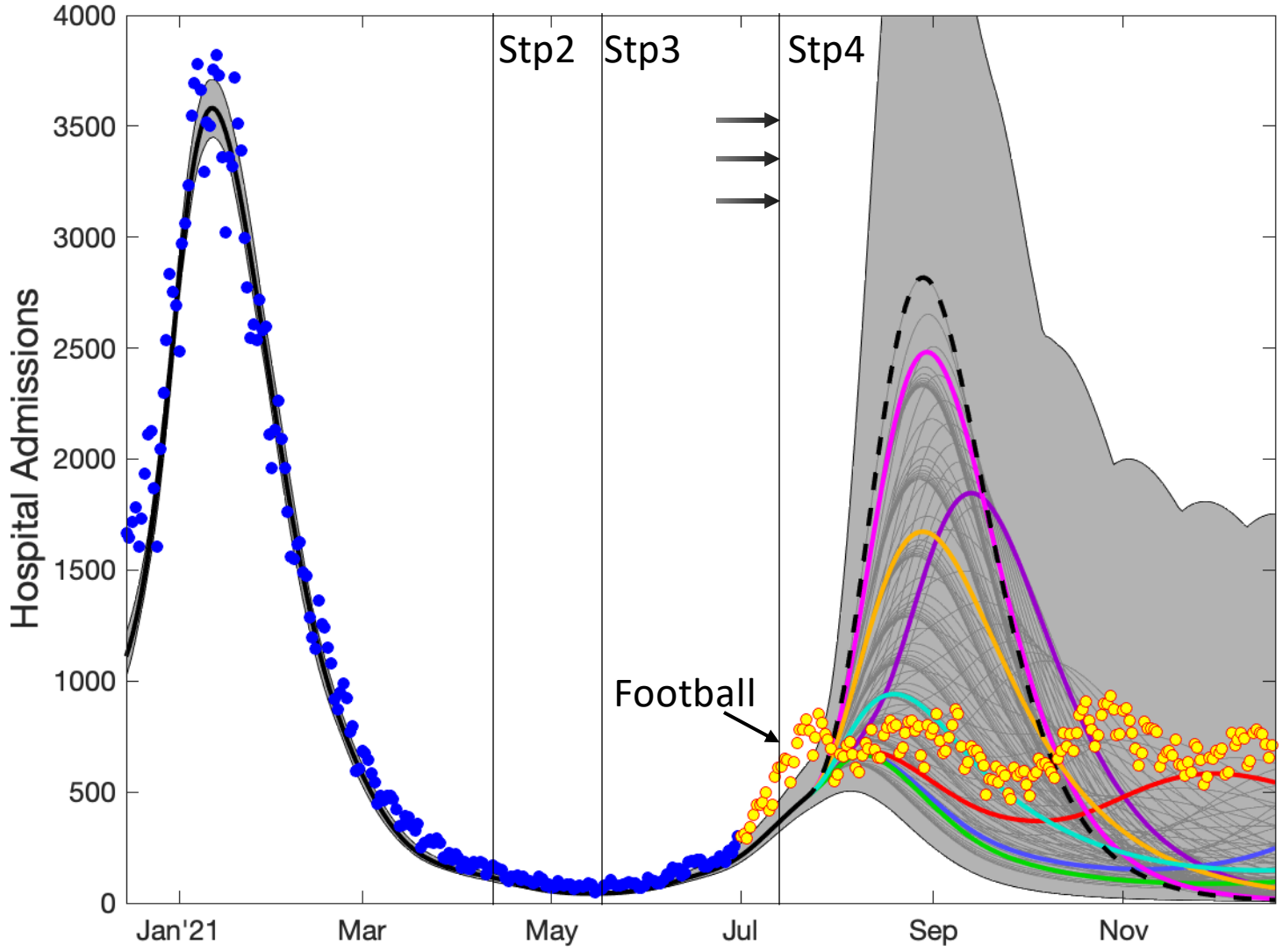
Data post simulation

Keeling *et al* medRxiv 2022.03.17.22272535

Roadmap for Relaxation

Data:
Better data on Delta and vaccine efficacy.

Policy:
How do we 'safely' remove controls



Roadmap 4b

By now we had sufficient data to see that the response to each relaxation Step was slow – the public were still cautious, we therefore modelled multiple speeds of relaxation.

Some parameter sets capture the long oscillatory plateau, but we failed to predict the steep rise due to football celebrations.

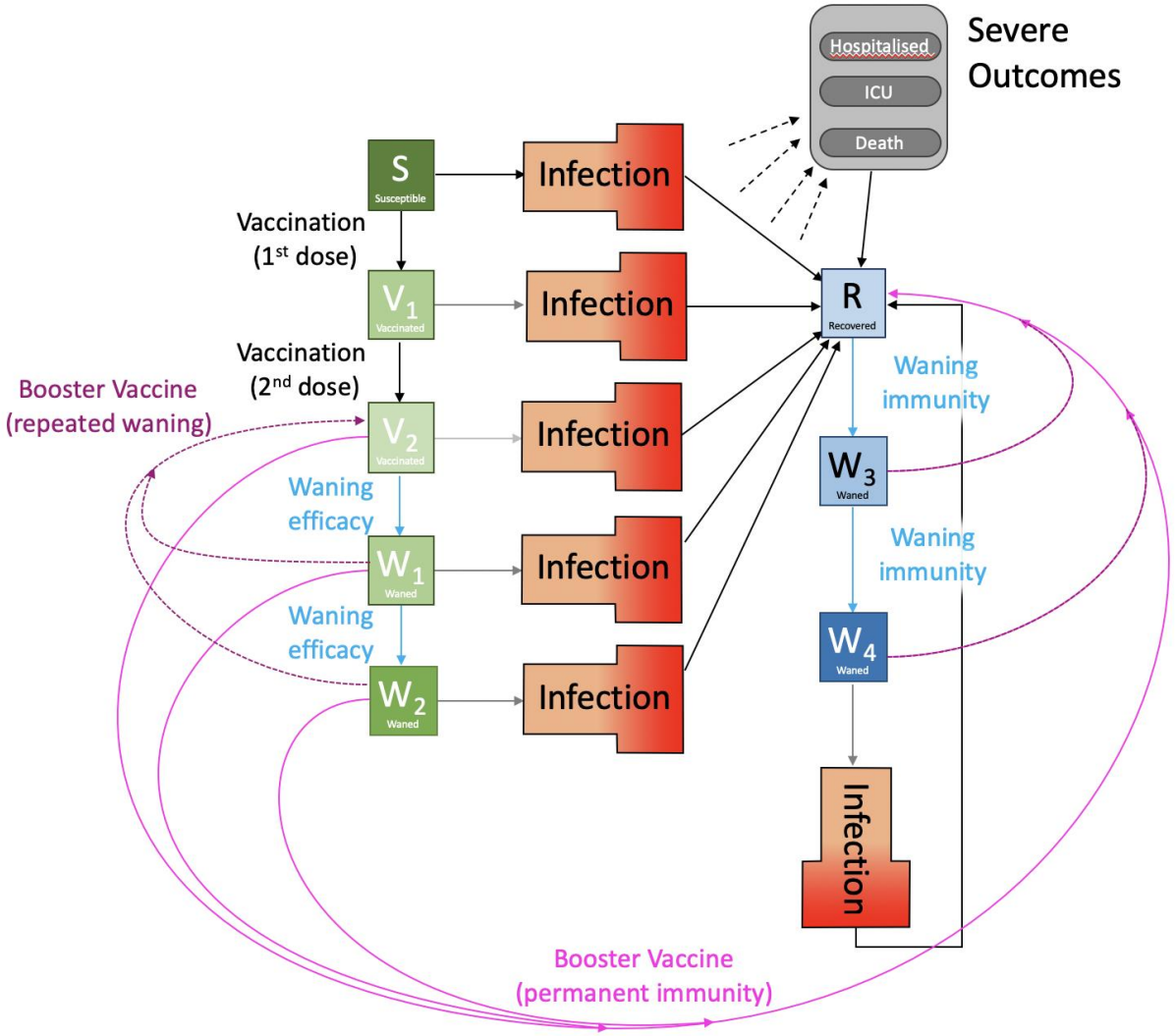
- Data used for inference
- Data post simulation

Keeling *et al* medRxiv 2022.03.17.22272535

Omicron and Beyond

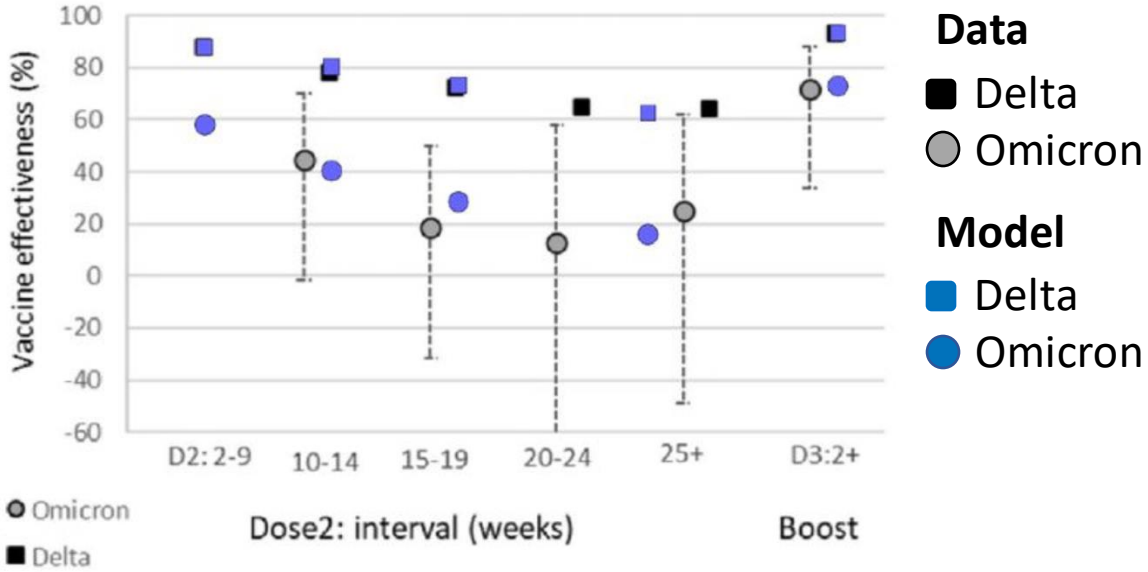
Data:
Waning immunity & novel variants.

Policy:
Do we need to react?



Omicron was detected in the UK on 27th November, by 21st December we were being asked to make detailed policy forecasts.

Models now took into account waning vaccine efficacy and waning immunity following infection; and the booster.



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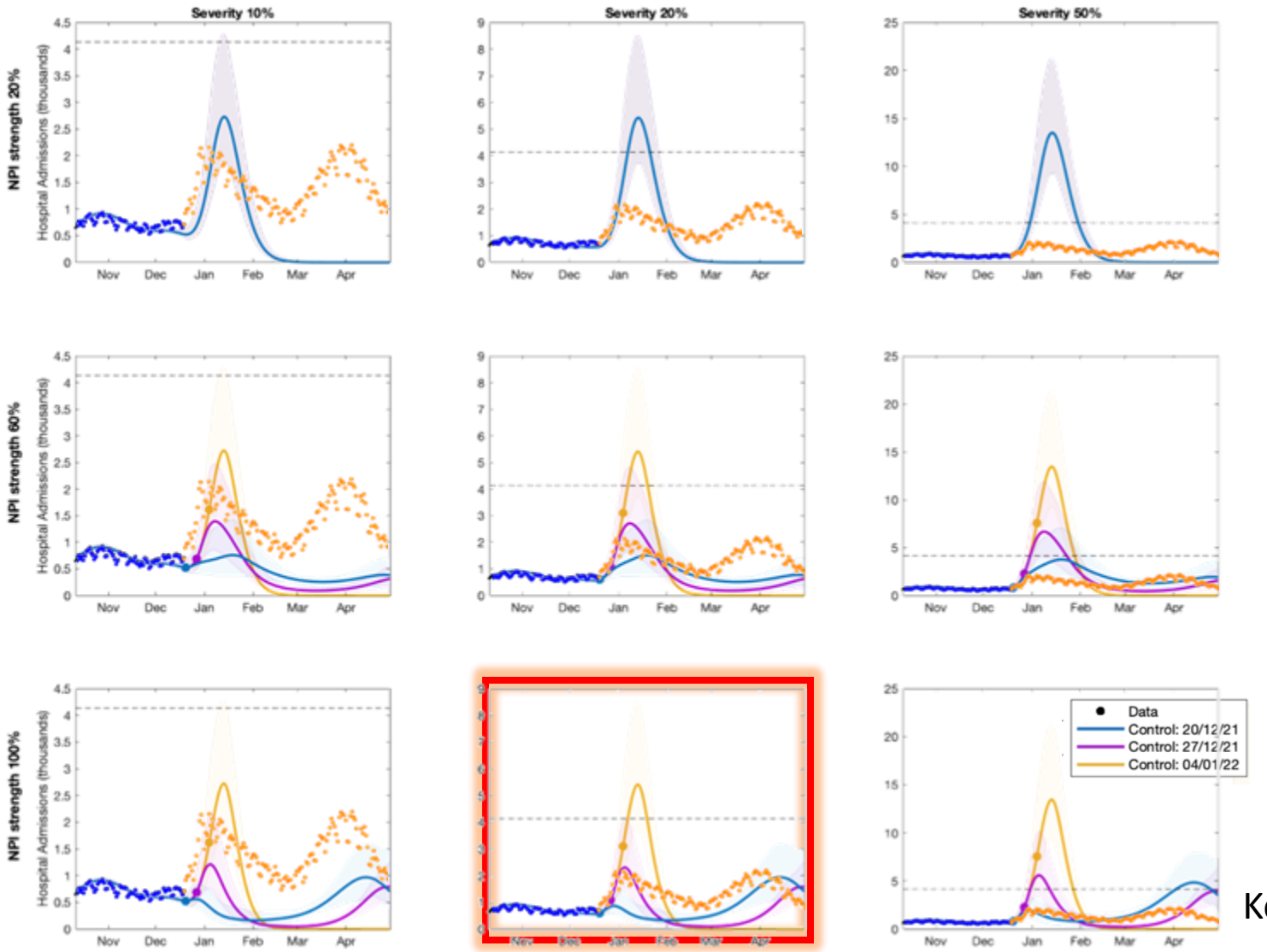

Omicron was detected in the UK on 27th November, by 21st December we were being asked to make *detailed* policy forecasts.

We considered different severity (columns) and different strengths of control (rows) with different start dates, with gradual relaxation.

No policy change occurred, but on 16th December Chris Whitty (CMO) made a plea for restrained behaviour and mass-testing over Christmas.

Keeling *et al* medRxiv 2021.12.30.21268307 (Dec 21)

Lessons for Future Pandemics

1) **Develop a thick-skin**. Models are projections of what might happen – they will be scrutinized, compared to any unfolding epidemic and criticised.

2) **You can't predict human behaviour**. The EUROs football, the pingdemic, the response to Chris Whitty in December 2021 – were all unexpected and unpredictable.

3) **Models <u>will</u> be wrong, but should be useful**. The departure of data from models can often hint at underlying changes in behaviour.

4) **Data is key**. Models are nothing without data, use all available sources. Genomic & immunological data is still being under exploited. Individual-level data is often extremely useful but ethically challenging.

5) **An holistic approach is best** – ideally modellers should think about all aspects of control: health, wealth and well-being. This is not always feasible.

6) **Team work is vital**. In the UK we were lucky to have SPI-M-O to integrate projections from multiple groups – shared responsibility. I've also been luck to be part of the JUNIPER consortium and a large supportive team in Warwick.

Modelling to Support Resilience for Pandemics

1) Inter-institutional teams for pooled knowledge, skills and resources – JUNIPER.
2) Science for policy vs Science for the public.
3) Suite of models as building blocks for the next pandemic / outbreak.
4) Excellent inference methods.
5) DATA (caveat: modellers always want more data!)
    1) Each of our insights during the COVID-19 pandemic has been due to new data (vaccine efficacy, S-gene target failure, waning immunity, repeat infections).
    2) Ideal would be seamless data access with UKHSA, NHS and other data providers; but this raises ethical and data privacy issures.
    3) Compromise is a freely available surrogate data, together with a secure “data warehouse” that has the processing power to run complex models and inference.

Any Questions?