Why Does a Variant Die Out When a Better One Arrives (What are they Competing for in an Exponentially Expanding Epidemic?)

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Overview

- My approach to modelling COVID-19 and brief introduction of Covasim
- Quantifying the progressive transmissibility of emerging variants in England between September 2020 and March 2022
- Explore the impact of the transmissibility and immune escape characteristics of Omicron on Omicron's doubling rate in England from November 2021

Modelling….

- Is a tool for answering complex questions.
- Gives technical framework to simulate various scenarios subject to caveats and assumptions.
- Can inform science and offer scientific advice to policy decision makers.

Modelling questions in 2020

- Q1 (in February 2020): Is the new virus spreading exponentially and will strict social distancing measures suppress it?
- Q2 (in March/April 2020): How to incorporate Test-Trace-Isolate (TTI) strategies within an SEIR framework?
- Q3 (in May/June 2020): Is it safe to reopen schools, Universities and workplace
- Q4 (in July 2020): How do we balance protecting lives and livelihoods?
- Q5 (in August 2020): Should masks be compulsory when schools reopen in September?
- Q6 (in September 2020): Can circuit-breakers reduce the resurgence of the virus or do we need another national lockdown?
- Q6 (in October 2020): How different levels of compliance and length of isolation affect SARS-CoV-2 transmission?
- Q7 (in November 2020): What are the characteristics of the new variant?
- Q8 (in December 2020): What is the impact of different vaccination strategies?

Modelling questions in 2021

- Q1 (in February/ March 2021): What is the impact of different vaccination strategies?
- Q2 (in March 2021): Is it safe to proceed with the different steps of the Reopening Roadmap?
- Q3 (in May/June 2021): Do we need to delay the Step 4 of the Reopening Roadmap?
- Q4 (in June/July 2021): What would be the impact of vaccination of 12-15 years old?
- Q5 (in August 2021): Should masks be compulsory when schools reopen in September 2021?
- Q6 (in October/November 2021): What is the transmissibility of Omicron?
- Q7 (in October/November 2021): What would be the impact of a lockdown or circuit breaker over Christmas 2021?
- Q7 (in November/December 2021): What would be the impact of booster vaccinations in Omicron's growth?

Modelling questions in 2022

- Q1 (in January 2022): Is it safe to reopen schools in January 2022?
- Q2 (in February 2022): What would be be impact if we reopened society fully at the end of March 2022?
- Q3 (in March 2022 and beyond): What would be the impact of different strategies against different emerging variants?
- Q4 (in March 2022 and beyond): What is the impact of the COVID-19 tracing App?

Case studies

Quantifying the progressive transmissibility of emerging variants in England

- **Statistical analysis of COG-UK data combined with Covasim modelling**
- Paper on B.1.177 vs Alpha vs Delta transmissibility difference accepted (subject to revisions) at Phil Trans Roy Soc A and preprint at https://doi.org/10.1101/2021.12.30.21267090
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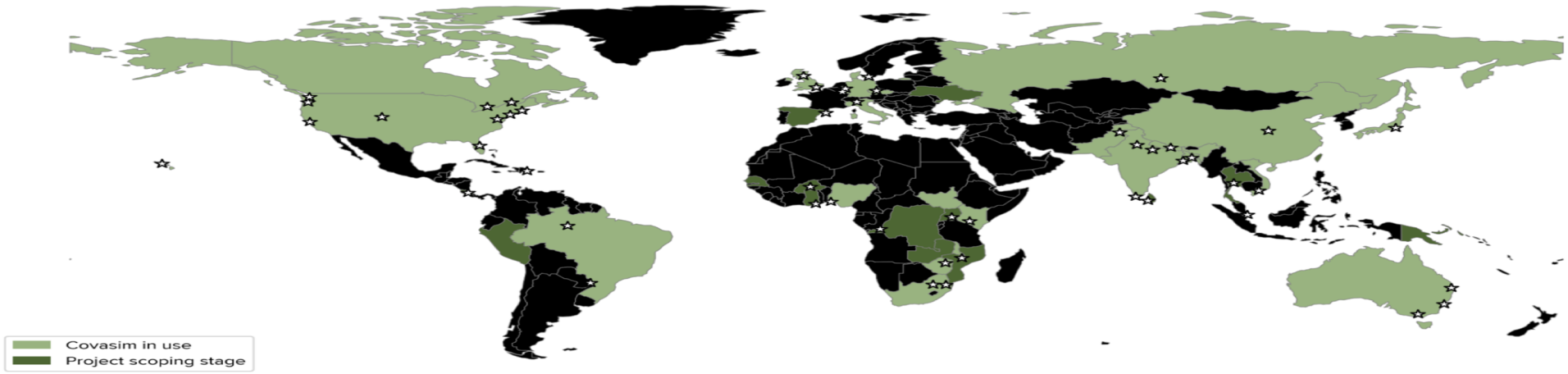
Covasim model

- Developed by the Institute for Disease Modelling at the Bill & Melinda Gates Foundation's Global Health Division
- UK specific model developed and lead by me since the onset of the pandemic
- One of the models used by SPI-M and UK Health Security Agency for nowcasting the epidemic and producing medium term projection



What is Covasim?

COVID-19 **A**gent-based **Sim**ulator

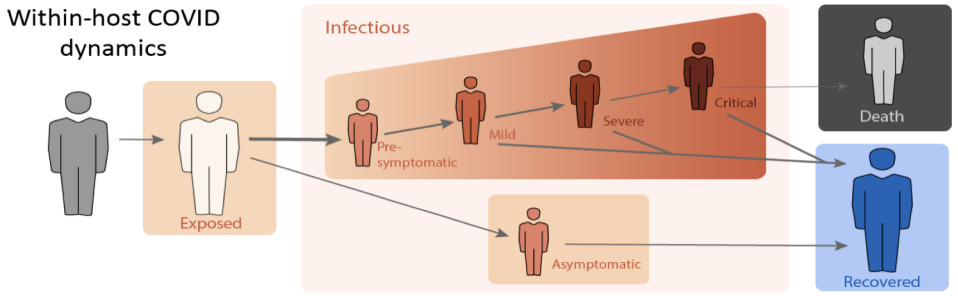
http://covasim.org

- Agent-based
- Stochastic
- Open source
- Pure Python
- Straightforward installation (`pip install covasim`)
- Tested & fully documented
- Designed in partnership with public health officials, epidemiologists, & software developers

How does Covasim work?

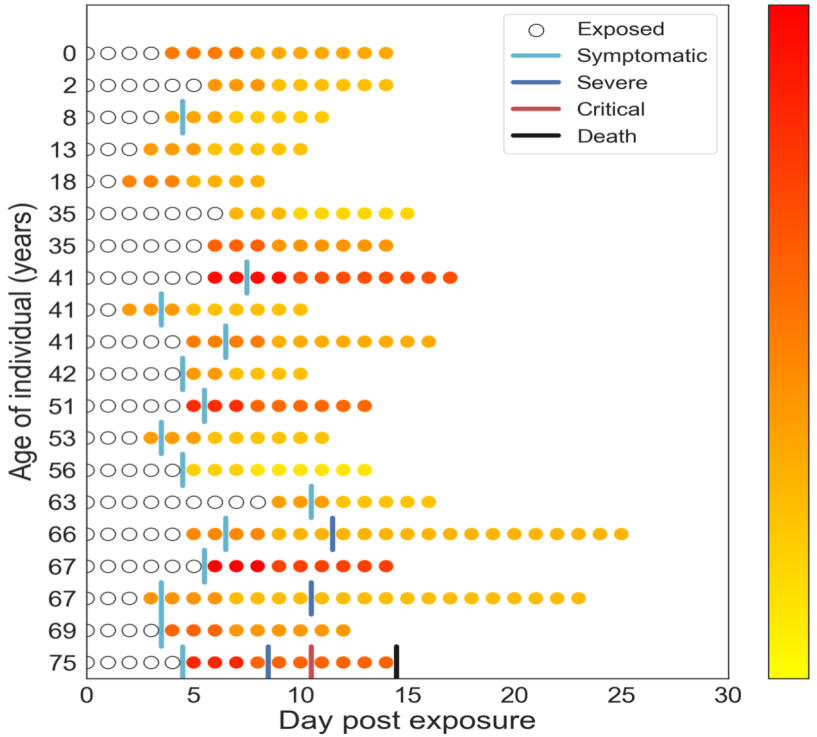
Disease progression

- Individuals progress through disease states: susceptible, exposed, infectious (asymptomatic, presymptomatic, mild, severe, critical), recovered, dead
- Progression depends on age and comorbidities



Disease transmission

- Viral load varies over time and individuals => affects transmissibility

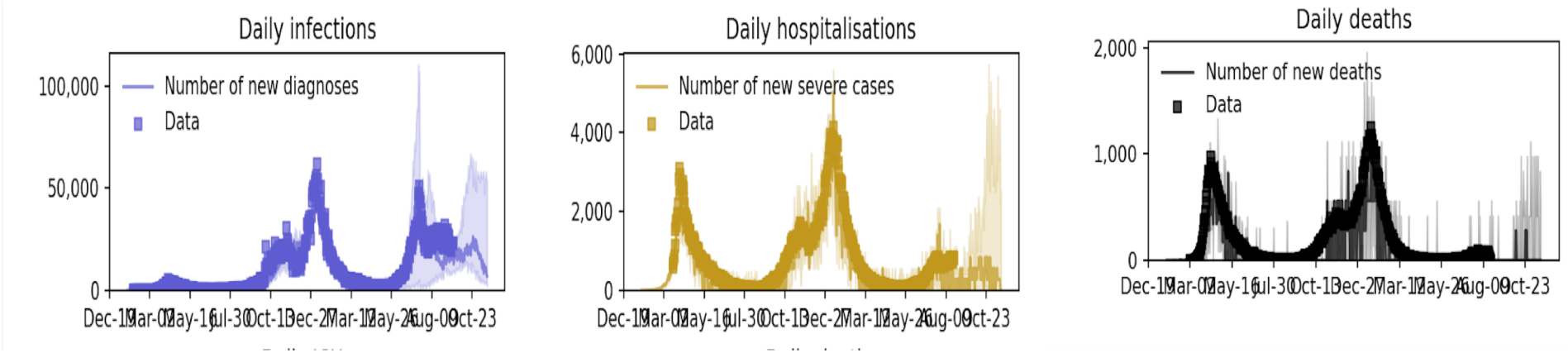


Application of Covasim to the UK

- UK (until December 2020) and England specific models tracking the epidemic since March 2020
- Calibrated to daily reported cases, hospital and ICU admissions from https://coronavirus.data.gov.uk/ and LFDs (i.e. asymptomatic testing) and PCR (i.e. symptomatic testing) tests as well as different variants timeseries using genomic data
- Modelled vaccine efficacy as per SPI-M models and age-specific vaccine rollout
- Waning of immunity included
- Modelling a number of important policy decision eg reopening after the 1st, 2nd and 3rd national lockdown, schools reopening in Sep 2020 and school closure in January 2021, reopening at different stages of the Roadmap, impact of different vaccination strategies
- Models for Wales, Scotland and Northern Ireland in development

Calibration

- Calibrated to COVID-19 dashboard data on daily infections, hospital admissions, hospital occupancy and deaths from https://coronavirus.data.gov.uk/
- Using Optuna - A hyperparameter optimization framework seeking optimal values of parameters related to initial seeded infections, transmission probability and monthly testing probabilities, contact-tracing and isolation level.
- Social mobility data used to inform ranges of social mixing parameters at points of change eg around Christmas 2020 and opening/closing of schools.
- Genomic Surveillance data used to match the seeding of different variants at different timepoints and for statistical analysis.



Examples

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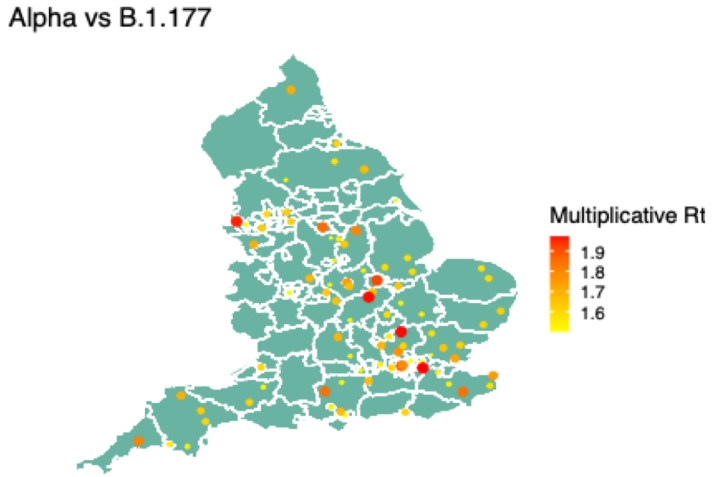
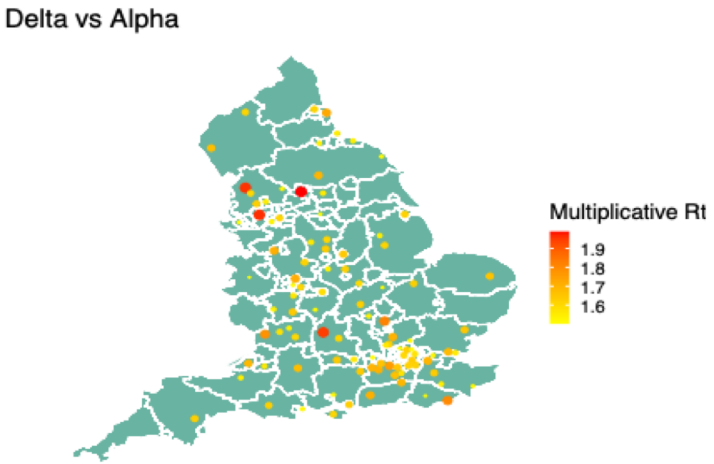
Methodology

- Publicly available data from the COG-UK Consortium between September 01, 2020 and July 12, 2021.
- Multivariate regression analysis on the count of the variant cases in each of the 311 lower tier authorities (LTLAs) using hierarchical generalized additive models (HGAM) quantified the transmissibility of the B.1.177, Alpha and the Delta variants.
- Covasim was calibrated to match the epidemic trajectories, also quantifying the transmissibility of the B.1.177, Alpha and the Delta variants over the study period.

B.1.177 vs Alpha vs Delta

- B.1.177 was 20% more transmissible than the wildtype.
- Alpha was 50-80% more transmissible than B.1.177.
- Delta was 65-90% more transmissible than Alpha.
- Variants transmissibility was heterogeneous across the regions.

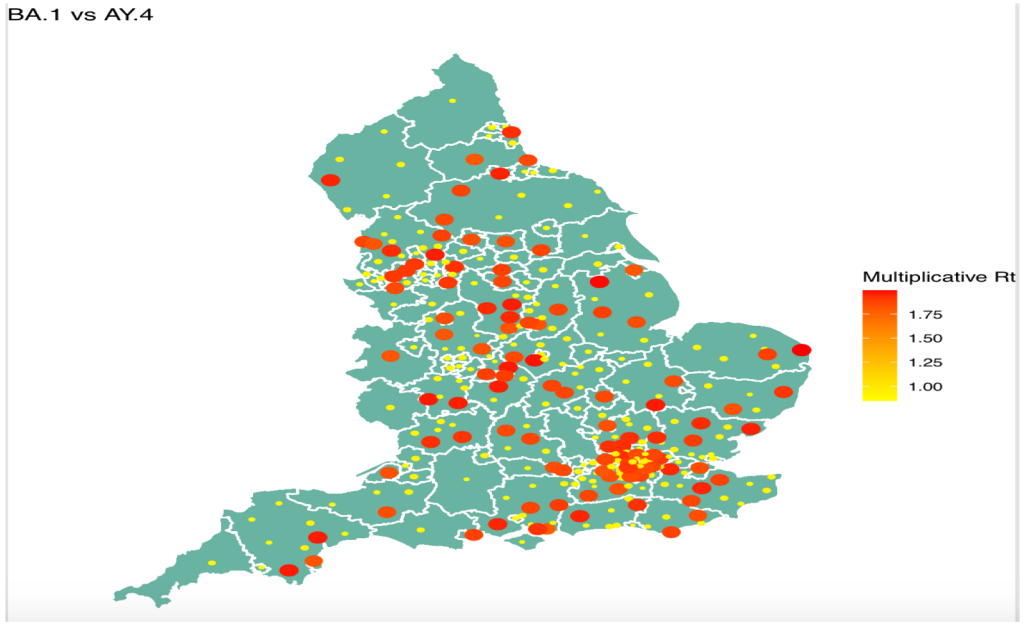


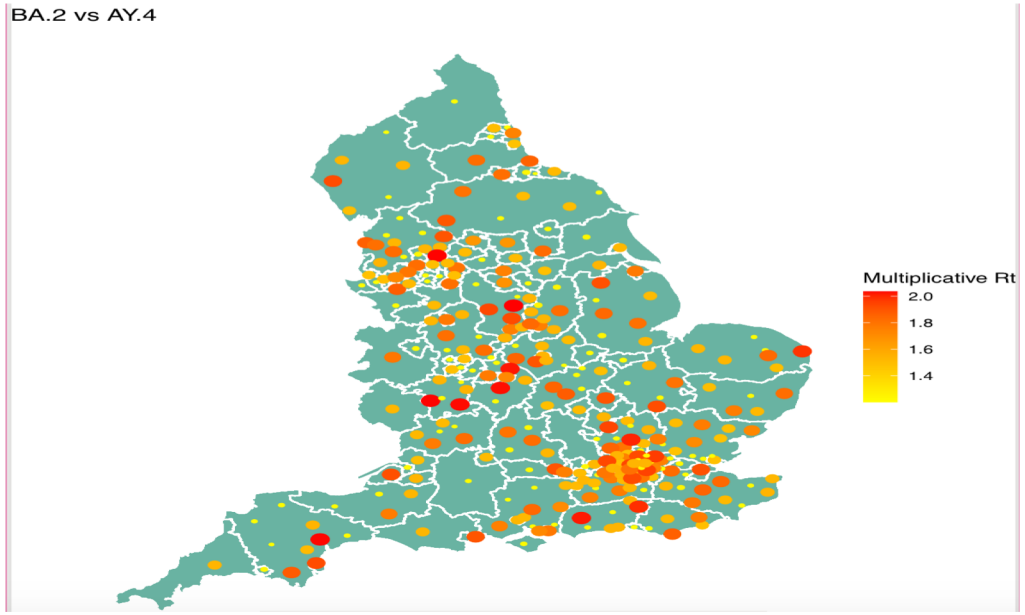


Invited submission to Phil Trans Roy Soc A RAMP special issue https://doi.org/10.1101/2021.12.30.21267090.

Delta vs Omicron

- B.1 is ~22% (-15% to 99%) more transmissible than Delta.
- B.2 is ~53% (20-100%) more transmissible than Delta.
- Spatial heterogeneity present in variants transmissibility across English regions.





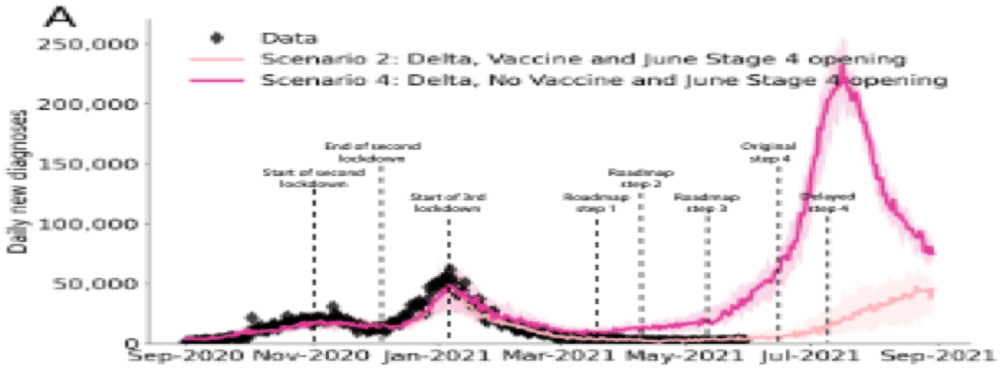
Paper in preparation with Ben Swallow (University of Glasgow)

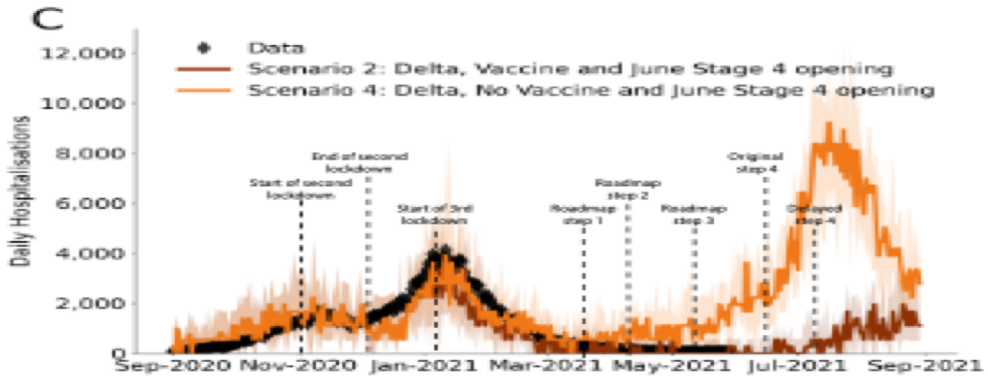
Application of the analysis

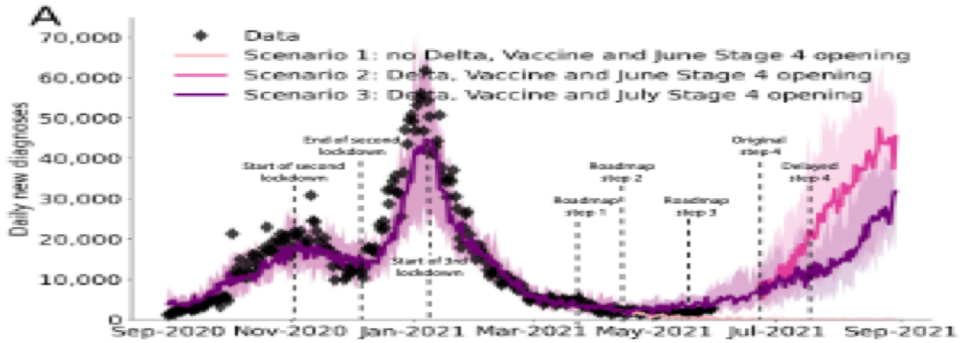
Is one month delay in the Roadmap necessary? What has been the impact of vaccination in early 2021?

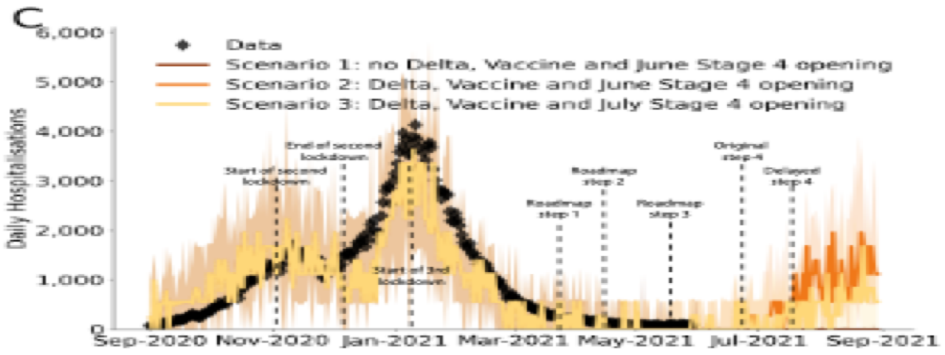
Results in June 2021: "…Vaccination has been imperative to controlling the third epidemic wave. One month delay to the Step 4 of the Roadmap was necessary to dampen the surge of the highly transmissible Delta variant."

Impact: Ongoing support to scientific and policy decision makers in the UK.









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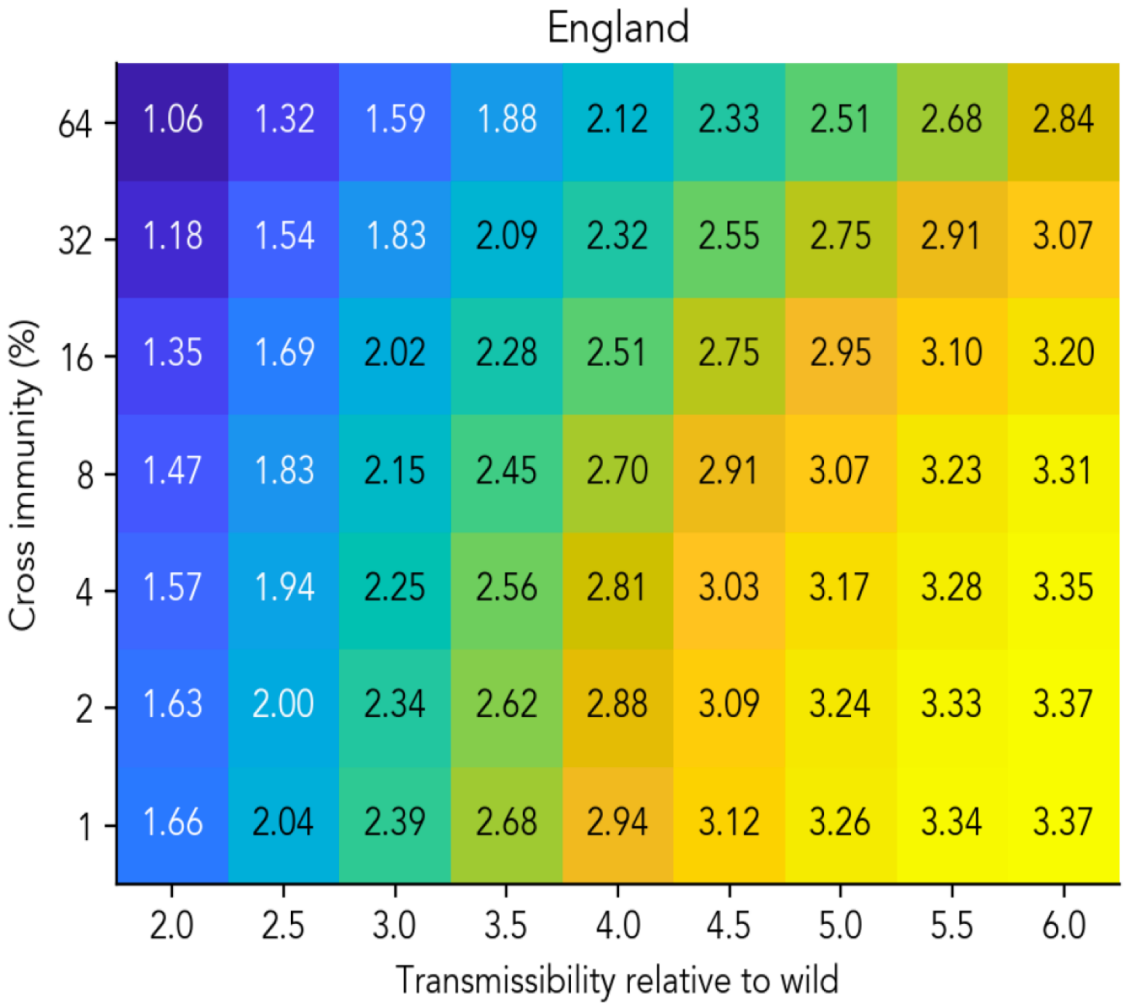
Methods

- We seeded 1,000 Omicron infections into the population with imprinted prior immunity on November 15, 2021 in England.
- We modelled Omicron to have a shorter latent period than prior variants (3 vs. 4 days) and to be 20% less likely to lead to severe.
- We varied the transmissibility and the degree of immune evasion to explore their effect on the weekly doubling rate.
- The transmissibility level varied between 2 to 6 times the level of infectiousness of the wildtype while the degree of immune evasion varied between 2- to 100-fold reduction in the level of Neutralising Antibodies (Nabs).

Doubling rate of Omicron in England over December 2021

- The observed doubling rate of 2.8 doubles per week for Omicron in England over December 2021 is a combination of transmissibility and cross-immunity.

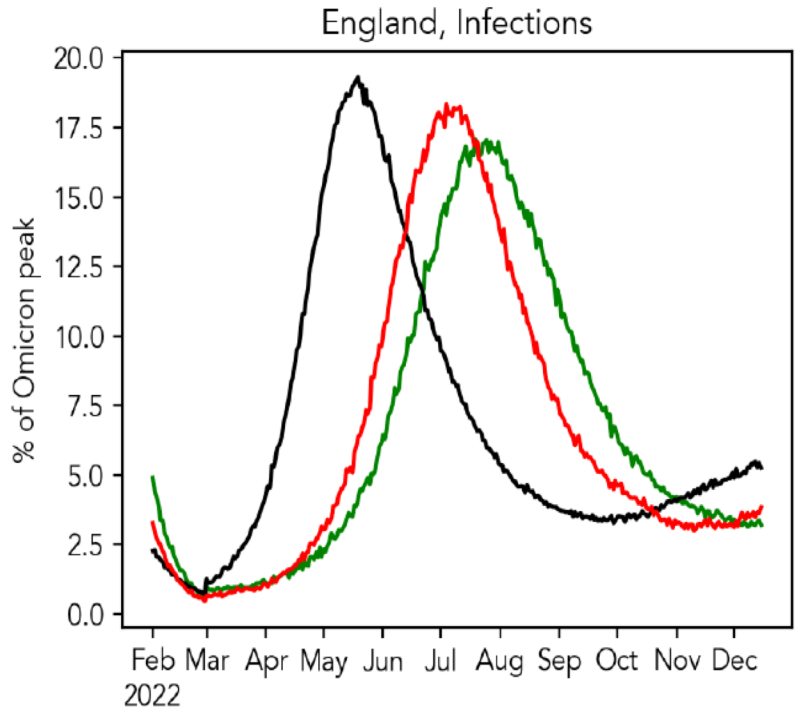
- A weekly doubling rate of 2.81 can be attained with transmissibility of 4 times higher than the wildtype and 4% cross-immunity, while a similar weekly double rate of 2.84 can be attained with much higher transmissibility of 6 times that of the wildtype and much higher cross-immunity of 64%.

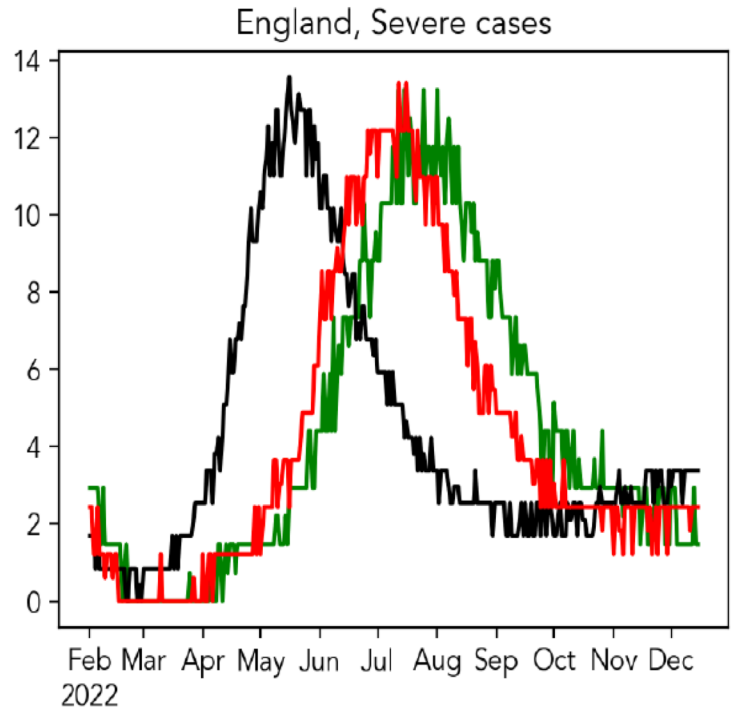


Results

- Follow-on Omicron wave driven by a highly transmissible but less immune evasive variant would have a two-months earlier and larger epidemic wave that a wave caused by a more immune-evasive but less transmissible variant (comparing the black and red curves)

Fitness advantage	Transmissibility	WT-cluster cross immunity
Intrinsic transmissibility (black curve)	5.5	64%
Combination of both (green curve)	4	8%
Immune evasion (red curve)	3.5	1%





Summary

- Statistical analysis and agent-based modelling suggest progressively increasing transmissibility maybe responsible for emerging SARS-COV-2 variants in England.

- Epidemic trajectories of Omicron are non-linear function of transmissibility and immune-escape properties of different Omicron sub variants.

- Both transmissibility and immune-escape characteristics of emerging variants are important when considering why one variant replaces another.

Thank you!

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