

Models and evidence synthesis for policy making

Marc Baguelin

Work done as part of the UK real-time modelling response team

WHO Collaborating Centre for Infectious Disease Modelling
MRC Centre for Global Infectious Disease Analysis
Jameel Institute

Imperial College London

- Established in 2007 → UK need for rapid responses to outbreaks
- Re-branded in 2017 → wider global health remit
- A core element of our mission: To undertake **applied collaborative work with national and international agencies to support policy planning and response operations against infectious disease threats.**
- Designated as a **WHO Collaborating Centre** in 2010, one of the aim being to provide **rapid analysis** of urgent infectious disease problems, notably outbreaks and events of international concern.

<https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis>

Early 2020

Novel coronavirus identified
Cases reported so far mainly in China

Report 1 - Estimating the potential total number of novel Coronavirus (2019-nCoV) cases in Wuhan City, China

WHO Collaborating Centre for Infectious Disease Modelling; MRC Centre for Global Infectious Disease Analysis; Abdul Latif Jameel Institute for Disease and Emergency Analytics; Imperial College London, UK

Summary

Many aspects of the COVID-19 (previously termed 2019-nCoV) outbreak are highly uncertain. However, the detection of three cases outside China (two in Thailand, one in Japan) is worrying. We calculate, based on flight and population data, that there is only a 1 in 574 chance that a person infected in Wuhan would travel overseas before they sought medical care. This implies there might have been over 1700 (3 x 574) cases in Wuhan so far. There are many unknowns, meaning the uncertainty range around

Key info

Date:

17 January 2020

Authors:

Natsuko Imai, Ilaria Dorigatti, Anne Cori, Steven Riley, Neil M. Ferguson

- Officially reported in Wuhan:
41 cases, with 3 in international travellers
- **Estimated:**
1,723 cases (95% CI: 427 – 4,471)
- Uncertainties about:
 - early event (large spillover event?)
 - H2H transmission & R0
 - “hidden” transmission
 - severity

Report 3 - Transmissibility of 2019-nCoV

WHO Collaborating Centre for Infectious Disease Modelling; MRC Centre for Global Infectious Disease Analysis; Abdul Latif Jameel Institute for Disease and Emergency Analytics; Imperial College London, UK

Note: This is an extended version of an analysis previously shared with WHO, governments and academic networks between 22/1/2020-24/1/2020.

Summary

Self-sustaining human-to-human transmission of the novel coronavirus COVID-19 (previously termed 2019-nCoV) is the only plausible explanation of the scale of the outbreak in Wuhan. We estimate that, on average, each case infected 2.6 (uncertainty range: 1.5-3.5) other people up to 18th January 2020, based on an analysis combining current estimates of the size of the outbreak in Wuhan with

Key info

Date:

25 January 2020

Authors:

Natsuko Imai, Anne Cori, Ilaria Dorigatti, Marc Baguelin, Christl A. Donnelly, Steven Riley, Neil M. Ferguson

Estimated R0: 2.6 (range 1.5-3.5)

Report 4 - Severity of 2019 novel coronavirus (nCoV)

WHO Collaborating Centre for Infectious Disease Modelling; MRC Centre for Global Infectious Disease Analysis; Abdul Latif Jameel Institute for Disease and Emergency Analytics; Imperial College London, UK

Summary

We present case fatality ratio (CFR) estimates for three strata of COVID-19 (previously termed 2019-nCoV) infections. For cases detected in Hubei, we estimate the CFR to be 18% (95% credible interval: 11%-81%). For cases detected in travellers outside mainland China, we obtain central estimates of the CFR in the range 1.2-5.6% depending on the statistical methods, with substantial uncertainty around these central values. Using estimates of underlying infection prevalence in Wuhan at the end of January derived from testing of passengers on repatriation flights to Japan and Germany, we adjusted the estimates of CFR from either the early epidemic in Hubei Province, or from cases reported outside mainland China, to obtain estimates of the overall CFR in all infections (asymptomatic or symptomatic) of approximately 1% (95% confidence interval 0.5%-4%). It is important to note that the differences in these estimates does not reflect underlying differences in disease severity between countries. CFRs seen in individual countries will vary depending on the sensitivity of different surveillance systems to detect cases of differing levels of severity and the clinical care offered to severely ill cases. All CFR estimates should be viewed cautiously at the current time as the sensitivity of surveillance of both deaths and cases in mainland China is unclear. Furthermore, all estimates rely on limited data on the typical time intervals from symptom onset to death or recovery which influences the CFR estimates.

Key info

Date:

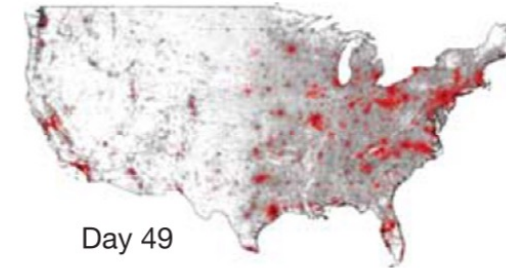
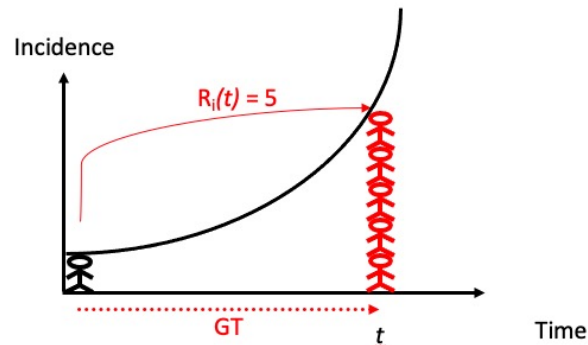
10 February 2020

Authors:

Ilaria Dorigatti*, Lucy Okell*, Anne Cori, Natsuko Imai, Marc Baguelin, Sangeeta Bhatia, Adhiratha Boonyasiri, Zulma Cucunubá, Gina Cuomo-Dannenburg, Rich FitzJohn, Han Fu, Katy Gaythorpe, Arran Hamlet, Wes Hinsley, Nan Hong, Min Kwun, Daniel Laydon, Gemma Nedjati-Gilani, Steven Riley, Sabine van Elsland, Erik Volz, Haowei Wang, Yuanrong (Raymond) Wang, Caroline Walters, Xiaoyue Xi, Christl Donnelly, Azra Ghani, Neil Ferguson*.

Estimated IFR: ~1%

What will we do when it hits the UK?



**Transmission
Mechanisms &
interventions**

Renewal equation based
(EpiEstim
Cori et al. AJE 2013)

?

Individual based model
(used for flu, Ebola,
Ferguson et al. Nature 2006)

Ability to fit to data

→ Development of an intermediate model

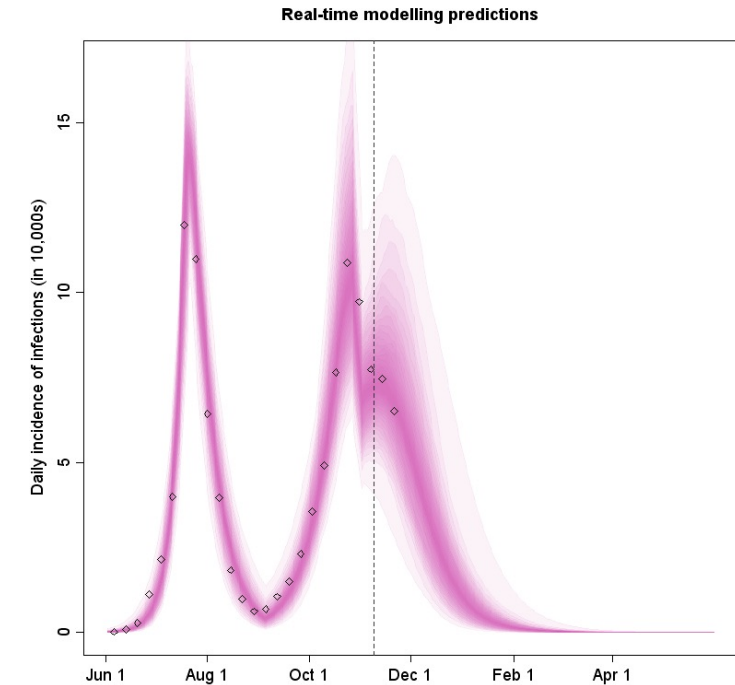
- Incorporating the most important transmission mechanisms
- Focusing on healthcare pathways
- With fine age structure
- Stochastic
- Able to fit multiple data streams



- Model used to link several data sources
- Holistic approach
- Bayesian methodology
- Must be able to fit to these data (inference)
- Use to look at alternative scenario of transmission (counterfactuals) and inform policy making
- Need to ensure that mechanisms (assumed causal relationships) are correctly informed by the data (e.g. reduction in severity can be imputed to better hospital practice, age at admission, vaccines, new variant etc)

Real-time “mechanistic” modelling

- Mechanistic model updated and fitted to an ongoing epidemic/pandemic
- Reflects what we know about the current epidemic
- Able to generate projections about future course of epidemic



*Example of real-time
modelling during 2009
influenza pandemic in
the UK*

SPI-M



SAGE



Government

Many UK academic modelling groups

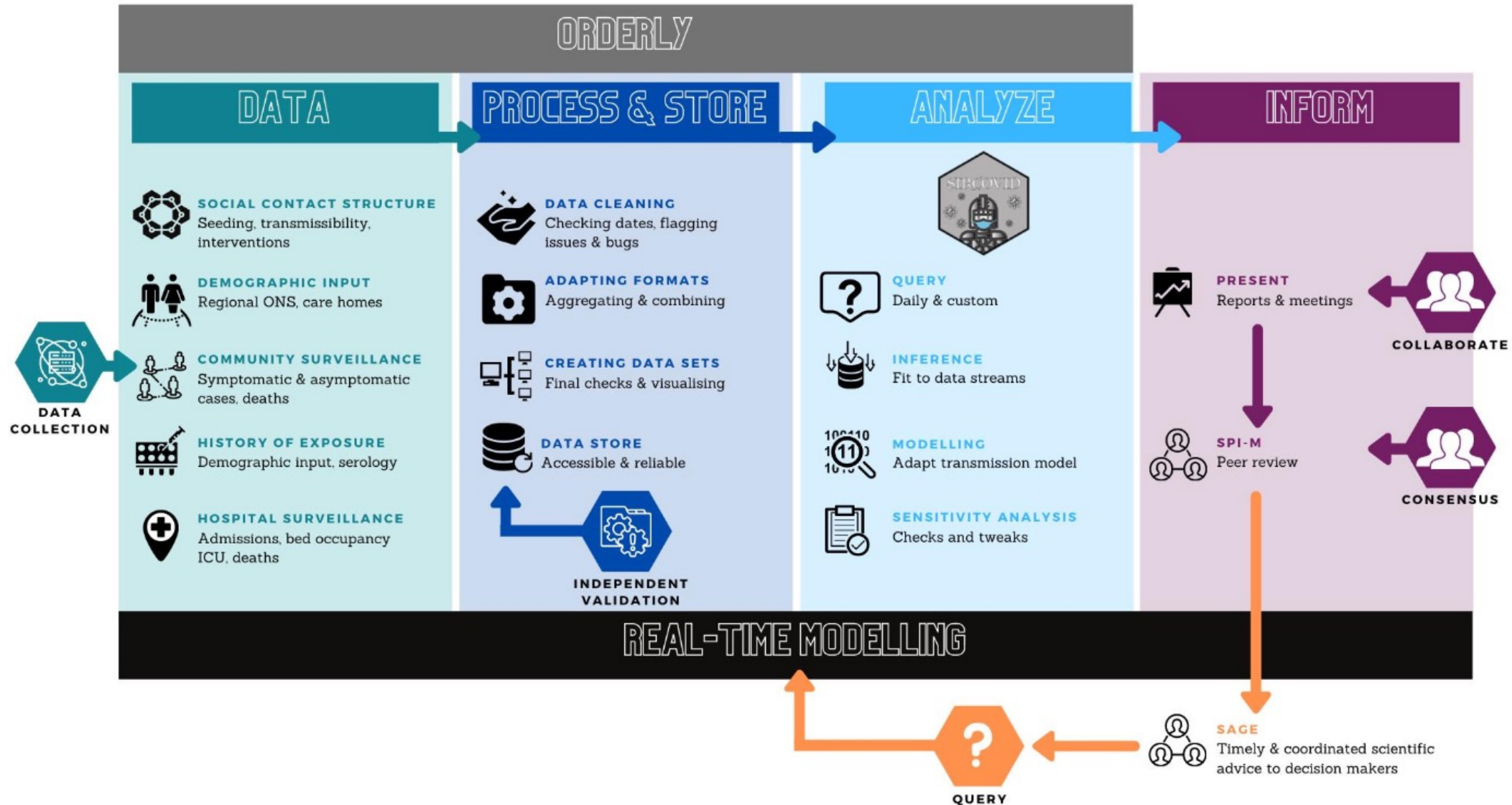
- meets weekly + many subgroups meetings
- produces regular epi estimates (R, incidence etc)
- produces consensus statements
- can be commissioned for specific tasks

Group with wider expertise, includes independent experts, NHS, civil servants, heads of SAGE sub-groups, CMO, CSA etc

→ First iteration of the model used late March to examine potential impact of lockdown (which started on March 23rd)

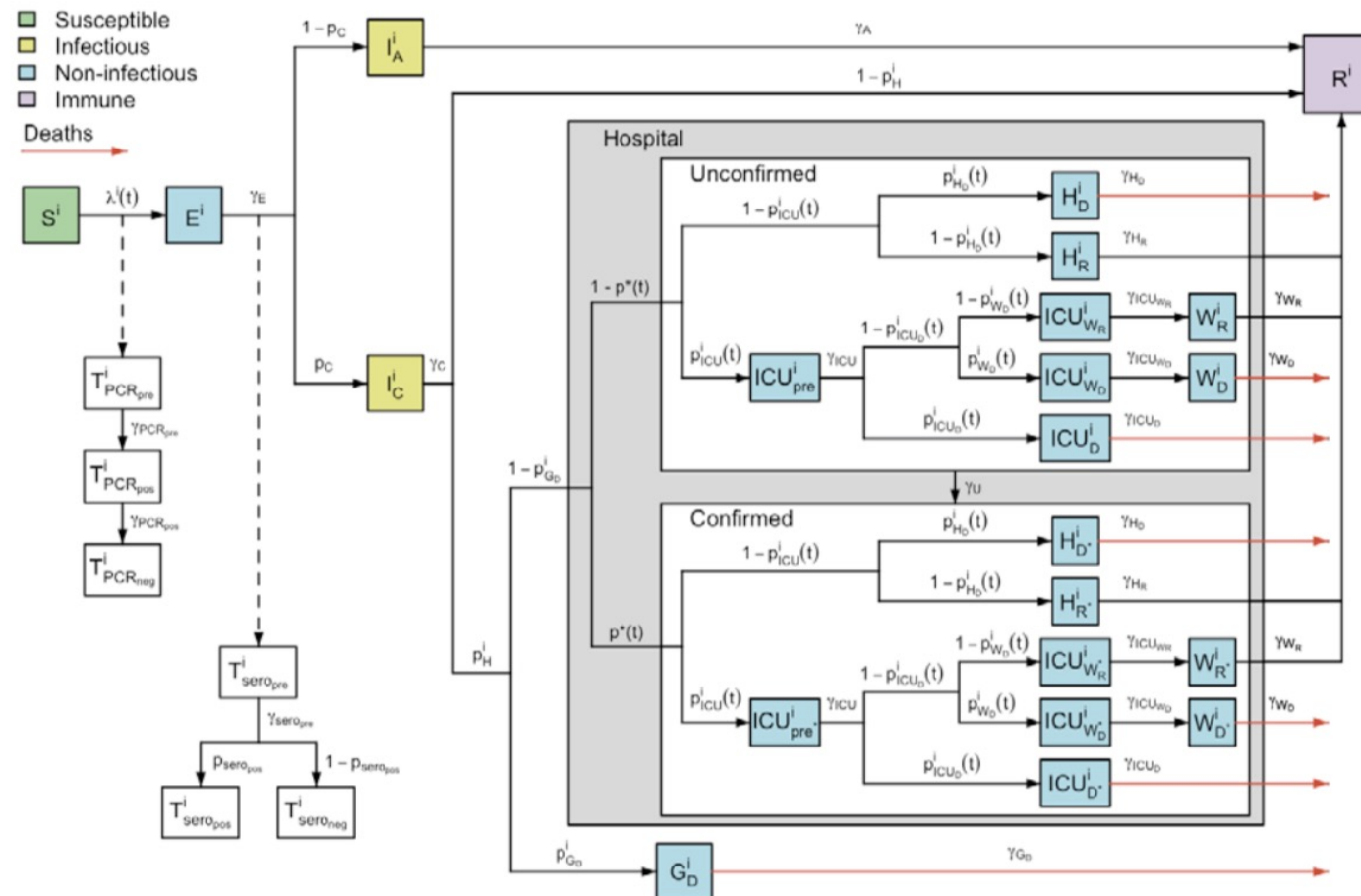
→ Used every single week since then to perform short term projections and address ad-hoc queries

A complex analysis pipeline



Our SARS-CoV2 transmission model

- SEIHR stochastic model, with symptomatic/asymptomatic, and detailed hospital pathways
- 17 age groups (0-4, 5-9, ..., 80+) + care home workers (CHW) & residents (CHR)
- 2 parallel flows for PCR and serology test results



- Inference of 26 parameters using particle MCMC
- Other parameters fixed to values from the literature

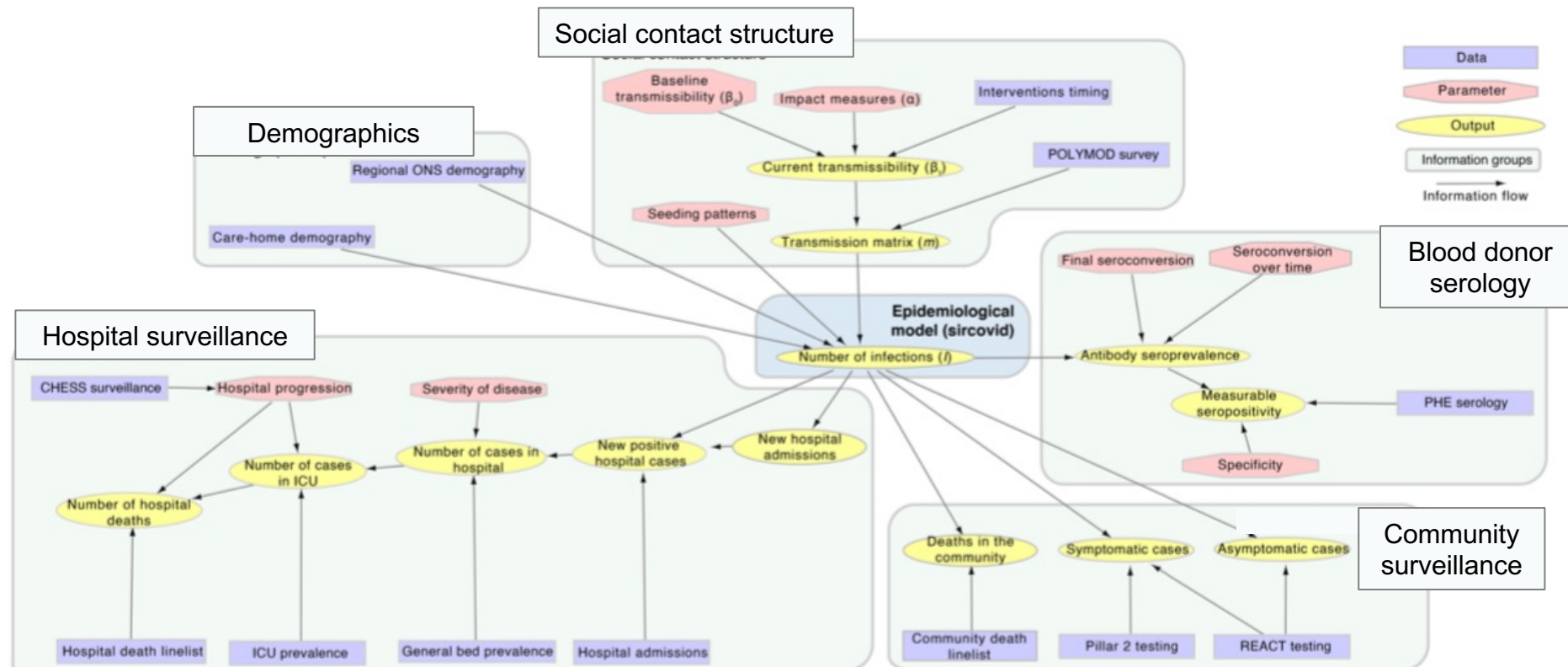
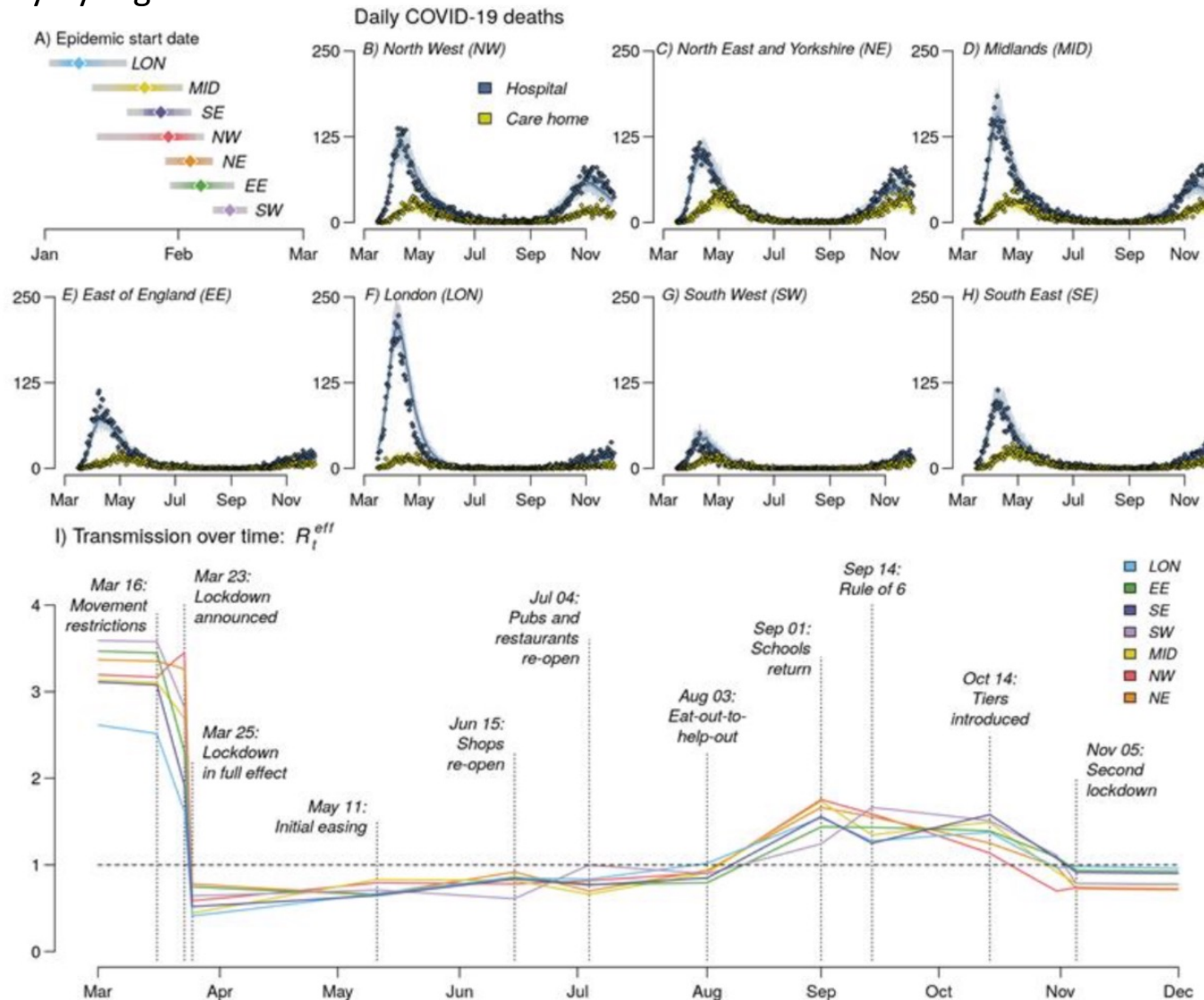


Figure S 1: Graph showing the functional relationships between data sources (rectangles), modelled outputs (ovals) and parameters (hexagons).

Inferred start date and transmissibility over time

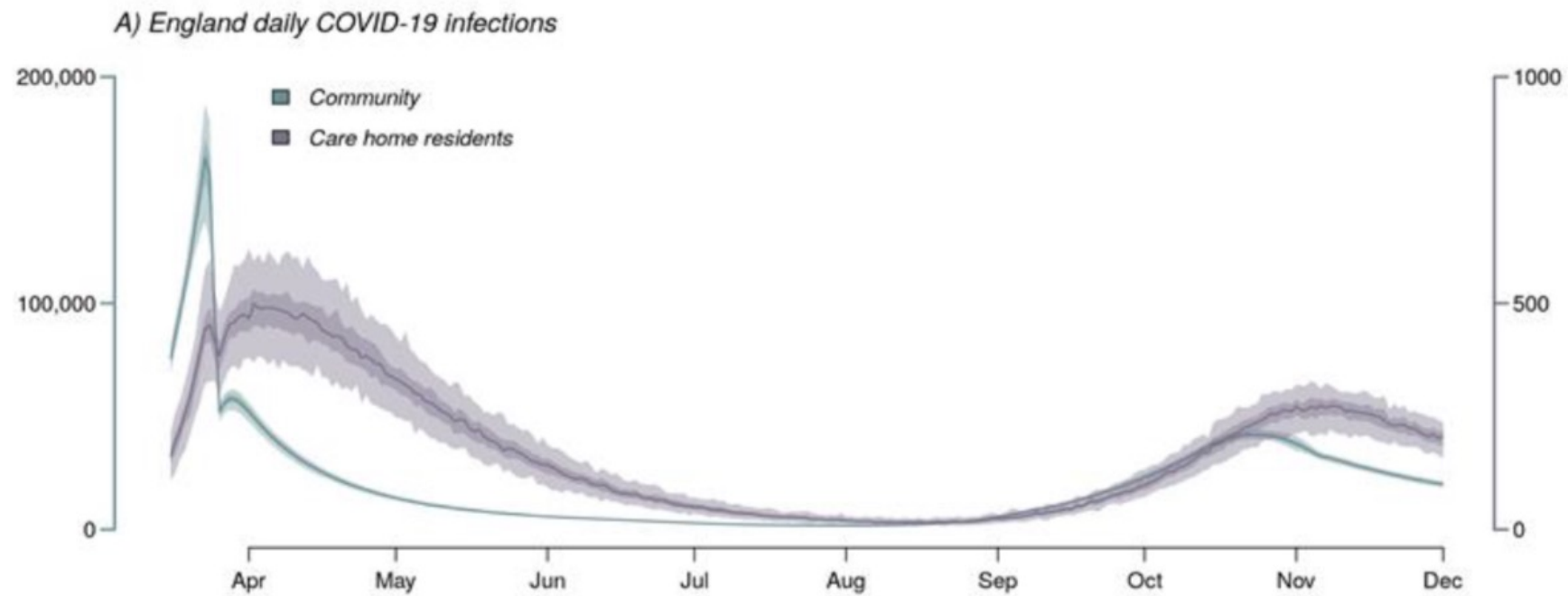
- Model fitted separately by region



→ Only national lockdown brought $R_t < 1$ consistently

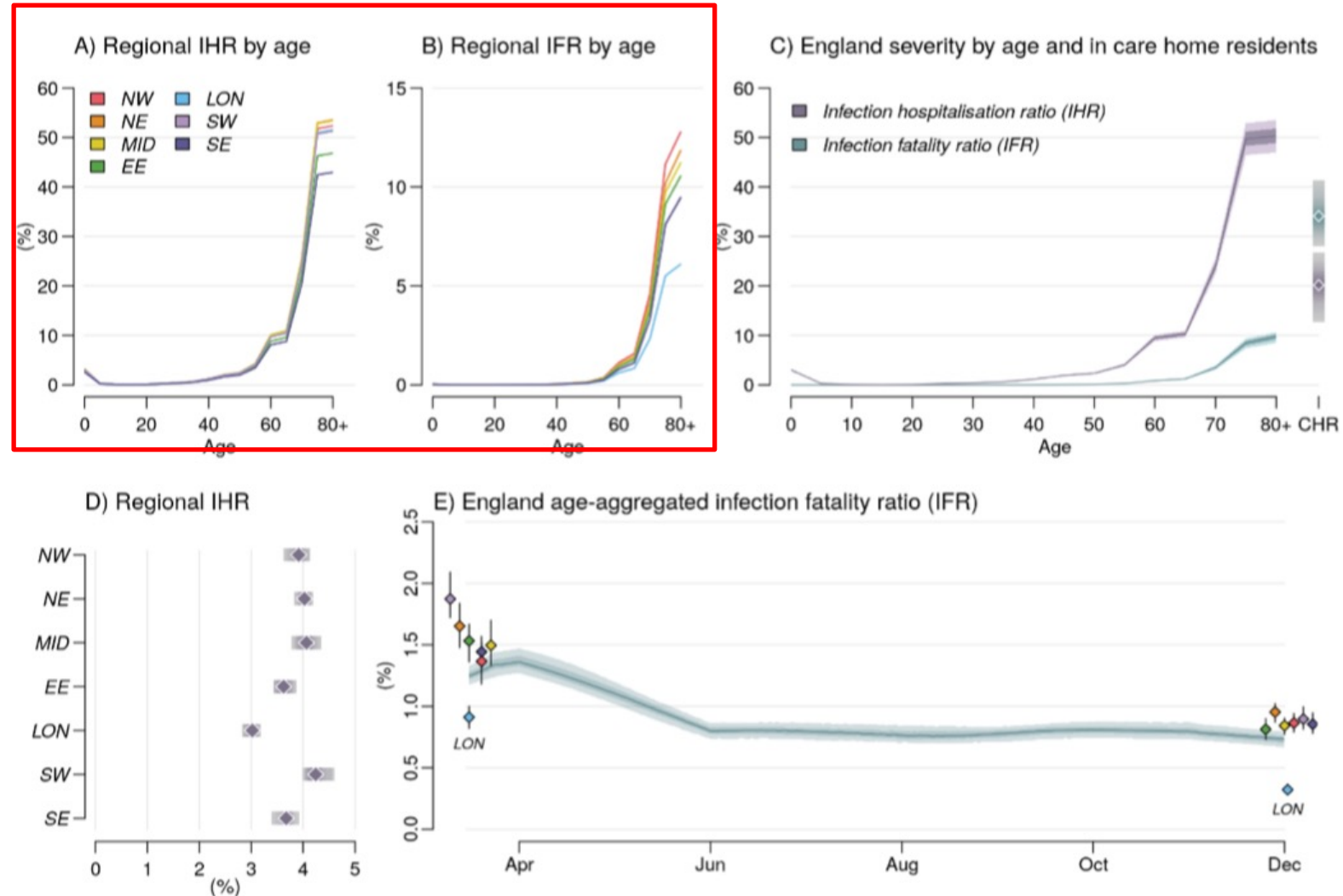
But in care homes...

- Infections continued to rise after lockdown



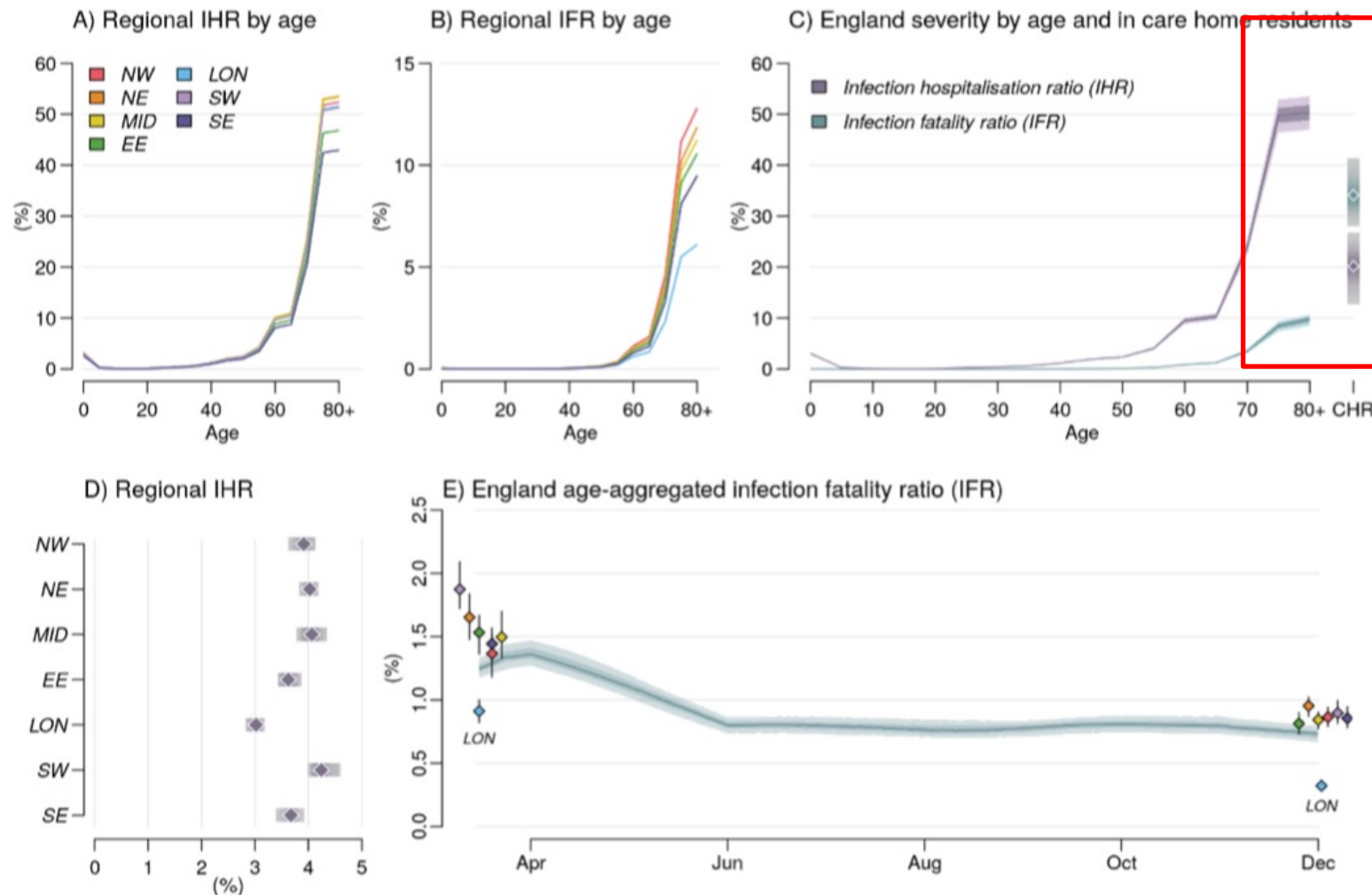
Hospitalisation and severity

- Highly age-dependant



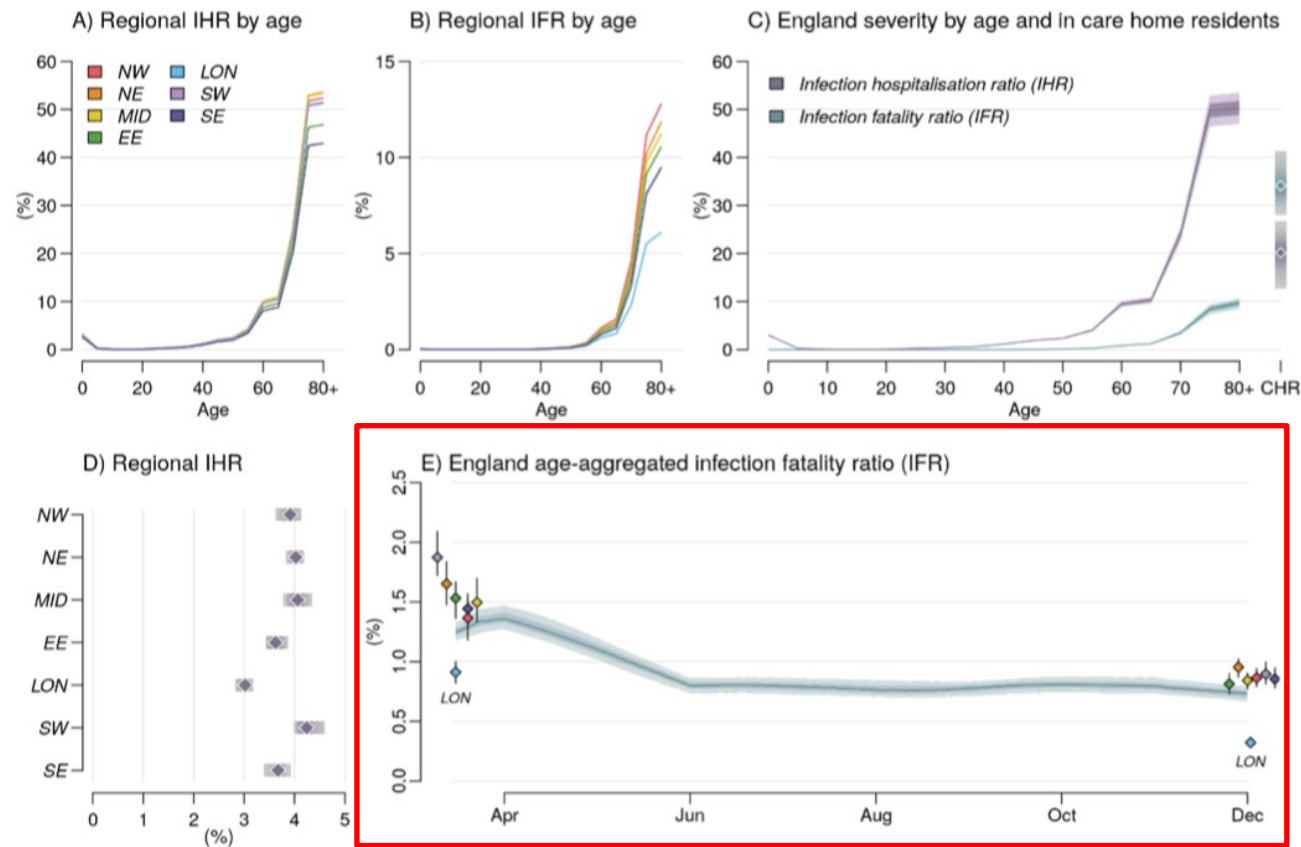
Hospitalisation and severity

- Highly age-dependant
- IFR 3.5 times higher in CHR than 80+ in the community



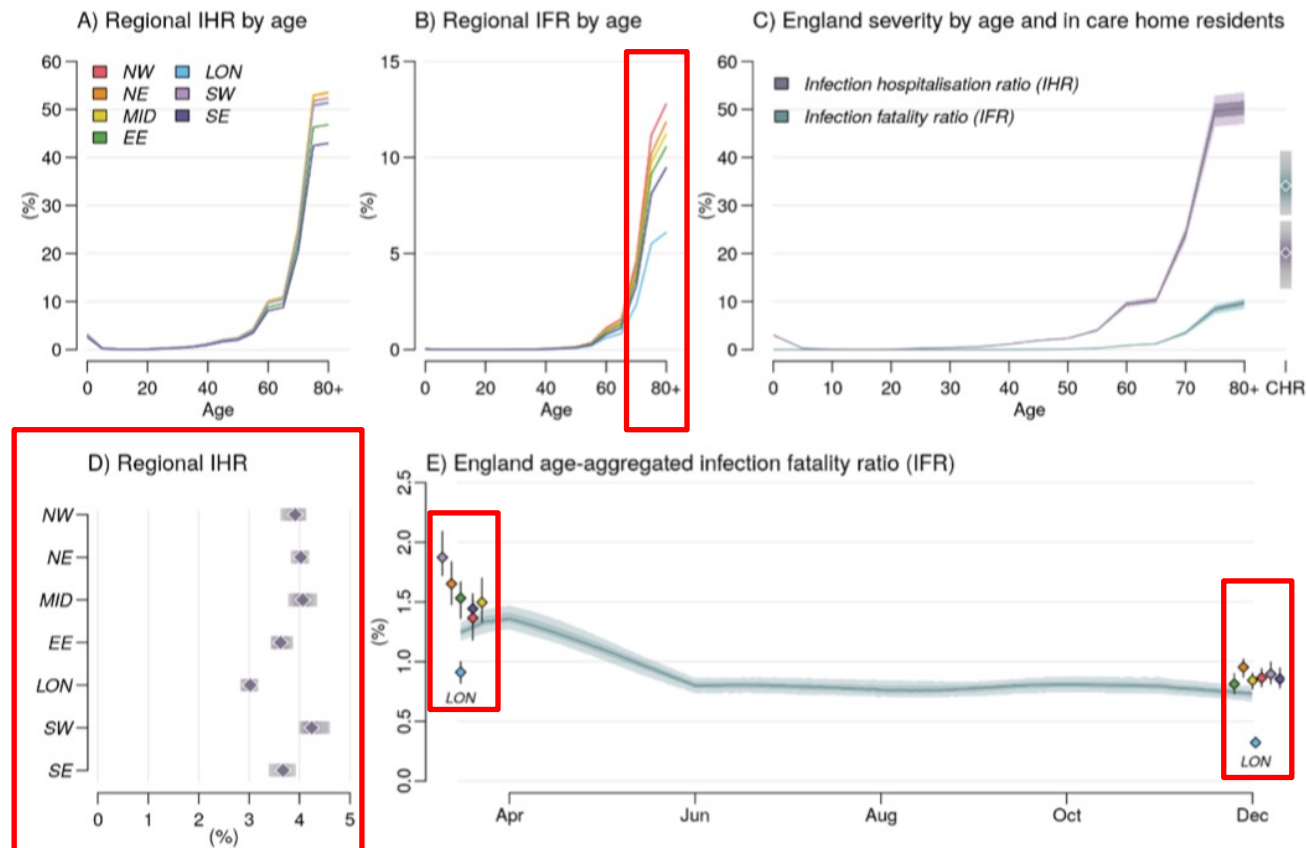
Hospitalisation and severity

- Highly age-dependant
- IFR 3.5 times higher in CHR than 80+ in the community
- IFR decreased from 1.25% to 0.77% (improved clinical management & fewer capacity constraints)



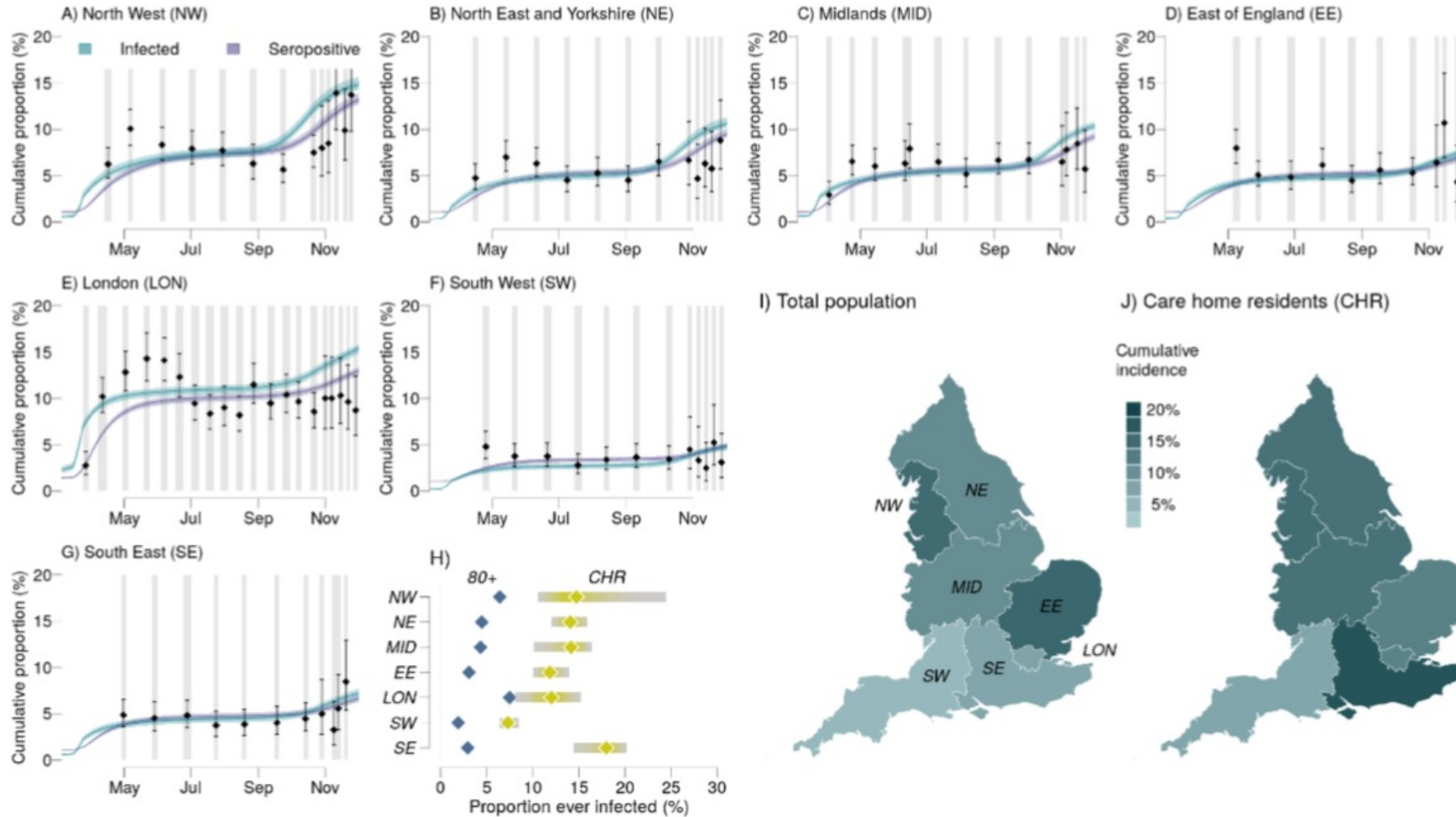
Hospitalisation and severity

- Highly age-dependant
- IFR 3.5 times higher in CHR than 80+ in the community
- IFR decreased from 1.25% to 0.77% (improved clinical management & fewer capacity constraints)
- Some differences between regions, not explained by demographics only



Attack rate far from herd immunity

- Between 4.8 and 15.4% across regions



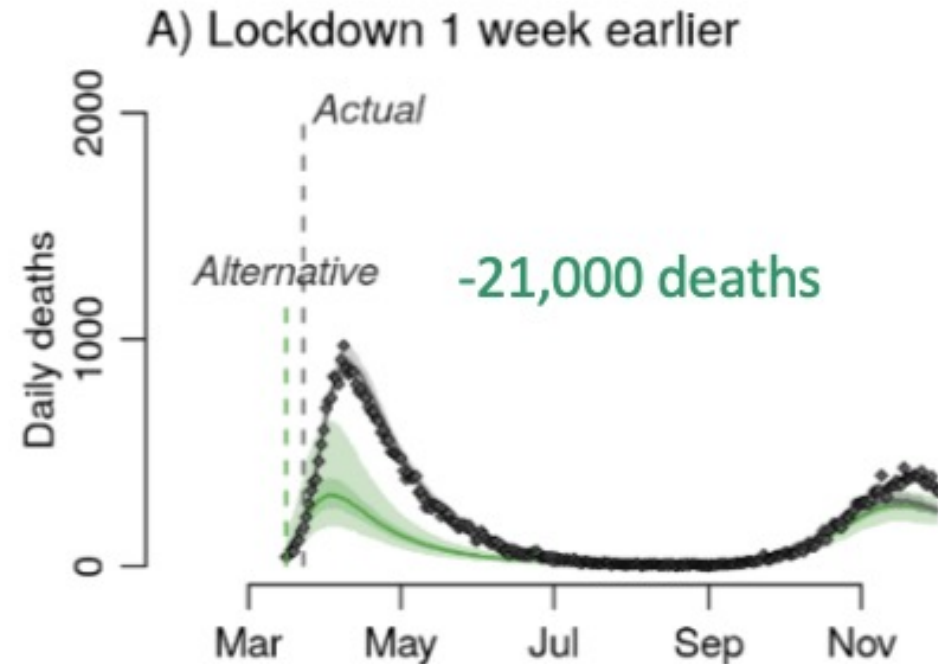
Counterfactual analyses: what if we had...

- Started lockdown 1 week earlier?
- Ended lockdown 1 week later?
- Reduced visits to care homes?

Counterfactual analyses: what if we had

- Started lockdown 1 week earlier?
- Ended lockdown 1 week later?
- Reduced visits to care homes?

Most effective measure



Summary so far

- R rapidly rising > 1 outside of lockdown
- Importance of timely initiation of control measures
- Population immunity far from herd immunity
- Decreased but still substantial severity
- Disproportionate burden among care home residents

UK approves Pfizer/BioNTech Covid vaccine for rollout next week

Sarah Boseley and Josh Halliday

Wed 2 Dec 2020 08:16 GMT



7,946

The UK has become the first western country to license a vaccine against Covid, opening the way for mass immunisation with the Pfizer/BioNTech vaccine to begin next week for those most at risk.

Christmas 2020

We have approved vaccines with high efficacy!

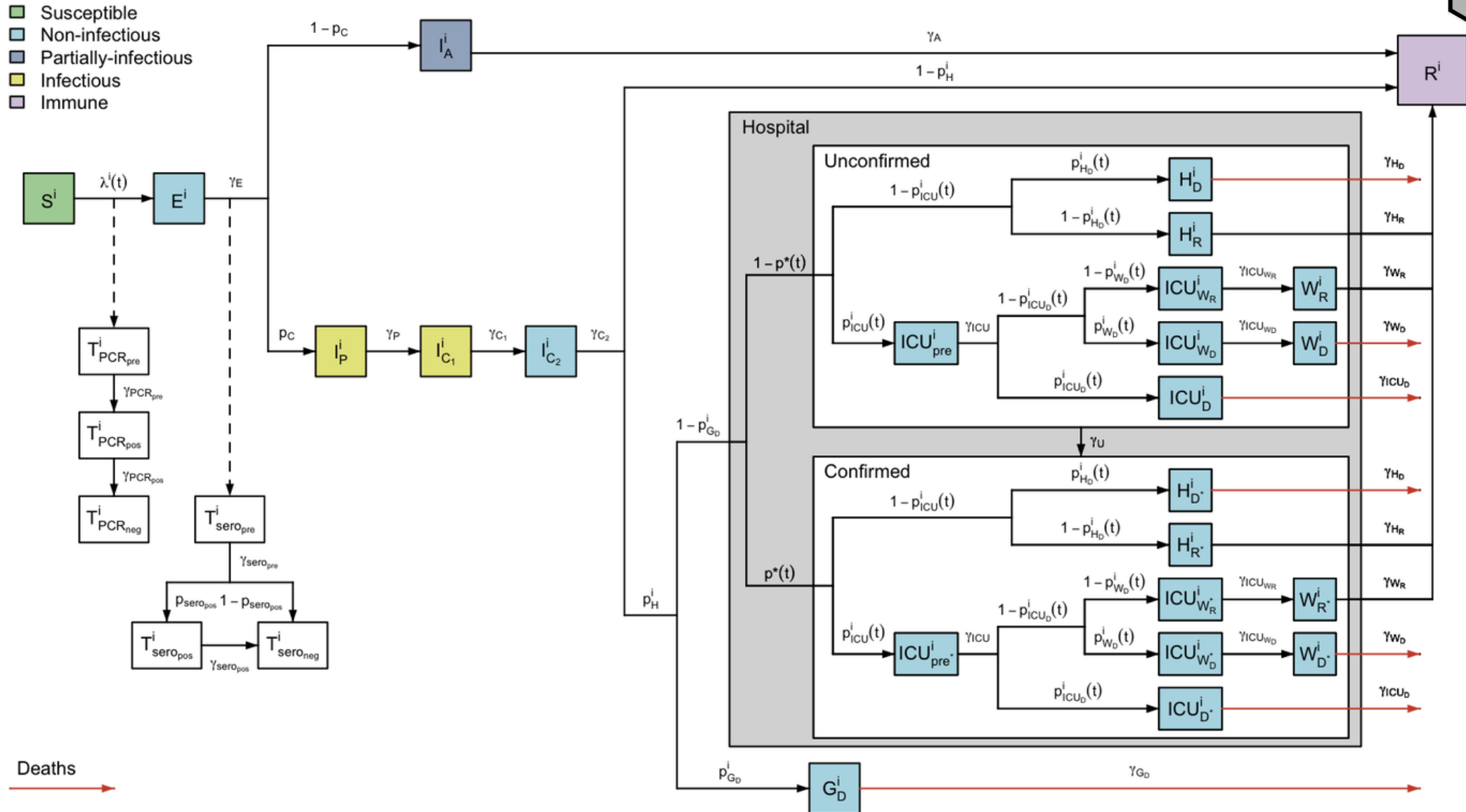
**But → novel variant, B.1.1.7 identified
Cases reported so far mainly in the UK**

On 6th January 2021, England enters their 3rd national lockdown

Key questions at that stage

- What is the expected impact of a vaccination campaign in the UK?
- How long will non pharmaceutical interventions (NPIs) need to remain in place?
- Model need to be adapted to include vaccination and a second variant

“Basic” layers of the model



More layers and Multiple data streams



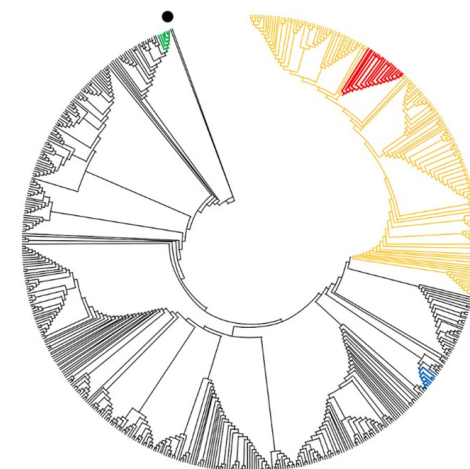
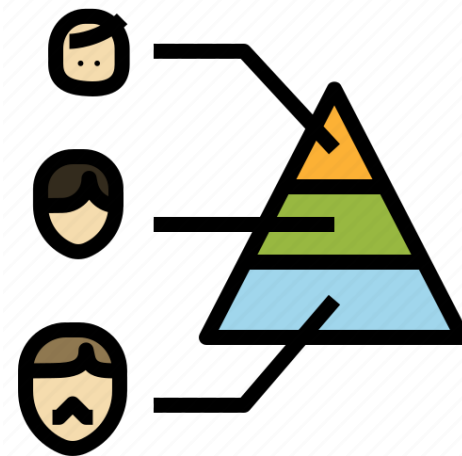
Pillar 2 cases (PCR positivity)
Prevalent infections (REACT)
Hospital admissions
Patients in general bed & ICU
Deaths (hospital & community)



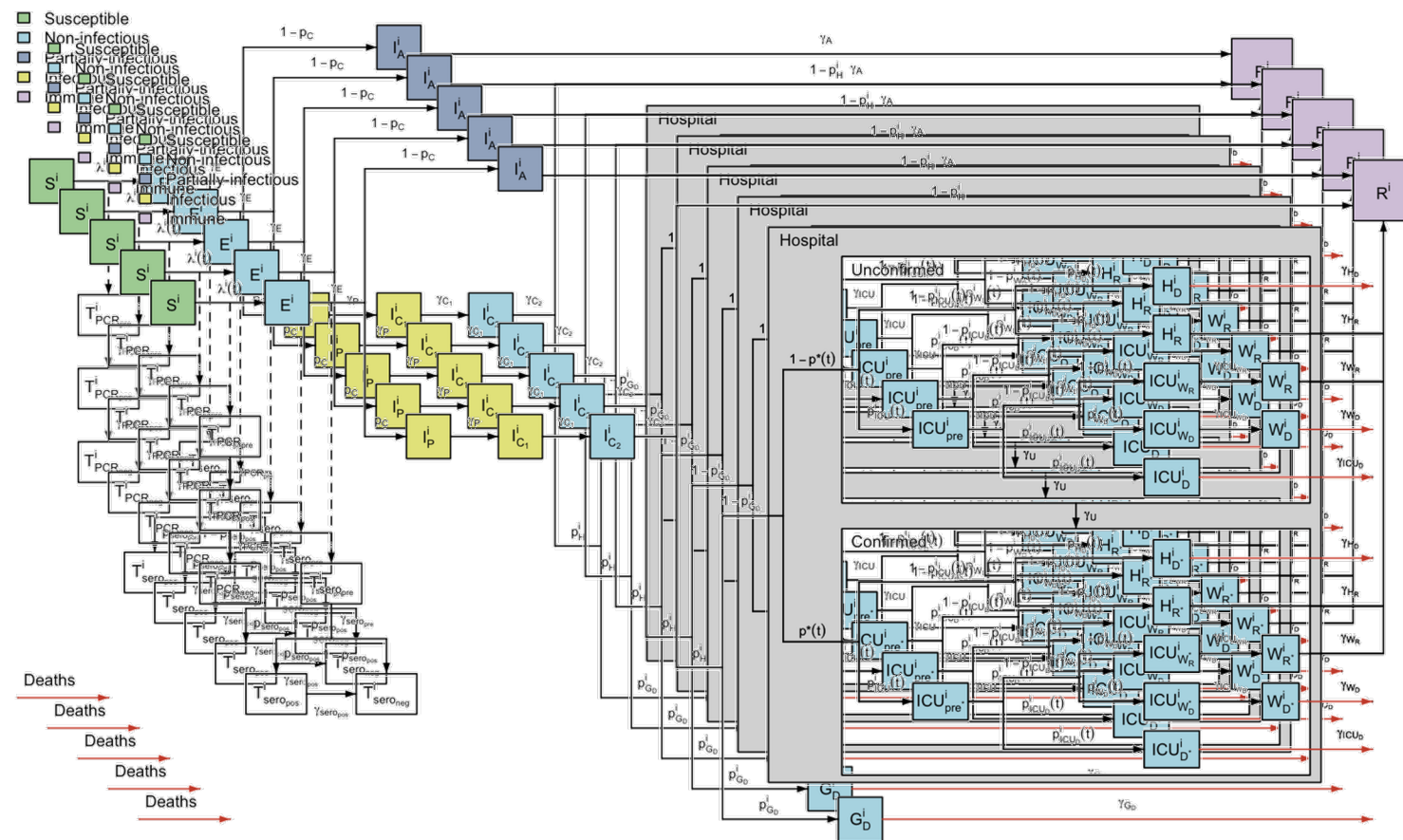
Daily 1st, 2nd and 3rd doses



VOC proportion (VAM)

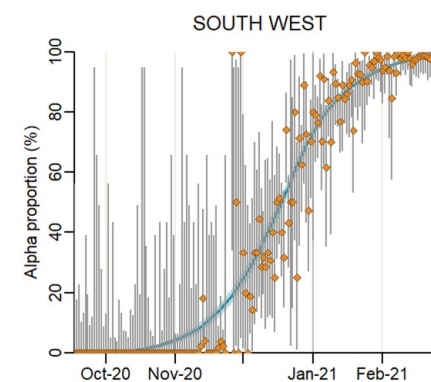
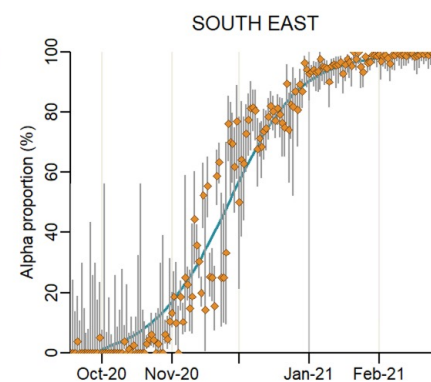
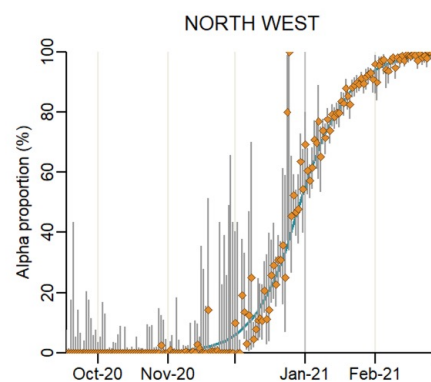
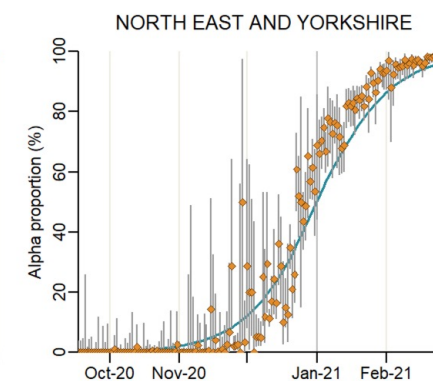
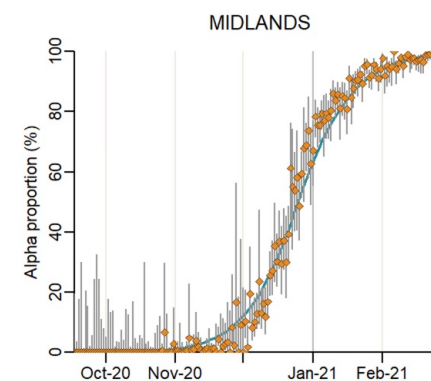
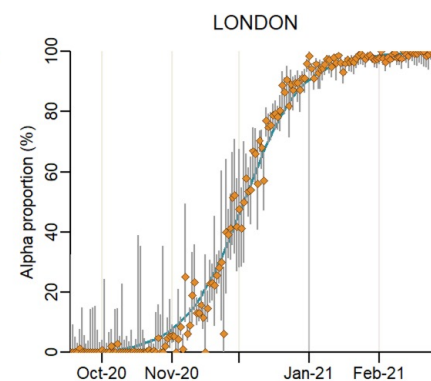
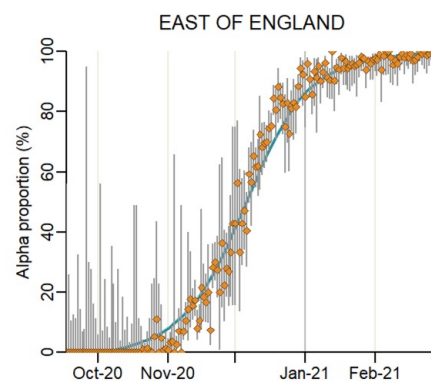
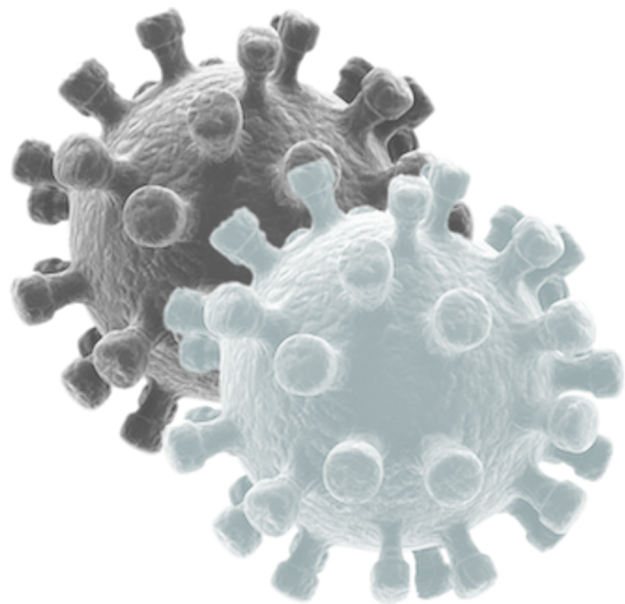


Vaccination



- Unvaccinated
- 1st dose protection
- 2nd dose protection
- Waned
- Booster protection
- Waned

Variant replacement





Sequential 2 strain models

Recovered compartments

- Strain 1
- Strain 2
- Strain 2 (reinfection)
- Strain 1 (reinfection)
- Historic variants

Fit (by NHS region):

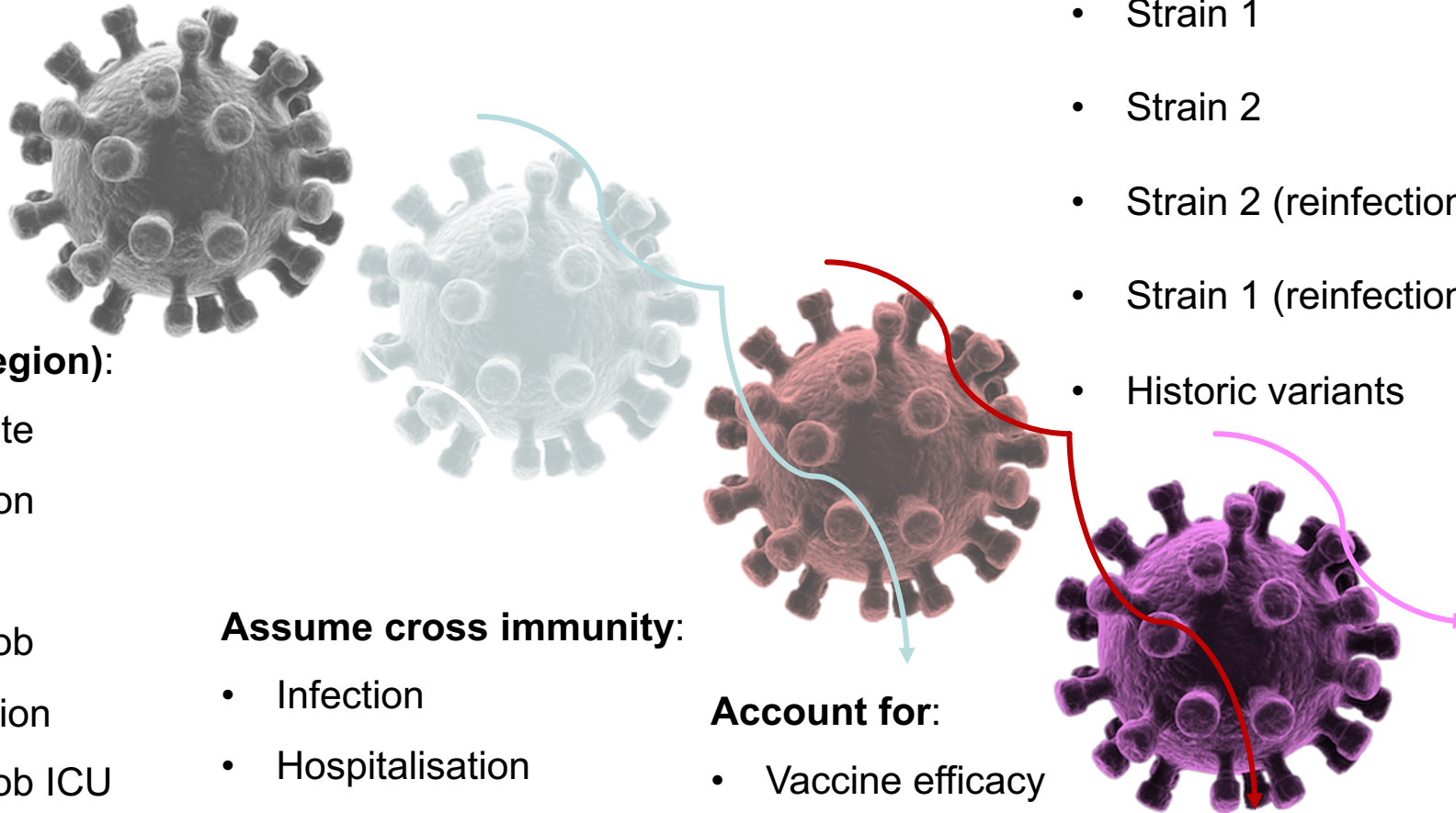
- Seeding date
- Transmission advantage
- Relative prob hospitalisation
- Relative prob ICU
- Relative prob death

Assume cross immunity:

- Infection
- Hospitalisation
- Death

Account for:

- Vaccine efficacy



MRC Centre for
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Disease Analysis

Imperial College
London

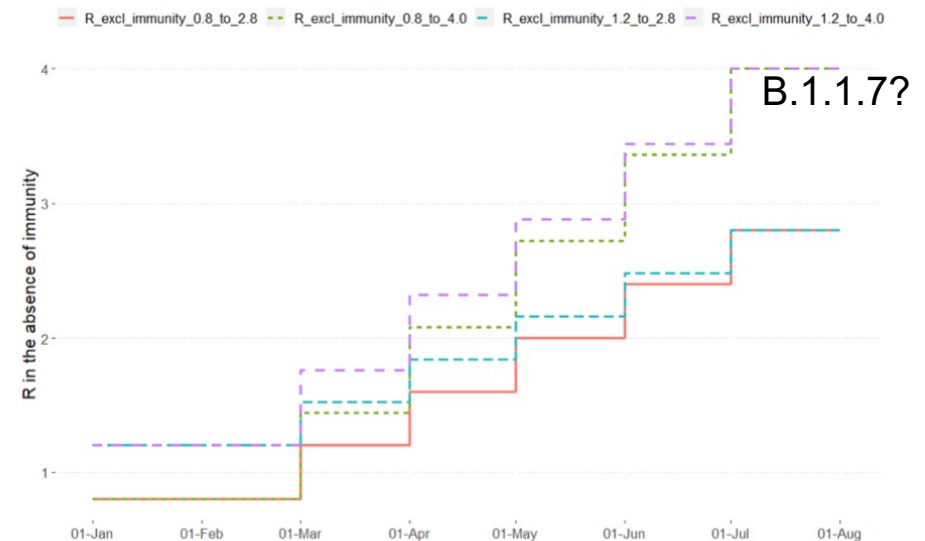
**Modelling of COVID-19
variants within a stochastic
compartmental model**

ES Knock, PN Perez-Guzman, M Baguelin

- 3 stages:

Period	Dec 2020:	Jan-March 2021:	April 2021 onwards: →
Target group	care homes	>50yo by decreasing age (+ frontline health/social workers and vulnerable)	<50yo
Vaccine	Pfizer-BioNTech	Pfizer-BioNTech / AstraZeneca	Astrazeneca (?)

- 3 vaccine roll-out scenarios
- 5 efficacy scenarios
(efficacy against disease & infection)
- Uptake ~85%
- 4 assumptions re gradual lifting of NPIs
over ~6 months



Vaccination is not the magic bullet

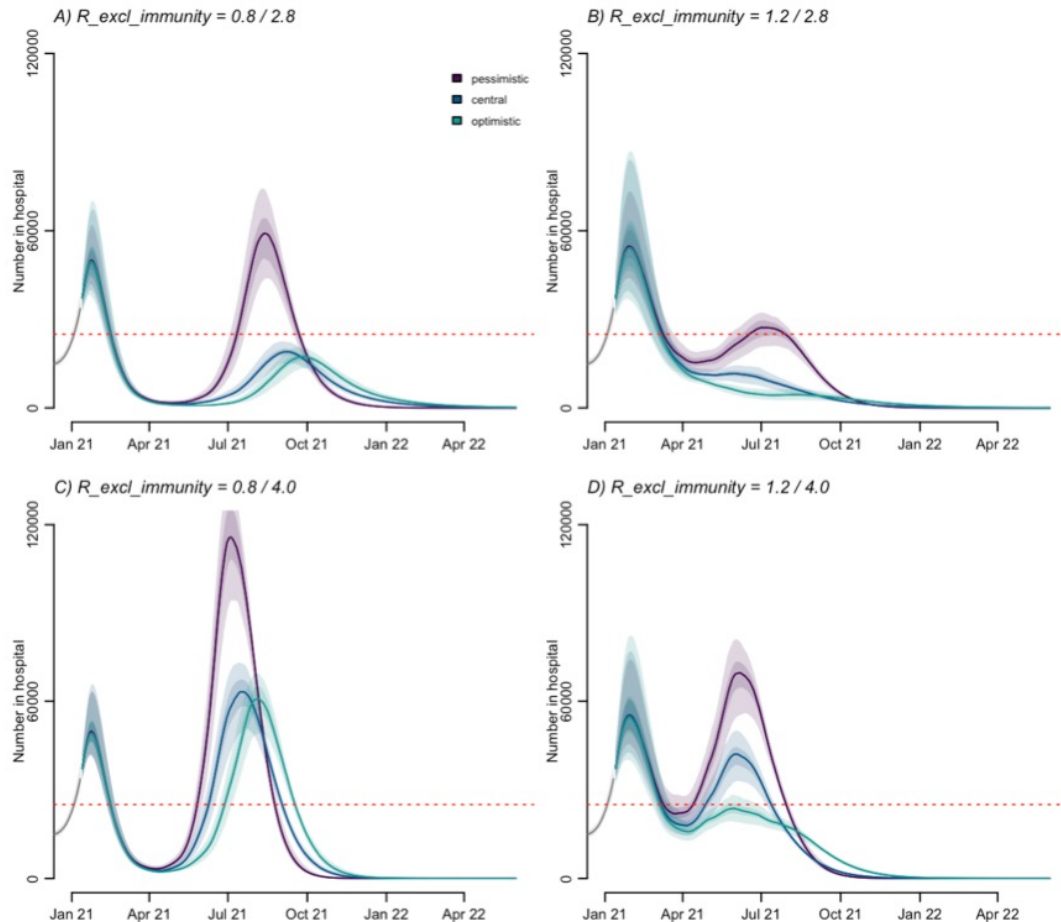


Figure 5: UK COVID-19 hospital occupancy (general wards and ICU) under a pessimistic (purple), central (blue), and optimistic (dark green) vaccine roll-out scenarios as described in Table 1. Each panel shows the impact of vaccination according to different levels of NPI relaxation translating to a gradual increase in the transmissibility ($R_{\text{excl_immunity}}$) with stepwise changes on the first of each month starting 1st March to 1st July 2021. $R_{\text{excl_immunity}}$ A) increasing from 0.8 to 2.8; B) increasing from 1.2 to 2.8; C) increasing from 0.8 to 4.0; and D) increasing from 1.2 to 4.0 as shown in Figure 3. The horizontal red dashed line denotes a threshold of 25,000 beds in the UK indicative of considerable stress for hospital capacity. N.B the y-axis is truncated to allow scenarios to be better differentiated. Thus, the peak is not shown for some scenarios.

- Even in the optimistic scenario, assumed efficacy and uptake levels not sufficient to prevent a third wave upon lifting NPIs.
- Uptake will need to be very high, and some form of NPIs to remain in place for some months

This work was considered at [SAGE 76](#) on 14 January 2021.

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/958913/S1024_SPI-M_vaccination_ask_Imperial_College.pdf

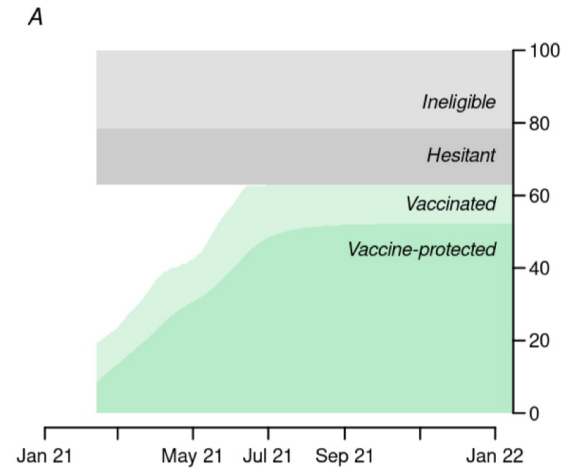
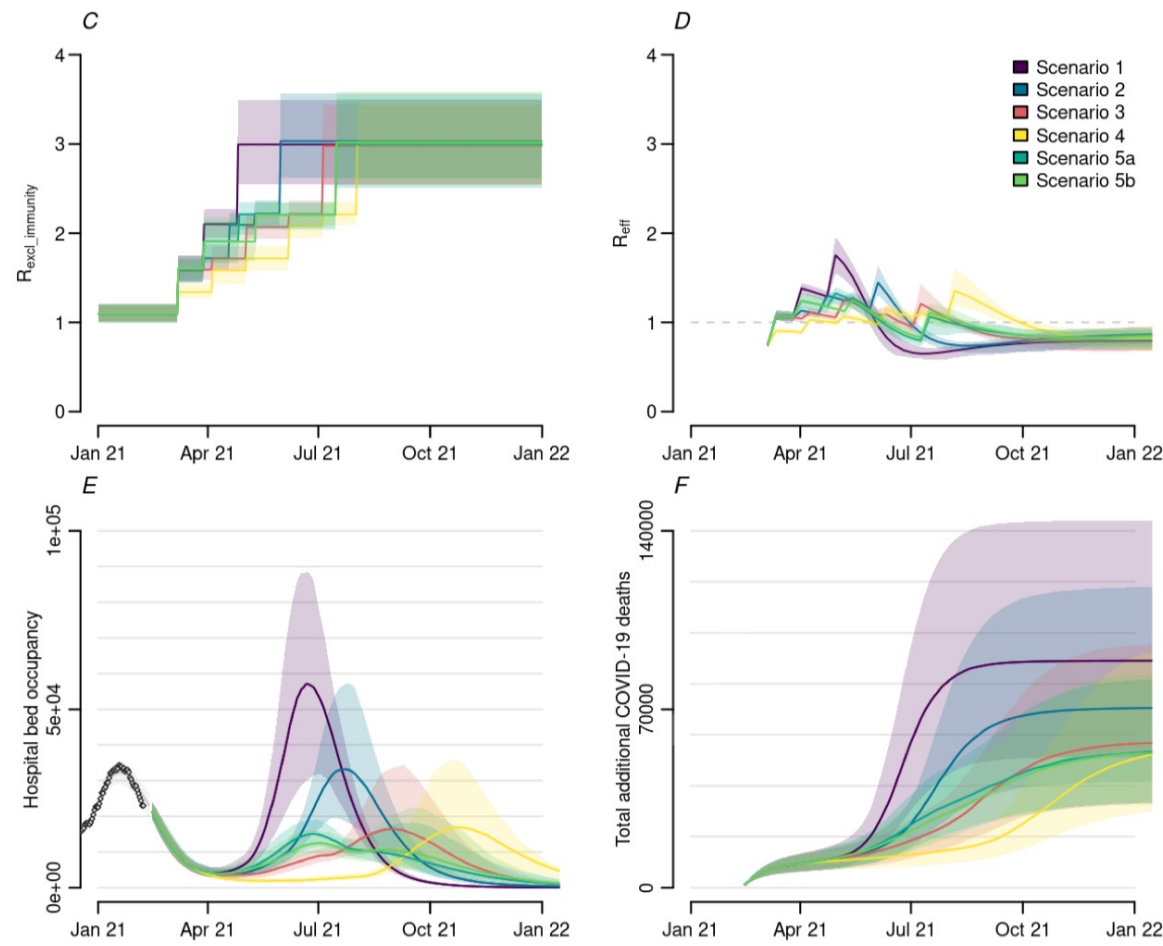
Modelling potential exit strategies

Table 1: Summary of all NPI easing scenarios where some restrictions are eased on specific dates resulting in an increase in transmissibility. The average transmissibility at each stage is shown. For the overall transmissibility and associated uncertainty see Table 2.

Date of NPI gradual release ("Full lift" still retains some baseline NPI measures such as TTI and hand hygiene^)						
Scenario 1. "Very fast"	8 March '21	29 March '21	26 April '21			
Level of NPI lifting	All schools	Tier 3 & 2	Full lift			
Average R (95% probability interval)*	1.60 (1.46-1.75)	2.10 (1.96-2.25)	3.00 (2.54-3.52) Lower adherence^: 4.00 (3.53-4.51)			
Scenario 2. "Fast"	8 March '21	29 March '21	19 April '21	10 May '21	31 May '21	
Level of NPI lifting	All schools	Tier 3	Tier 2	Tier 1	Full lift	
Average R (95% probability interval)*	1.60 (1.46-1.75)	1.70 (1.56-1.85)	2.10 (1.96-2.25)	2.20 (2.06-2.35)	3.00 (2.54-3.52) Lower adherence^: 4.00 (3.53-4.51)	
Scenario 3. "Medium"	8 March '21	5 April '21	3 May '21		7 June '21	5 July '21
Level of NPI lifting	All schools	Tier 3	Tier 2		Tier 1	Full lift
Average R (95% probability interval)*	1.60 (1.46-1.75)	1.70 (1.56-1.85)	2.10 (1.96-2.25)		2.20 (2.06-2.35)	3.00 (2.54-3.52) Lower adherence^: 4.00 (3.53-4.51)
Scenario 4. "Gradual"	8 March '21	5 April '21	3 May '21	7 June '21	5 July '21	2 Aug '21
Level of NPI lifting	Primary schools	All schools	Tier 3	Tier 2	Tier 1	Full lift
Average R (95% probability interval)*	1.35 (1.23-1.48)	1.60 (1.46-1.75)	1.70 (1.56-1.85)	2.10 (1.96-2.25)	2.20 (2.06-2.35)	3.00 (2.54-3.52) Lower adherence^: 4.00 (3.53-4.51)
Scenario 5. "New"	8 March '21 / "Step 1"	29 March '21 / "Step 2"	"Step 3"	5a: 27 April '21 **		
				5b: 11 May '21 **		
Level of NPI lifting	Schools + critical HE/FE, some children's activities	Tier 3-like + one guest per day per household indoors + outdoor hospitality	Tier 1-like			Full lift
Average R (95% probability interval)*	1.60 (1.46-1.75)	1.90 (1.62-2.21)	2.20 (2.06-2.35)			3.00 (2.54-3.52) Lower adherence^: 4.00 (3.53-4.51)

* Mean R calculated for the population according to the changes of transmissibility. ** Roll out dates of the easing strategy. For details see Table 2. ^ Lower adherence to NPI measures.

Relaxing NPIs too fast could lead to a very large third wave



This work was considered at [SAGE 81](#) on 18 February 2021.

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/958913/S1024_SPI-M_vaccination_ask_Imperial_College.pdf

England's roadmap out of lockdown

→ Published on 22 February 2021

→ 4 steps, with dates conditional on meeting predefined criteria related to

1) vaccine roll out, 2) vaccine efficacy 3) infection rates / hospitalisations 4) VOC

STEP 1 8 March 29 March	STEP 2 No earlier than 12 April At least 5 weeks after Step 1	STEP 3 No earlier than 17 May At least 5 weeks after Step 2	STEP 4 No earlier than 21 June At least 5 weeks after Step 3 All subject to review
EDUCATION 8 MARCH • Schools and colleges open for all students • Practical Higher Education courses	EDUCATION • As previous step	EDUCATION • As previous step	EDUCATION • As previous step
SOCIAL CONTACT 8 MARCH • Exercise and recreation outdoors with household or one other person • Household only indoors	SOCIAL CONTACT 29 MARCH • Rule of 6 or two households outdoors • Household only indoors	SOCIAL CONTACT • Maximum 30 people outdoors • Rule of 6 or two households indoors (subject to review)	SOCIAL CONTACT • No legal limit
BUSINESS & ACTIVITIES 8 MARCH • Wraparound care, including sport, for all children	BUSINESS & ACTIVITIES 29 MARCH • Organised outdoor sport (children and adults) • Outdoor sport and leisure facilities • All outdoor children's activities • Outdoor parent & child group (max 15 people, excluding under 5s)	BUSINESS & ACTIVITIES • Indoor hospitality • Indoor entertainment and attractions • Organised indoor sport (adult) • Remaining accommodation • Remaining outdoor entertainment (including performances)	BUSINESS & ACTIVITIES • Remaining businesses, including nightclubs
TRAVEL 8 MARCH • Stay at home • No holidays	TRAVEL 29 MARCH • Minimise travel • No holidays	TRAVEL • Domestic overnight stays • International travel (subject to review)	TRAVEL • Domestic overnight stays • International travel
EVENTS • Funerals (30) • Weddings and wakes (6)	EVENTS • Funerals (30) • Weddings, wakes, receptions (15) • Event pilots	EVENTS • Most significant life events (30) • Indoor events: 1,000 or 50% • Outdoor seated events: 10,000 or 25% • Outdoor other events: 4,000 or 50%	EVENTS • No legal limit on life events • Larger events

Delayed by 4 weeks following the emergence of Delta

<https://www.gov.uk/government/publications/covid-19-response-spring-2021/covid-19-response-spring-2021-summary>

<https://www.printweek.com/media/215988/lockdown-steps.jpg>

A retrospective modelling analysis of the roadmap out of lockdown

Aims:

- Quantify transmissibility over the course of the roadmap
- Assess the impact of Delta on the roadmap
- Evaluate the impact of the 4-week delay in step 4
- Project potential epidemic trajectories going forward
- Understand the main drivers of uncertainty in future epidemic burden

Restrictions maintained $R < 1$ until mid-May 2021 thanks to an increasing vaccine induced protection

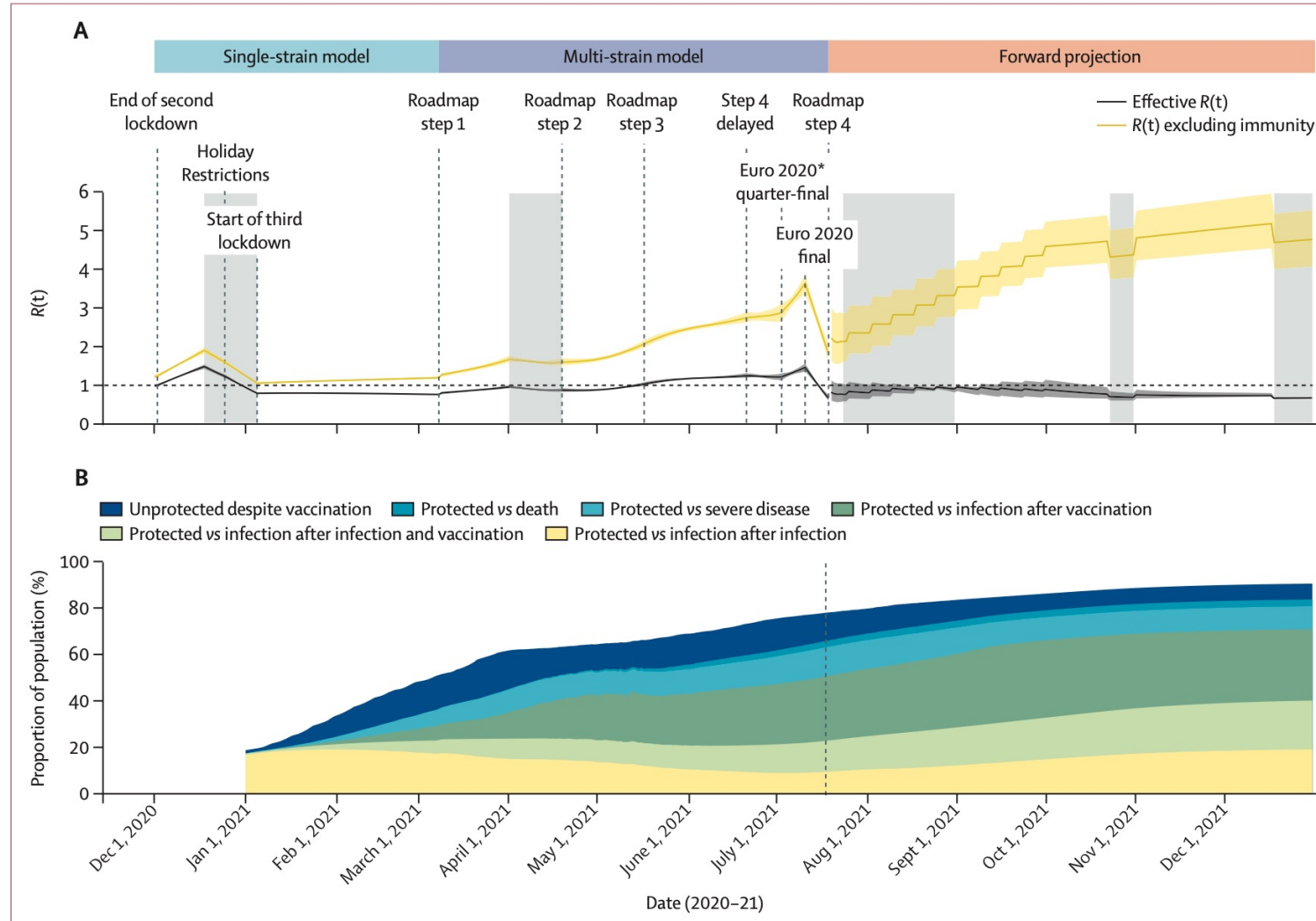


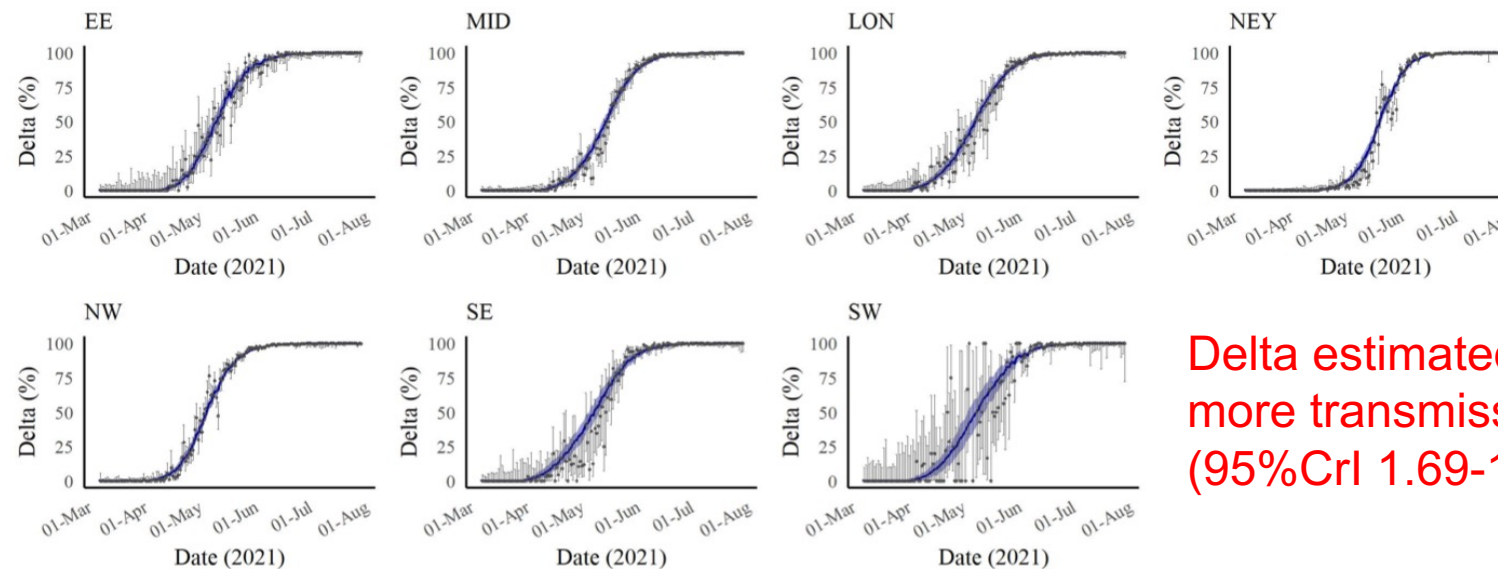
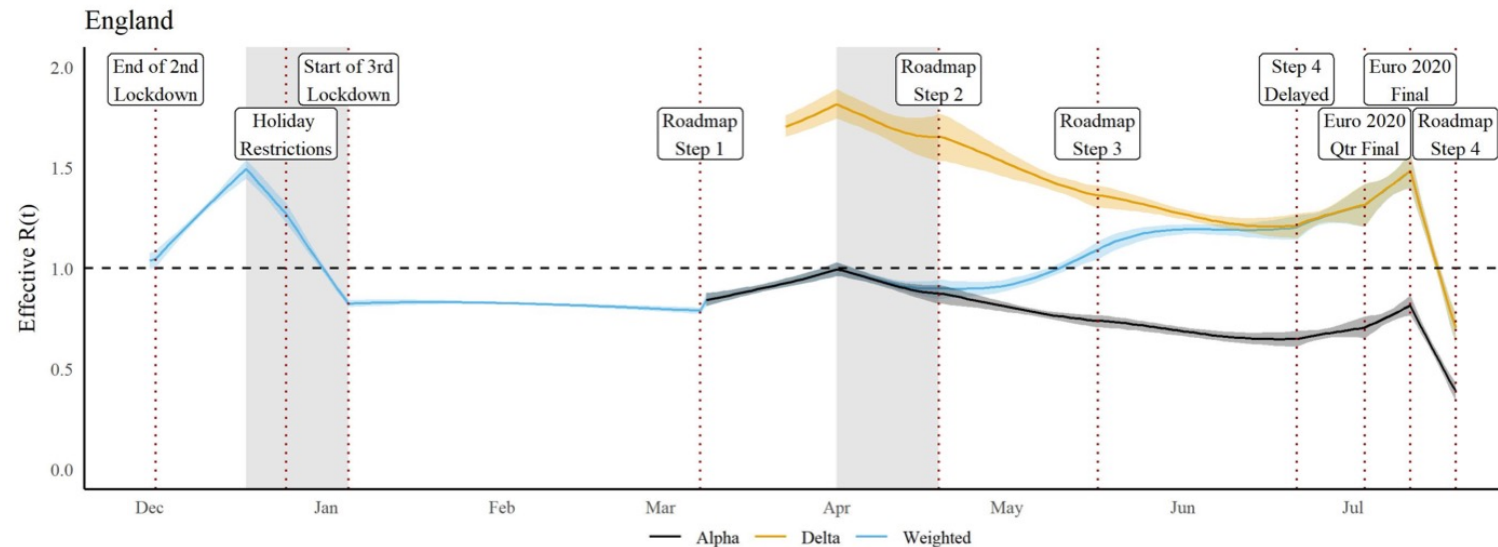
Figure 2: Prevalence-weighted effective $R(t)$ and $R(t)$ excluding infection-induced or vaccine-induced immunity (A) and proportion of the population in England protected after infection or vaccination against infection, severe disease, or death (B), over time

In the absence of Delta, R would have remained <1

MRC

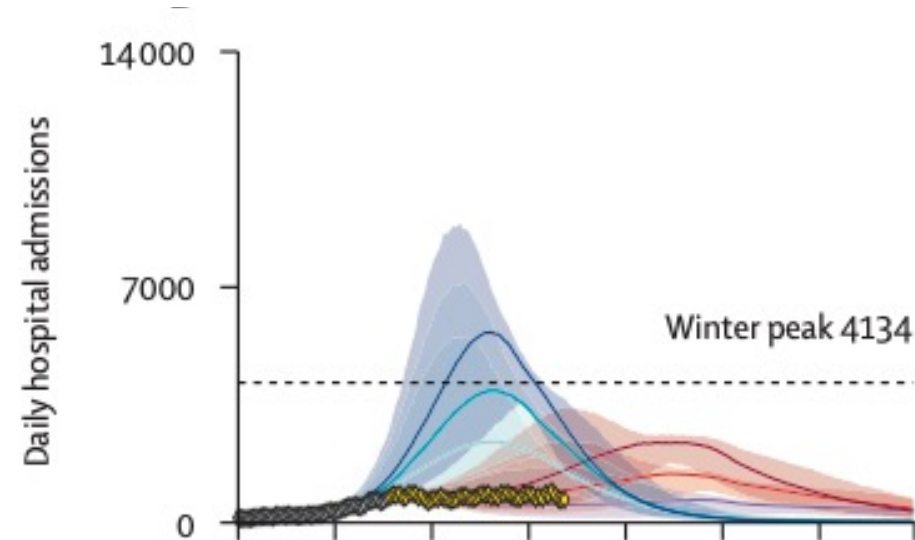
Centre for
Global Infectious
Disease Analysis

Imperial College
London



Delta estimated to be 1.76 times
more transmissible than Alpha
(95%CrI 1.69-1.83)

Delaying step 4 allowed a 3-fold reduction in peak hospitalisations



■ June (high transmissibility) ■ June (moderate transmissibility) ■ June (low transmissibility)
■ July (high transmissibility) ■ July (moderate transmissibility) ■ July (low transmissibility)

But large uncertainty remains regarding the future epidemic trajectory

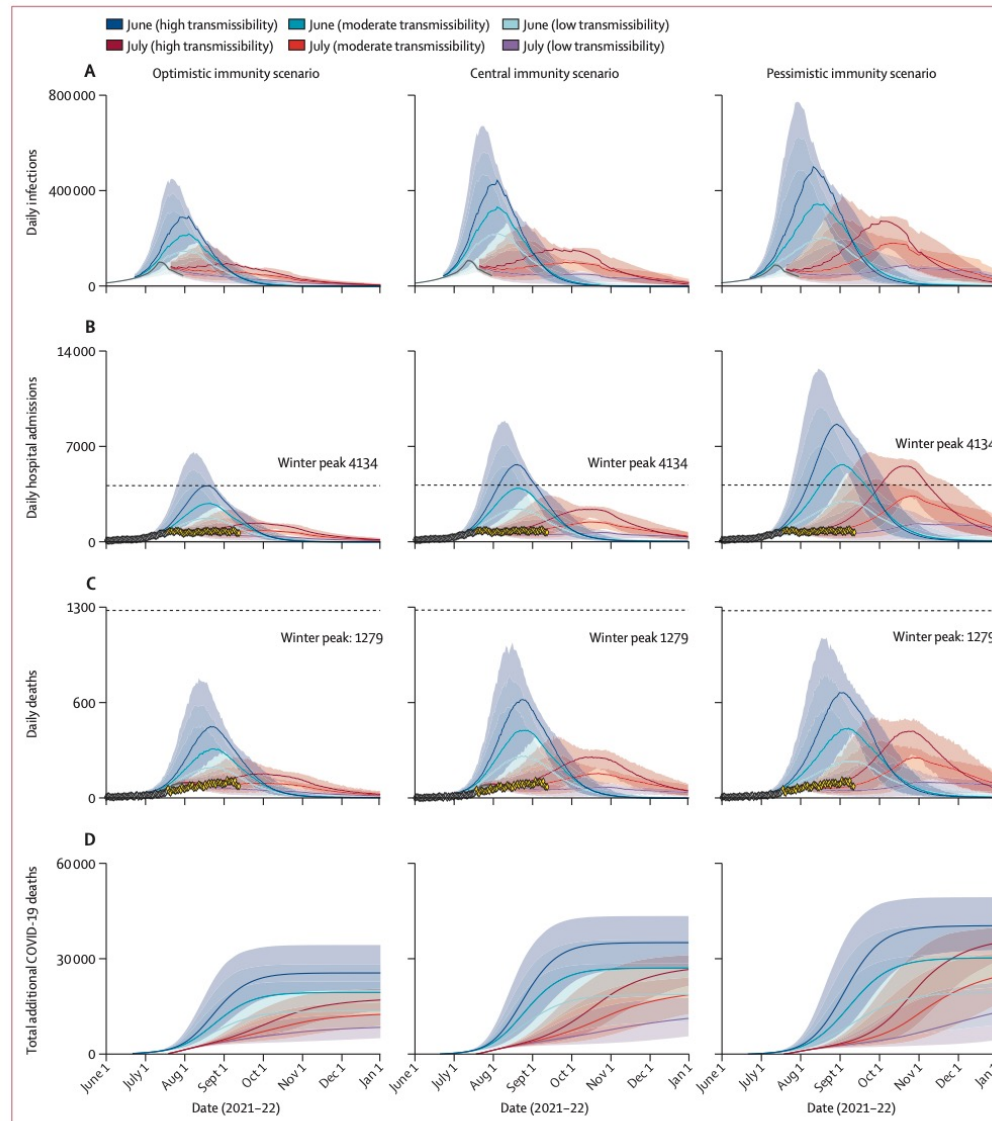


Figure 3: England COVID-19 daily infections (A), hospital admissions (B), deaths (C), and total additional deaths between June 21, 2021, and Jan 1, 2022 (D)

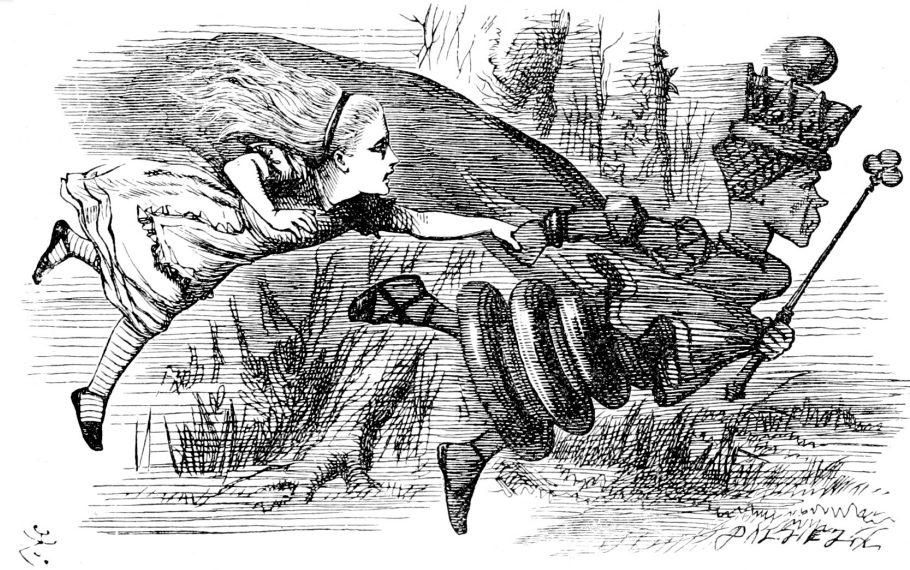
- Main sources of uncertainty:
- Levels of mixing after lifting NPIs
 - Estimates of vaccine effectiveness

Some of the challenges of real-time scenario modelling

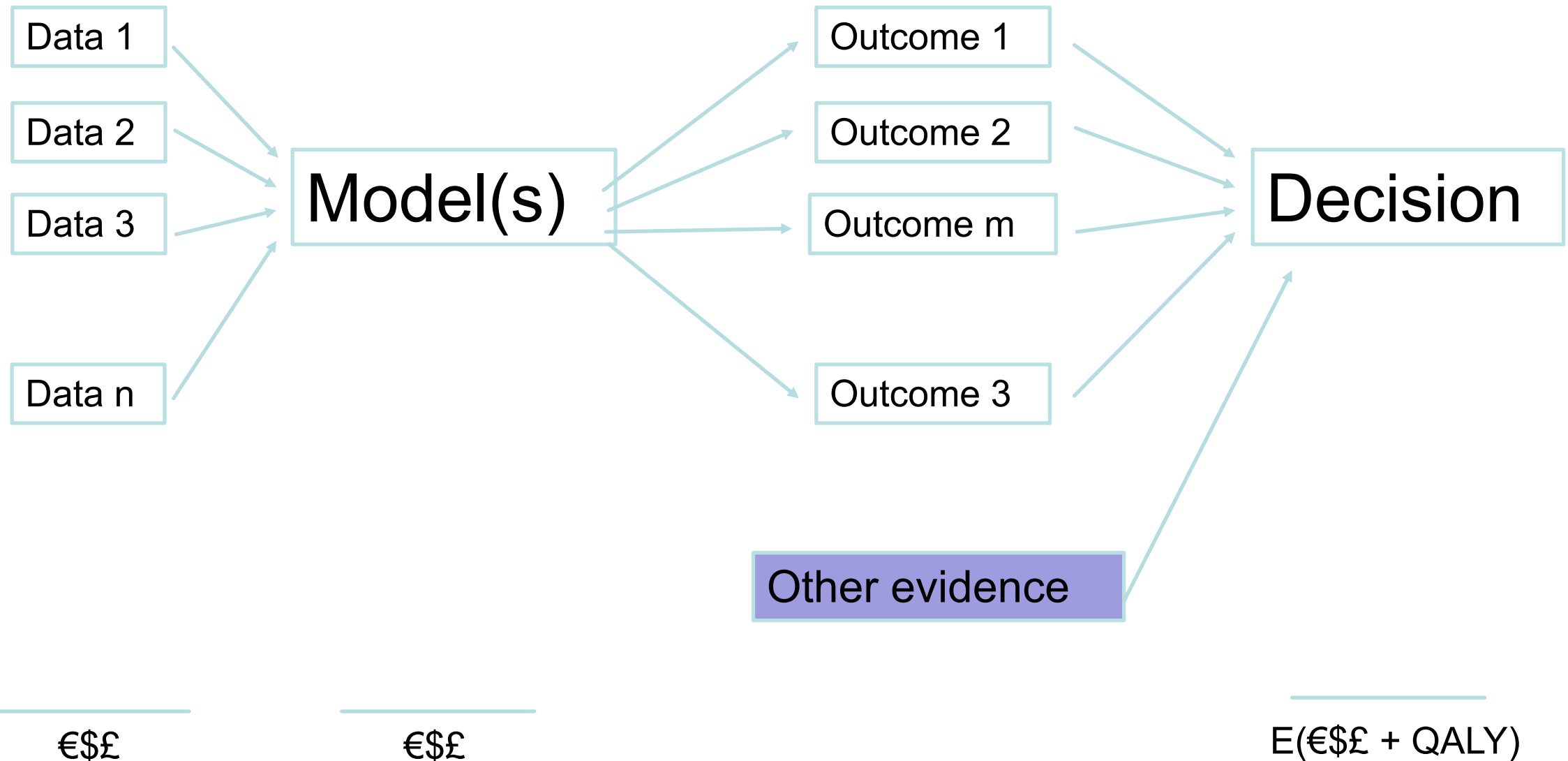
- Having to update data all the time (& data cleaning and formatting)
- Accounting for rapidly changing evidence supporting
 - model structure (e.g. variants)
 - parameter values (e.g. vaccine efficacy)
- Finding the right balance between
 - model complexity (e.g. how many age groups / how much can we save as model outputs)
 - flexibility (we refit and run forward simulation with the model at least once a week; currently a fit takes a couple of days on a high performance computing cluster)
- Conveying uncertainty
- Distinguishing scenario modelling from predictive modelling

A changing landscape

- Current model is more complex than original one:
 - Variant (WT, alpha, delta, Omicron)
 - Vaccines (and boosters)
- Effect becomes more complicated to predict
 - Immunity (vaccine and infection) waning
 - Cross immunity in a complex landscape
 - Population behaviour
- Time series are longer and longer (almost two years now)
- We need to include more data sets to inform different component of the model
- Big data but obsolete data?
 - In March 2020 we were lacking data
 - In December 2021 we couldn't inform the degree of immunity escape vs increased transmission and change in severity

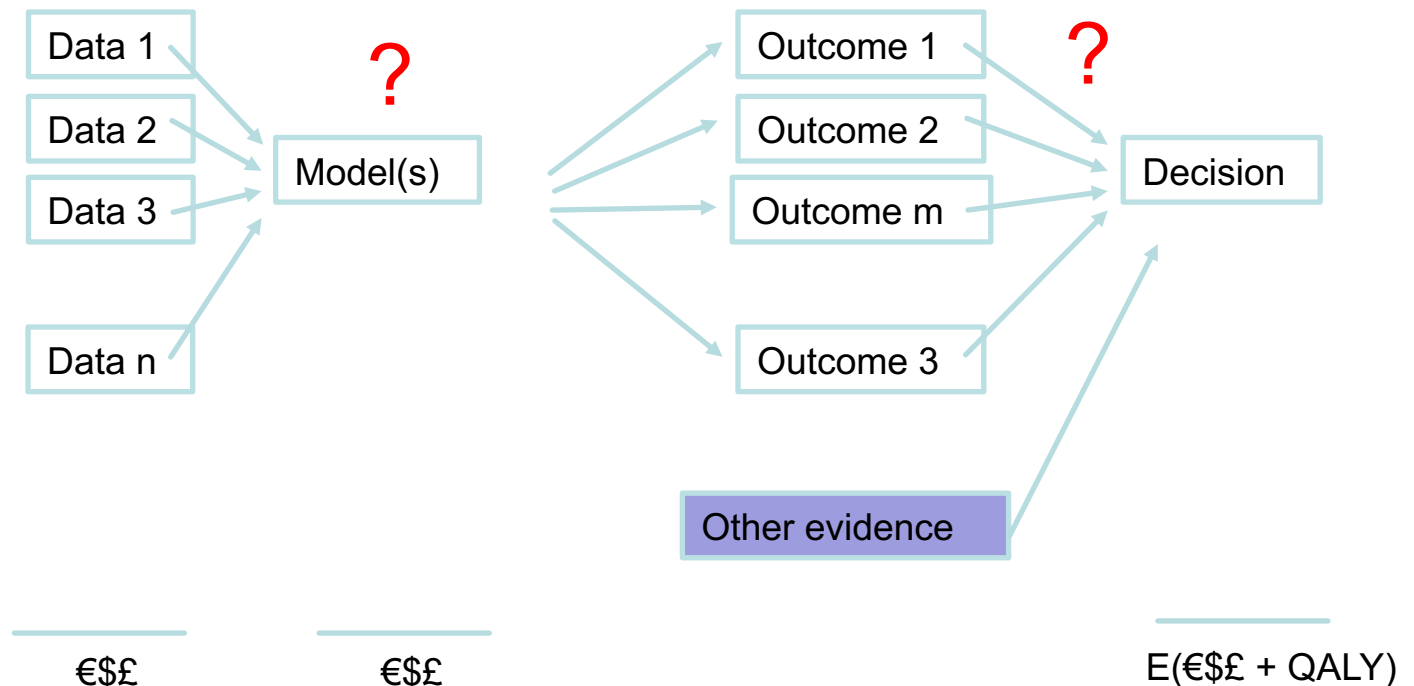


A need to understand the decision pipeline

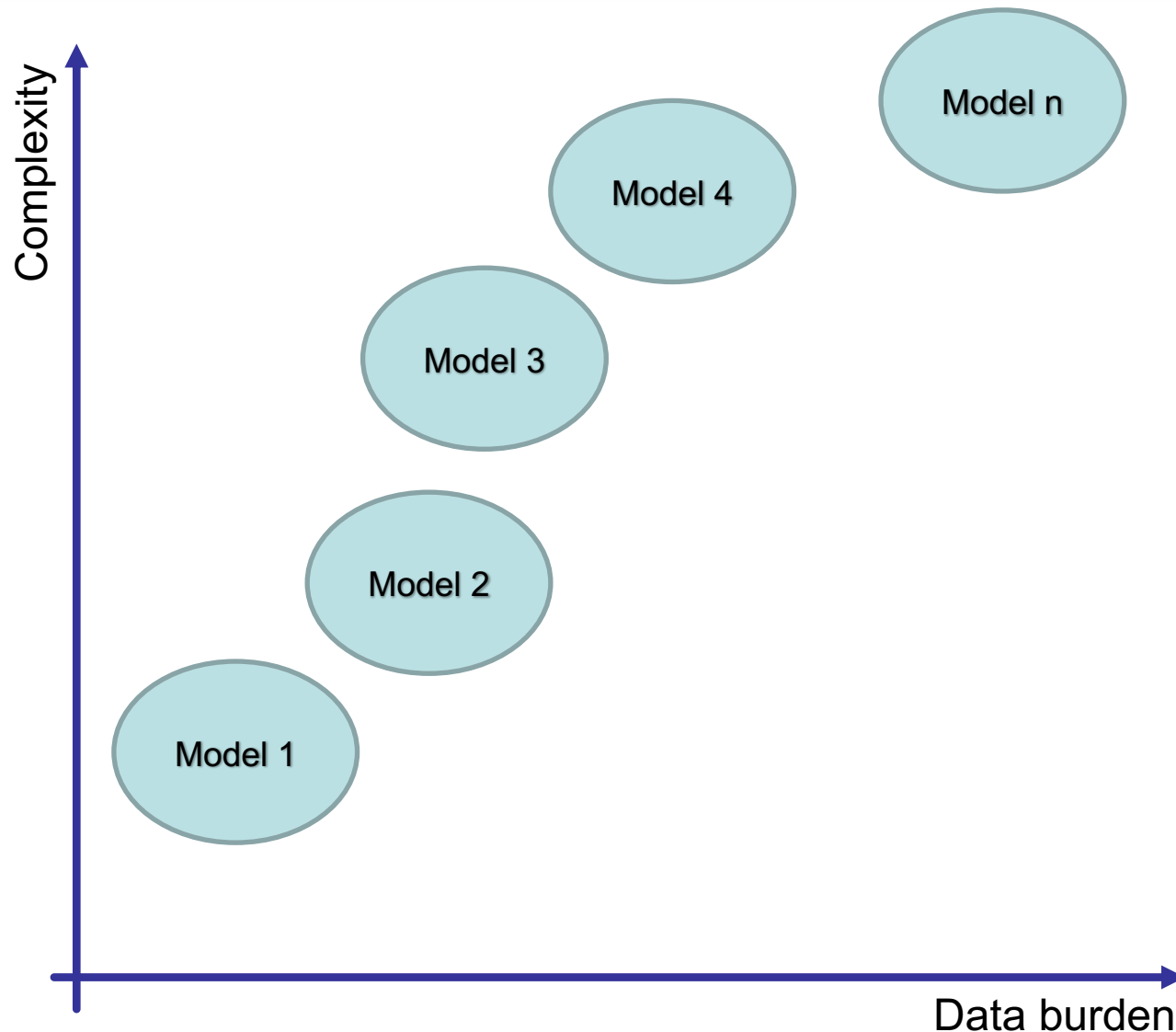


Further questions

- In order to (1) scale down **current surveillance** (2) plan for **future pandemics** we need to understand how each of the data stream informs the epidemiological outcomes and at what price
- We need to understand how the **choice of models** are driving these outcomes (model choice)
- We need to understand what outcome are **relevant for decision making** – this has likely changed during the pandemic (from deaths to pressure on the NHS)
- Importance of **public information**, data are necessary to monitor and explain decisions to the public
- Necessity of **multidisciplinary studies** including (health) economics, modelling, social sciences
- Can lead to more optimal and resilient surveillance systems



Challenges and further work



- Difficulties fitting complex models and large datasets
- Need for adapting inference methods
 - Earlier stochastic models using PMCMC with bootstrap filter
 - Current version using (for RT), hybrid deterministic-stochastic
- Difficult to do work in real-time
- Importance of expert-domain knowledge to identify mechanisms
- Danger of wrongly attributing observations
- Importance of evidence synthesis
- Importance of Bayesian framework and sensitivity analysis
- More formal model choice study?

- Mathematical models fitted in real-time to various data sources are useful to:
 - Provide an initial assessment of the level of threat posed by an emerging infectious agent
 - Continuously reassess the epidemiological situation (R, short term forecasts)
 - Use scenario modelling to compare different intervention packages (e.g. finding the right balance between pharmaceutical and non-pharmaceutical interventions)
 - Detect changes in the properties of the pathogen over time (treatments, variants)
 - Reassess the situation and control options in light of those changes
- But: very costly in terms of computer and manpower!
- Hard to sustain over time
- Automated pipelines and code testing helps
- Added value of complementary analyses using different data sources (e.g. genetic data) and performed by different groups

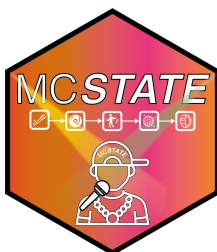
Check our tools

Our work has led to several R packages:



Efficient coding of compartmental models (deterministic or stochastic):
odin

Simple iteration of stochastic models (e.g. as part of a particle filter):
dust



Easy SMC inference for odin models:
mcstate

A stochastic SARS-CoV-2 transmission model, coded in odin:
sircovid



SOFTWARE TOOL ARTICLE



REVISED Reproducible parallel inference and simulation of stochastic state space models using odin, dust, and mcstate [version 2; peer review: 2 approved]

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*All our analyses are done using the R package **orderly**, which facilitates reproducibility*

<https://mrc-ide.github.io/odin/>
<https://github.com/mrc-ide/dust/>
<https://github.com/mrc-ide/mcstate/>
<https://github.com/mrc-ide/sircovid>
<https://github.com/vimc/orderly>

All our reports are available at:

<https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/covid-19-reports/>

Report 41 including the first part of what I presented:

<https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/report-41-rtm/>

SAGE reports summarizing the rest:

[https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/958913/S1024 SPI-M vaccination ask Imperial College.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/958913/S1024_SPI-M_vaccination_ask_Imperial_College.pdf)

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[M Imperial College London Evaluating England s Roadmap out of Lockdown.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/975910/S1183_SPI-M_Imperial_College_London_Evaluating_England_s_Roadmap_out_of_Lockdown.pdf)

Our R packages:

<https://mrc-ide.github.io/odin/>

<https://github.com/mrc-ide/dust/>

<https://github.com/mrc-ide/mcstate/>

<https://github.com/mrc-ide/sircovid>

<https://github.com/vimc/orderly>

Papers:

[1] Fitzjohn et al. Wellcome Open Research, 2021

[2] Knock et al. Science Translational Medicine, 2021

[3] Sonabend et al. The Lancet, 2021

[4] Imai et al. Lancet Public Health 2022

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