Possible future waves of SARS-CoV-2 infection generated by variants of concern with a range of characteristics

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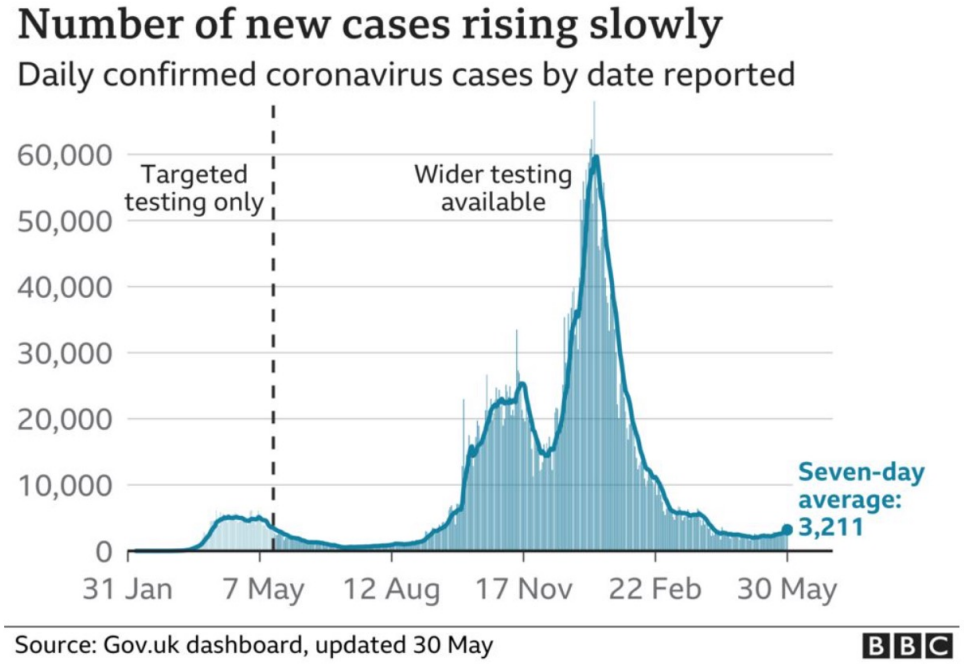
Variants of Concern: UK context

- The early phases of the outbreak in the UK consisted of:
  - An initial wave suppressed by a lockdown in March 2020
  - Relaxations in Summer 2020, followed by lockdown November 2020
  - B.1.1.7 (Alpha) emerged in November, followed by lockdown in January 2021

- "Roadmap" out of lockdown in 2021, with planned relaxations on 8th March, 29th March, 12th April and 17th May.
- Planned relaxation for 21st June was postponed in response to emergence of B.1.617.2 (Delta) variant.



What can mathematical models tell us?

- We investigate two ways in which variants may be concerning:
  - they may be more transmissible;
  - that they may evade immunity (infection- or vaccine-derived).

Table: Transmissibility and immune escape properties for illustrative VOC scenarios.
*VOC E+LH displays full efficacy against hospitalisations.

	Description	Relative transmissibility	Proportional vaccine efficacy	Proportional prior-infection efficacy
VOC MT	More transmissible	1.5	1	1
VOC E	Immune escape	1	0.75	0.75
VOC E+LH	Immune escape, hospitalisation efficacy unadjusted	1	0.75*	0.75*
VOC LT+E	Less transmissible and immune escape	0.8	0.75	0.75

Talk outline

(1) Exploring parameter space and discerning general principles

- Analysed using a parsimonious deterministic compartment model with homogeneous mixing.

(2) Potential effects of variants on burden of severe cases

- Deterministic compartmental model with age-structure, matched to epidemiological data in the UK.

(3) Timing of VOC targeted vaccines

- Stochastic VOC importation model & parsimonious model with a VOC targeted vaccine.

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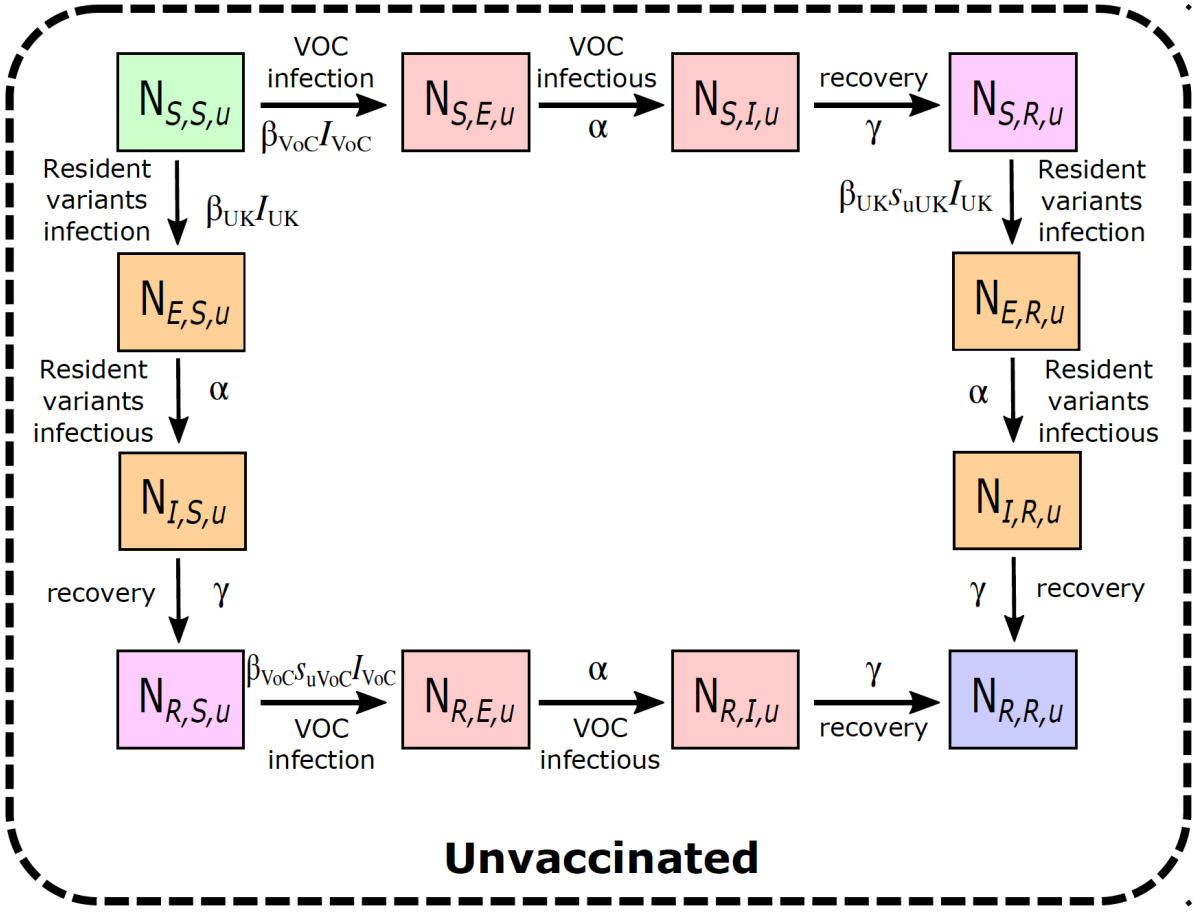
Parsimonious SARS-CoV-2 transmission model schematic



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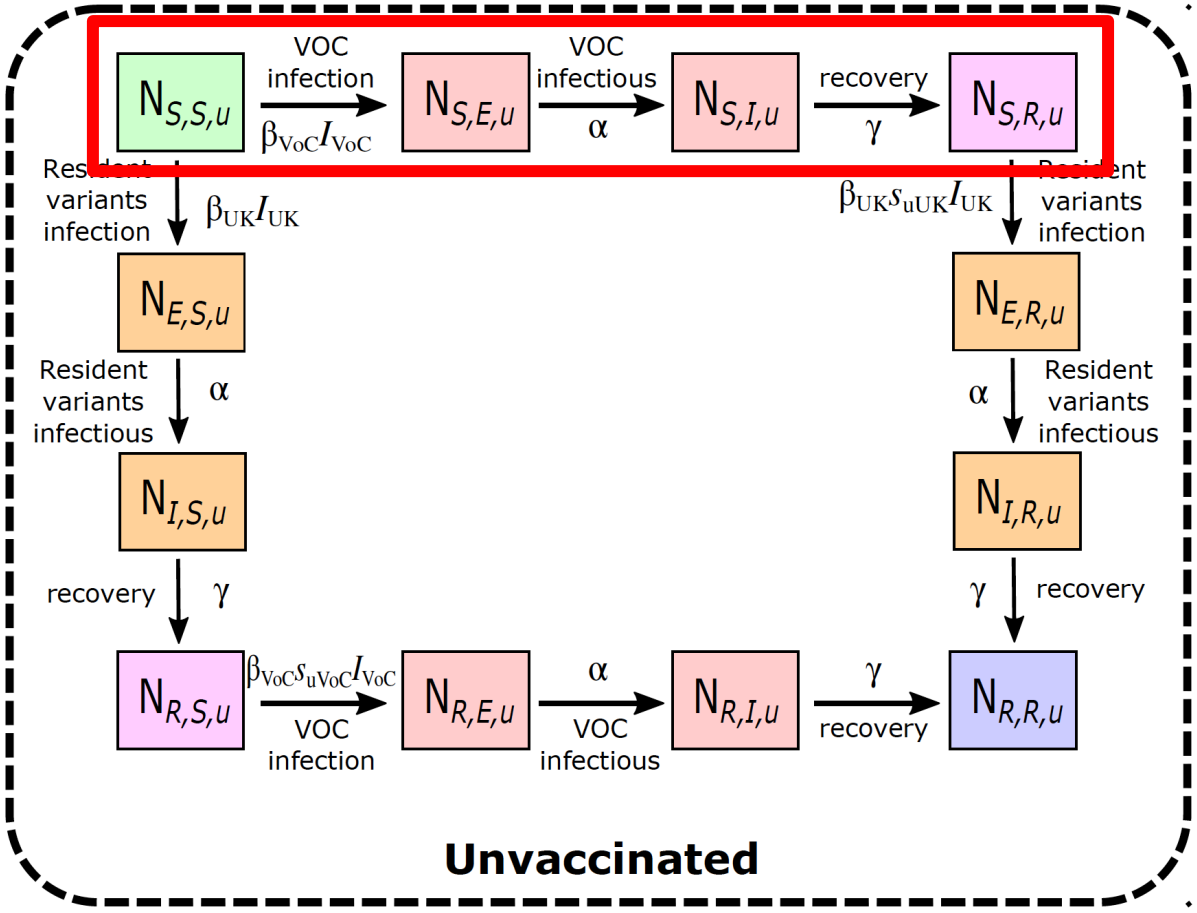

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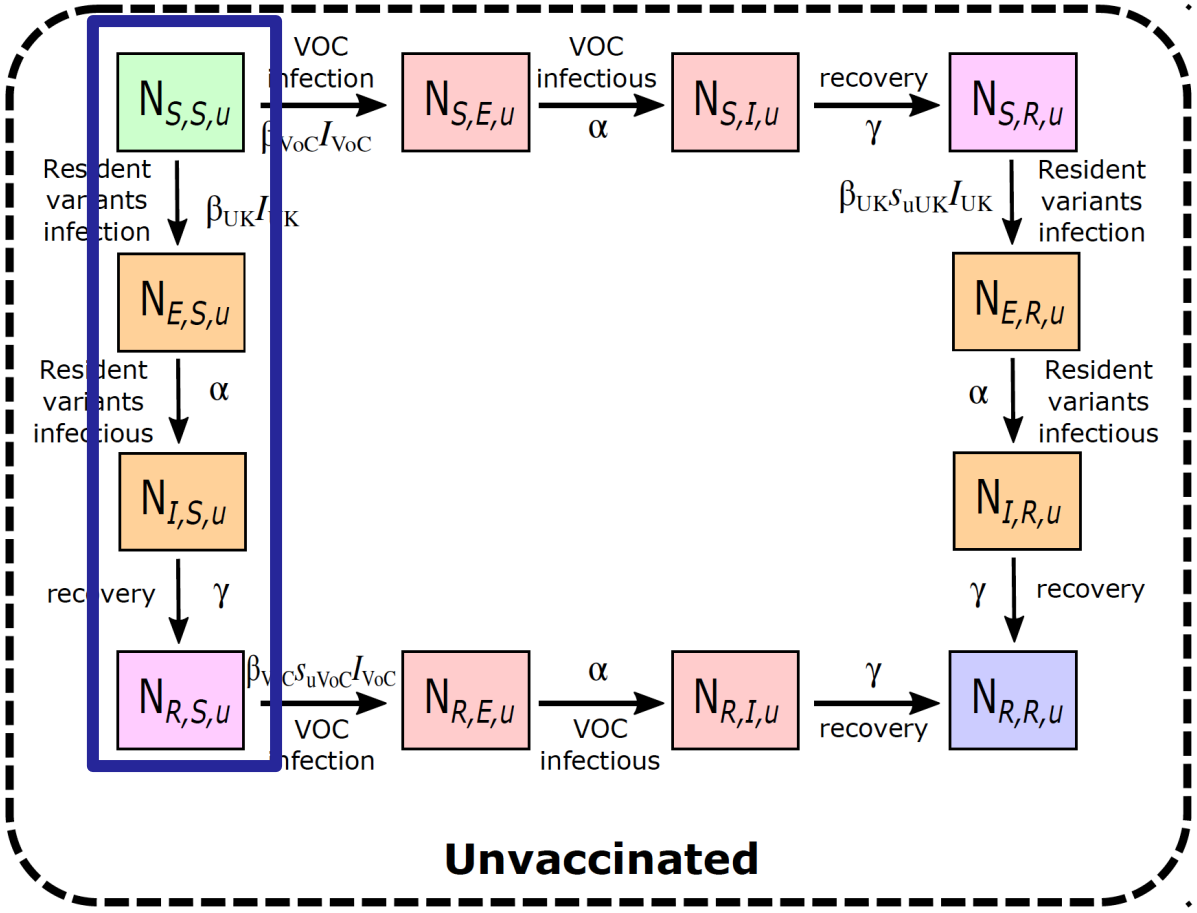

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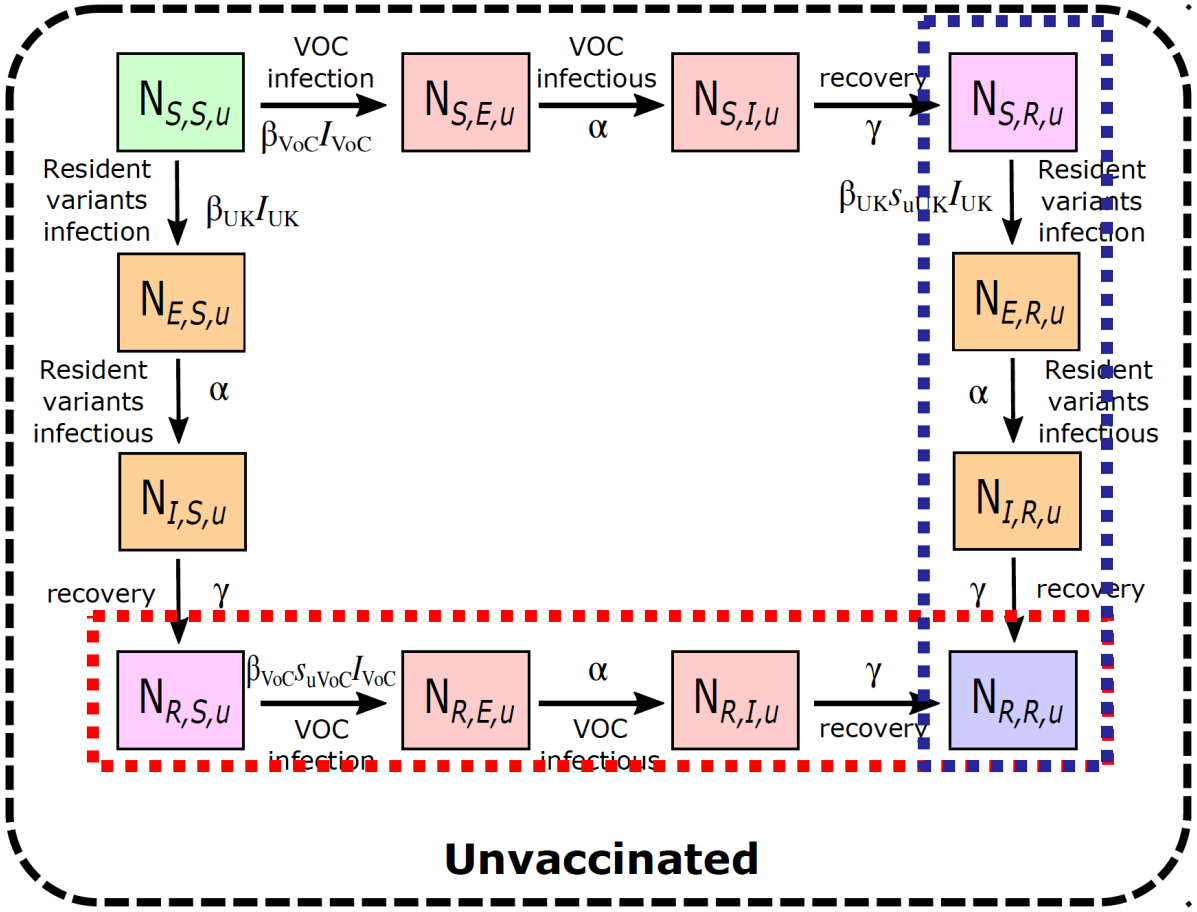

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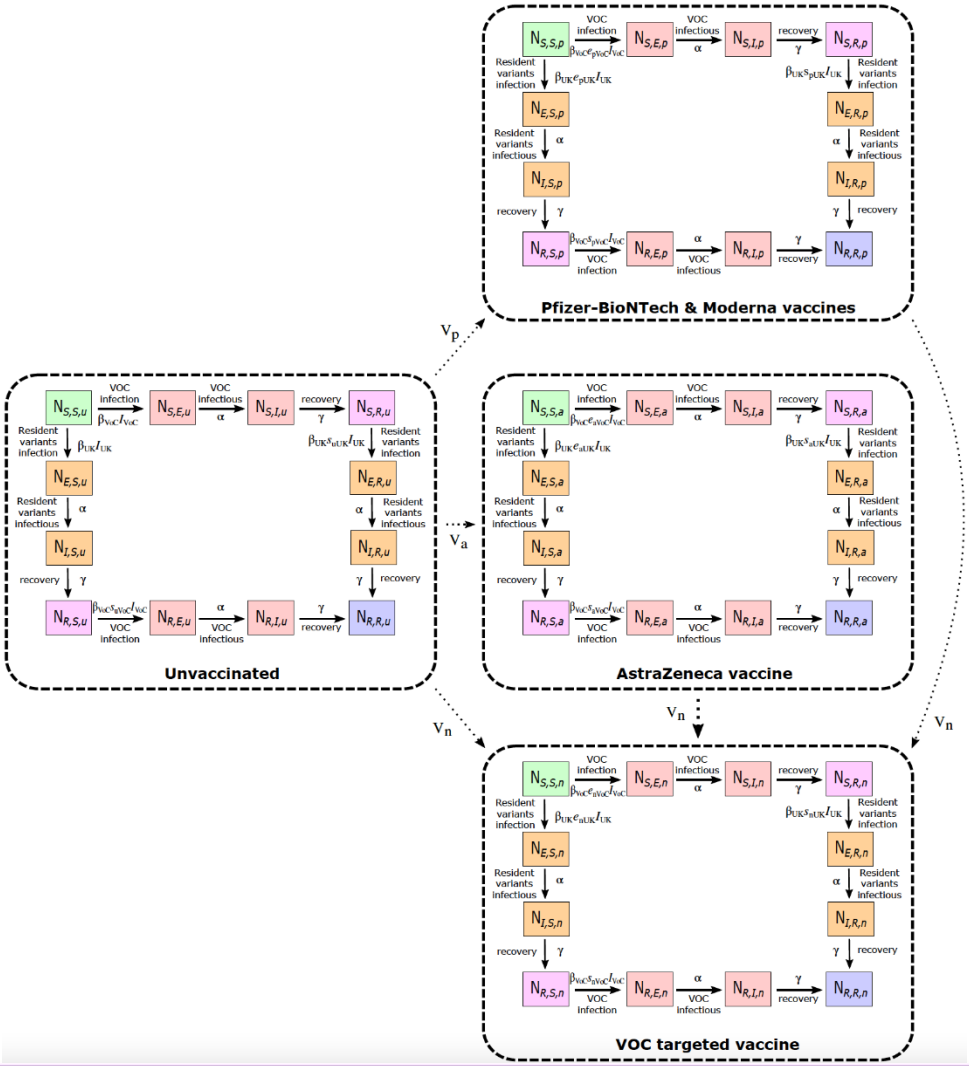
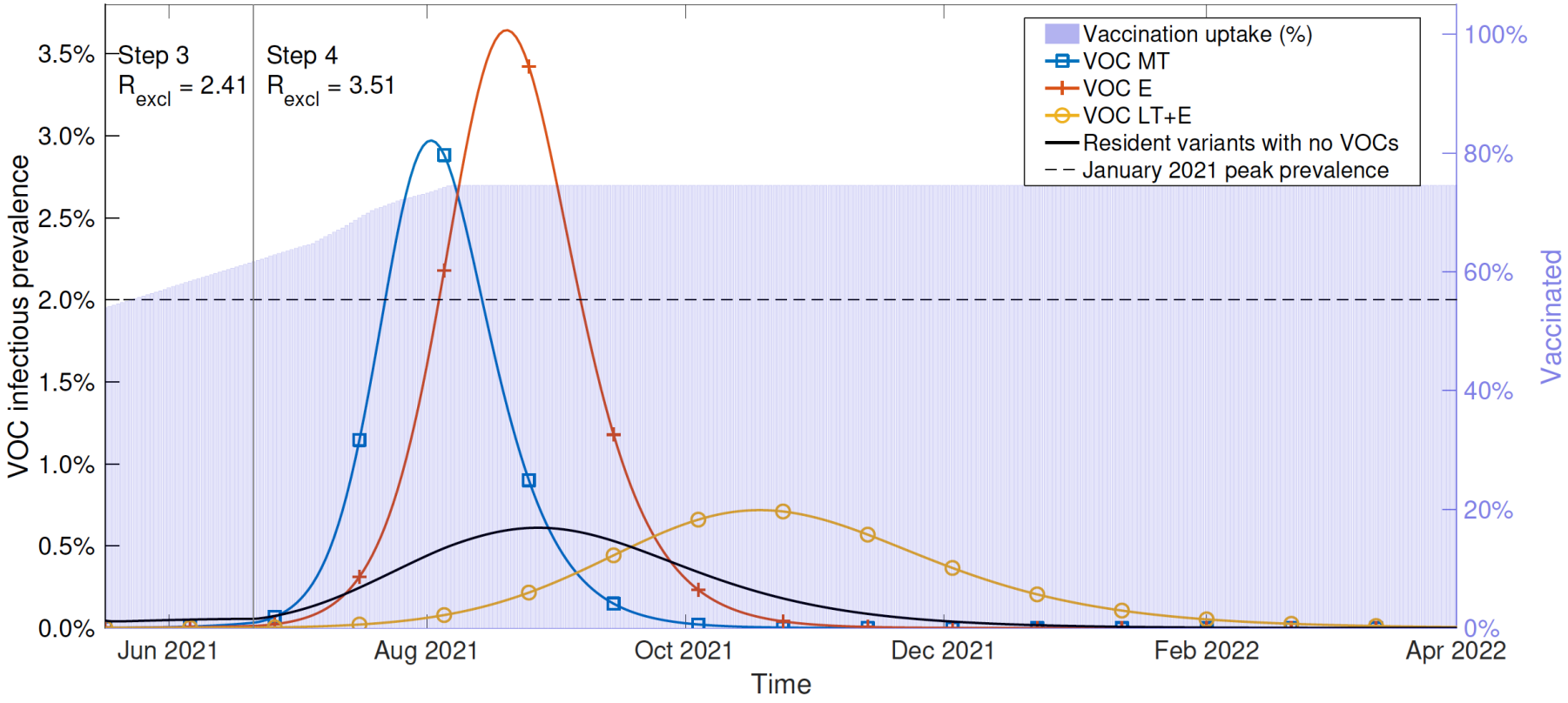


Simulation overview

- **Population:** 56 million.
- **Time horizon:** Beginning 17th May 2021, for 365 days.
- **VOC initial infecteds:** Have 2,000 VOC infected on 17th May 2021.
- **NPIs:** Level of NPIs acting on the population is captured by "R excluding immunity", which increases on the earliest date each step of the relaxation Roadmap may be enacted.
- **Vaccination:** Vaccine action acts to prevent infection.

VOC transmission dynamics

Figure: Temporal profiles of the infectious prevalence for the illustrative VOCs.



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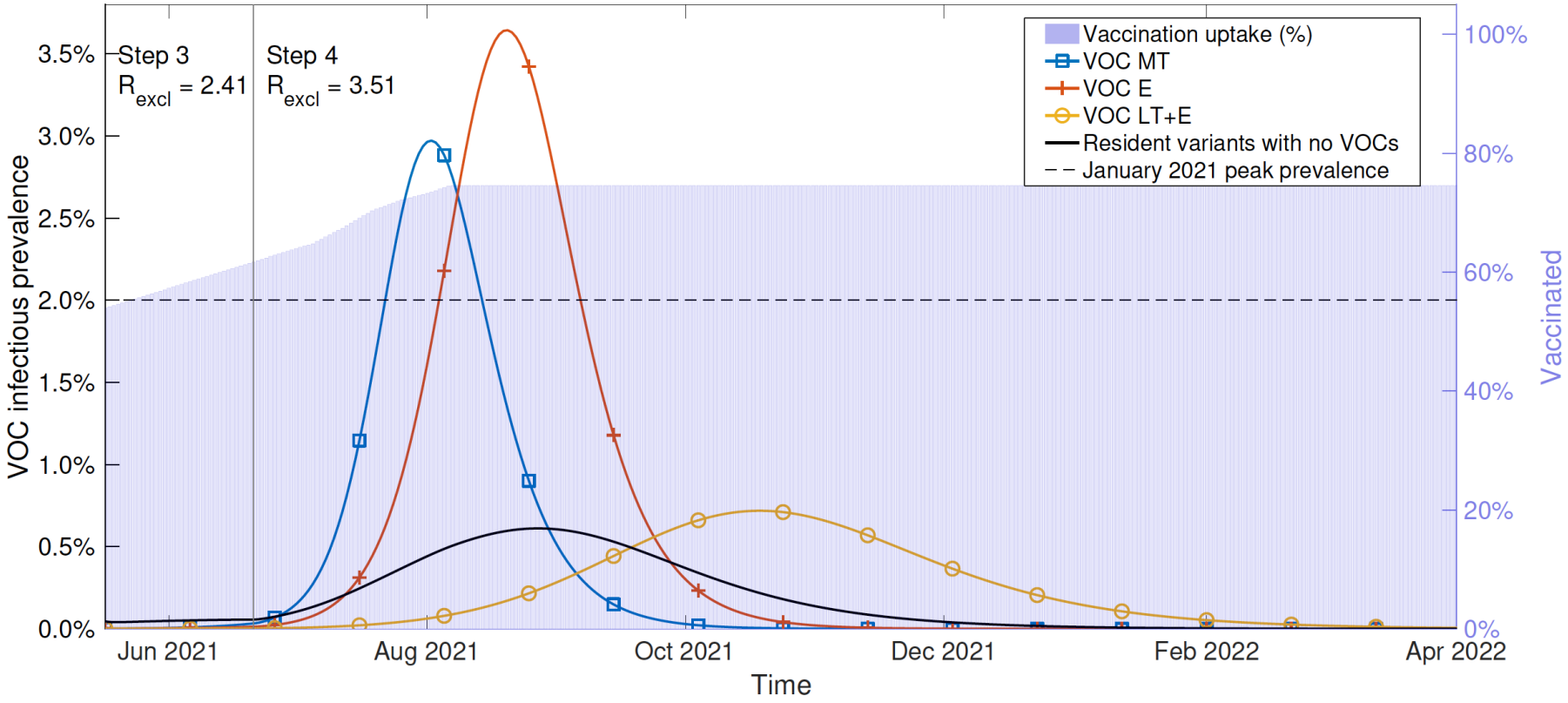
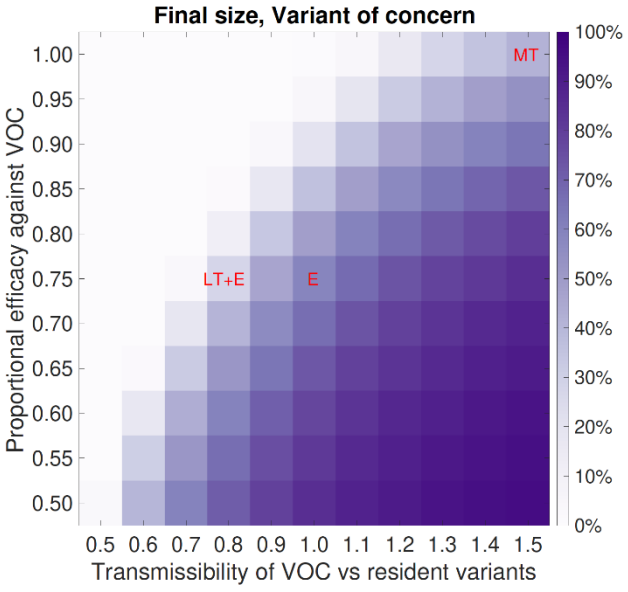
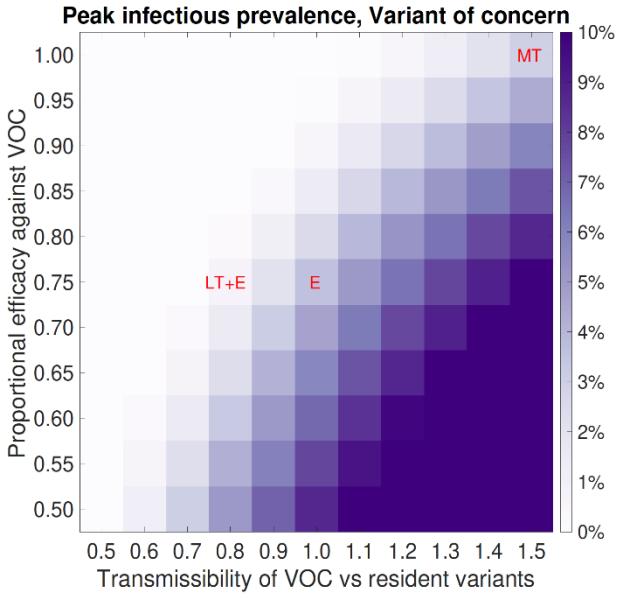


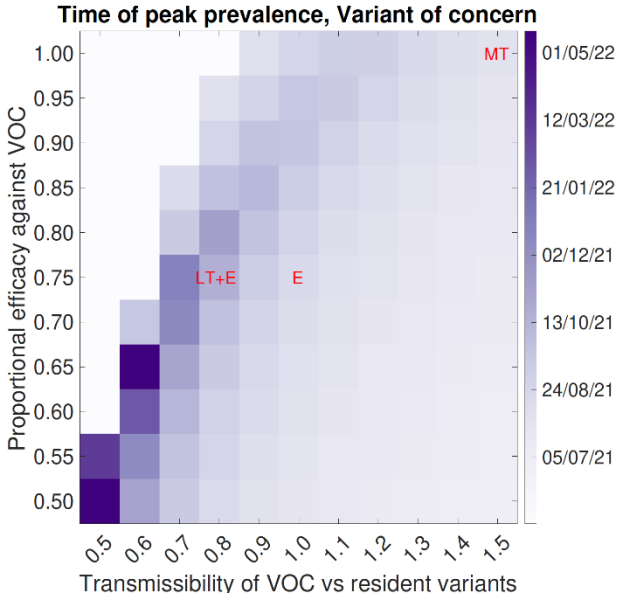
- Novel variants can lead to waves of infection beyond what we would expect from the resident strains (including Alpha).

Sensitivity to VOC assumptions

Figure: Sensitivity of epidemiological measures to relative transmissibility of the VOC versus the resident variants and proportional efficacy (vaccine and natural-immunity) against the VOC.







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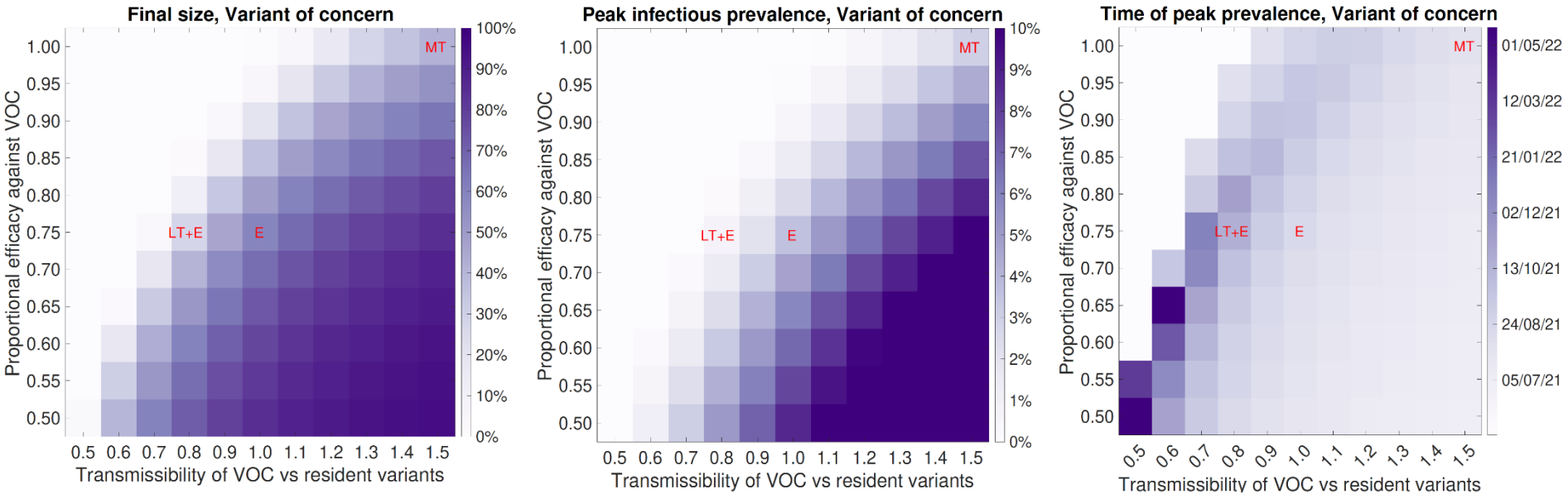

- Both the outbreak size and peak in infectious prevalence for VOCs were sensitive to the transmissibility and ability to evade existing immunity.

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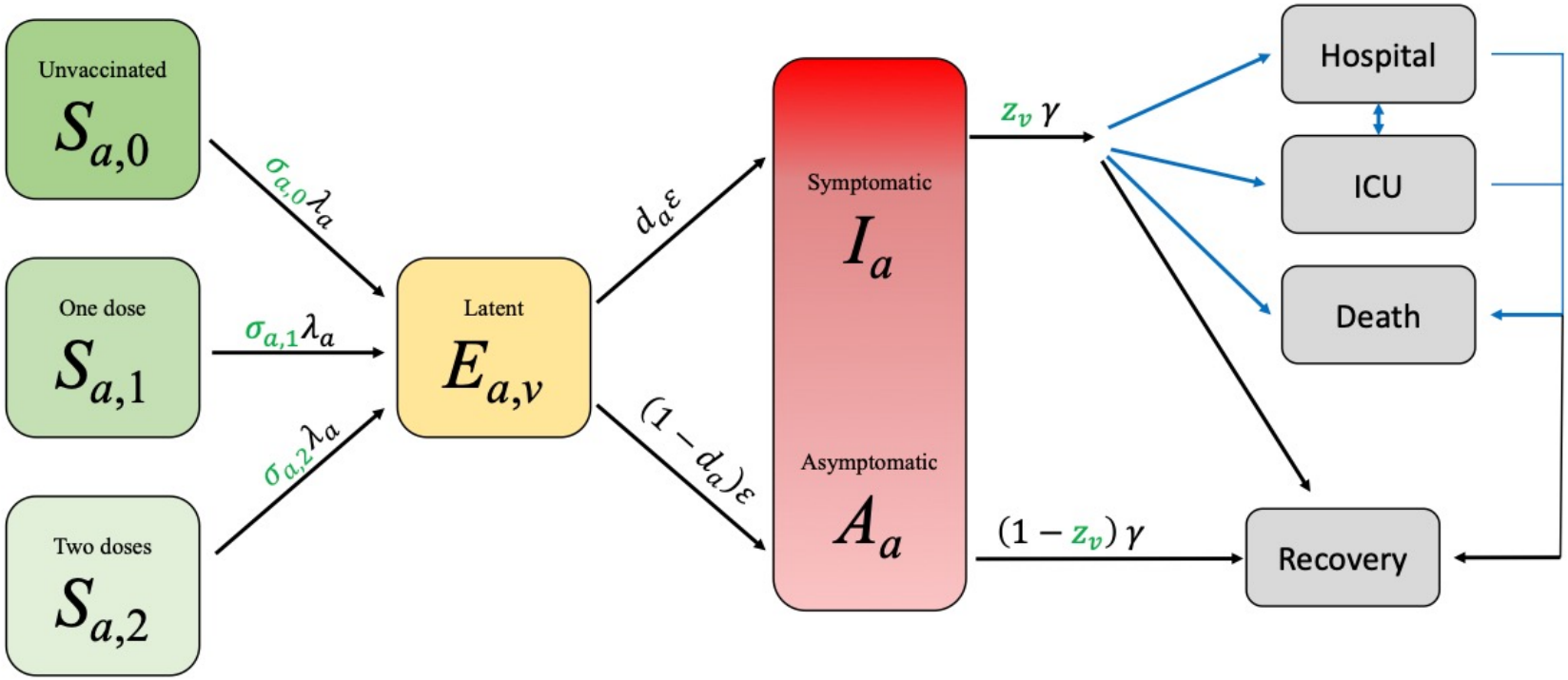
Full age-structured model

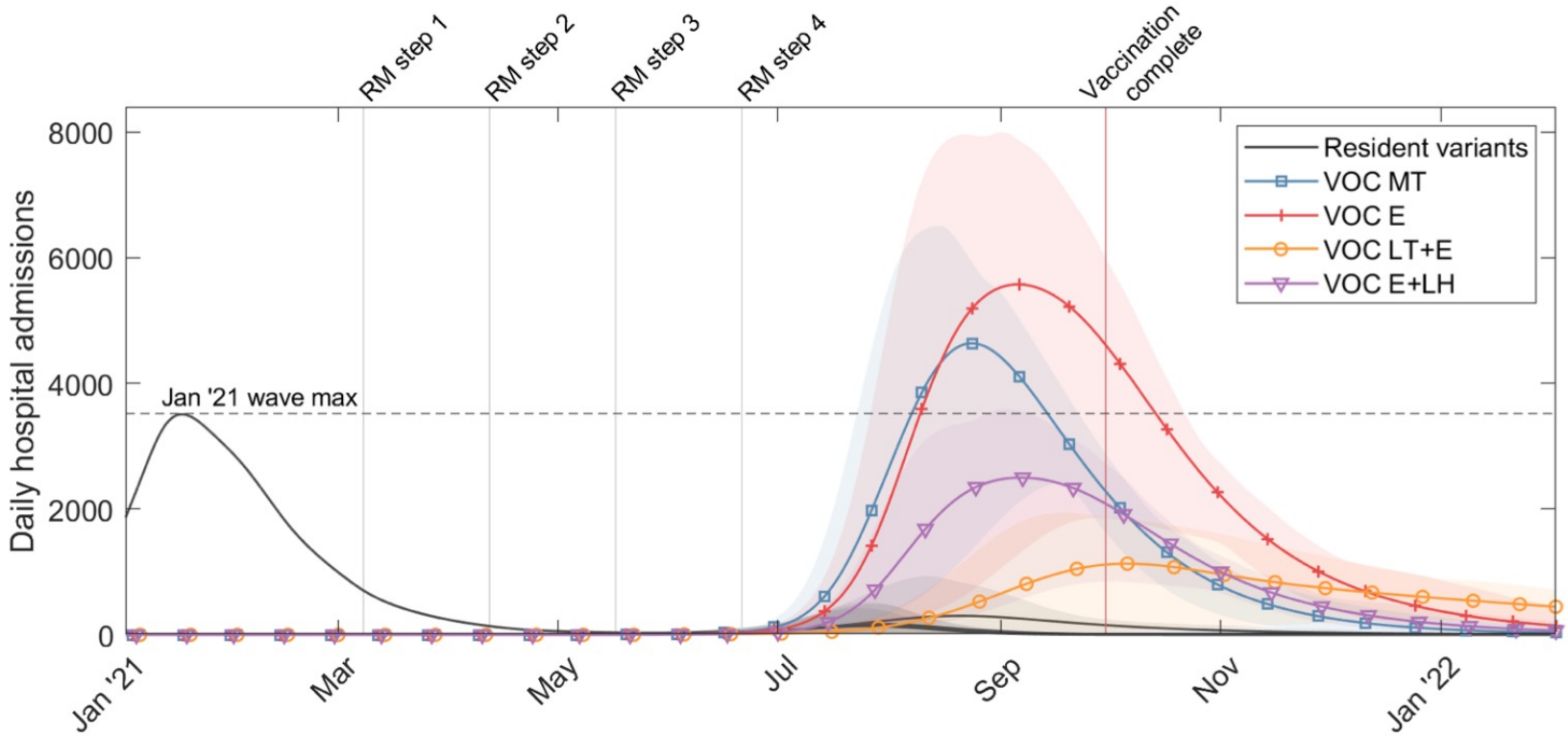


Vaccination and non-pharmaceutical interventions for COVID-19: a mathematical modelling study
Moore *et al.* (2021)
Lancet Infectious Diseases.
doi:10.1016/S1473-3099(21)00143-2

Sam Moore

Full age-structured model

Figure: Time series of daily hospital admissions (thousands). Solid lines show the mean at each timepoint and the shaded ribbons the 95% prediction intervals.



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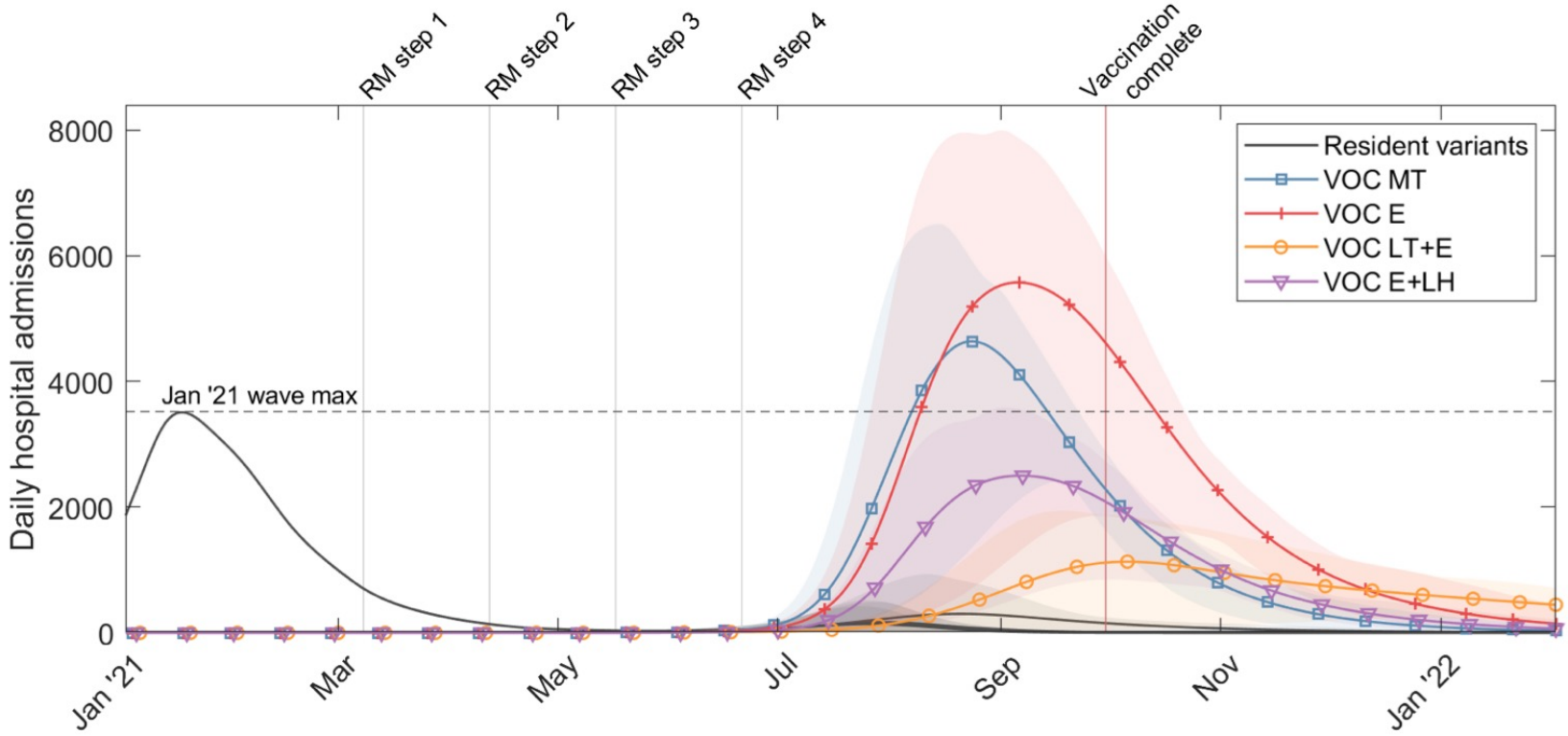
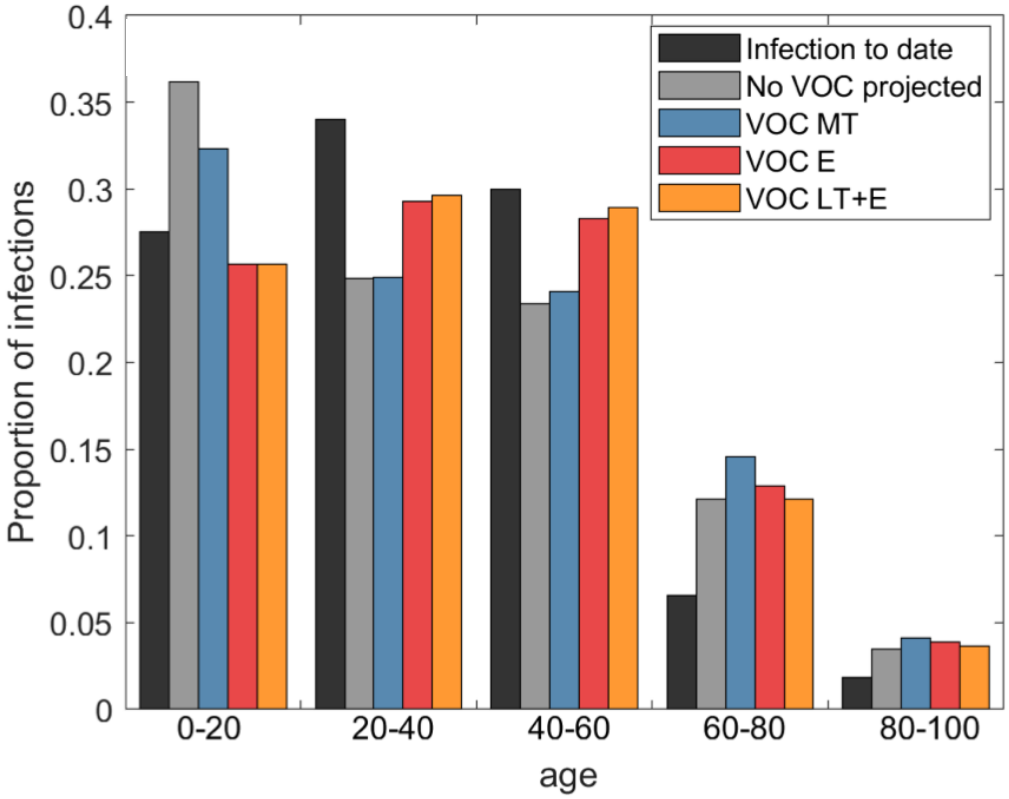


- Even though the vaccines protect against severe infection, the number of infections can be high, and so the number of hospitalisations can be high.

Full age-structured model

Figure: Age distribution of infections for historical data (black bars), projected distributions for the resident variant in the absence of any VOCs (grey bars) and each VOC scenario.



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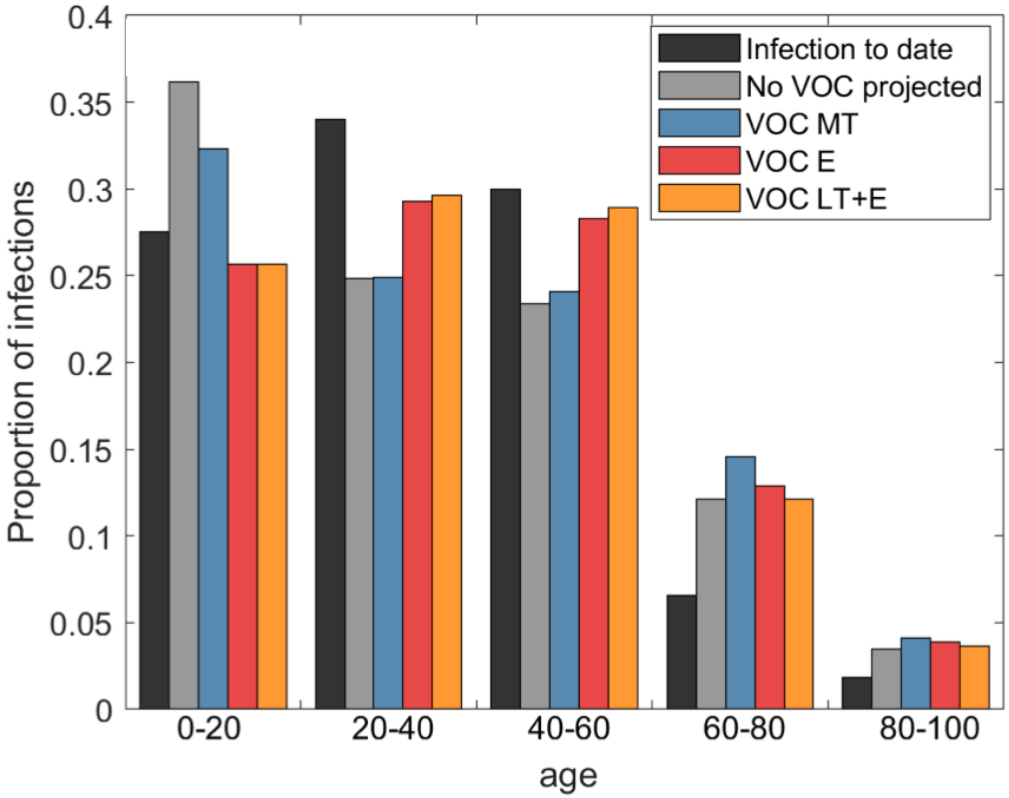

- Higher transmissibility variant quickly becomes apparent, while immune escape may not be recognised until it is 'washed up' by NPI relaxations.

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Stochastic importations

Jacob
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Lorenzo
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Thomas
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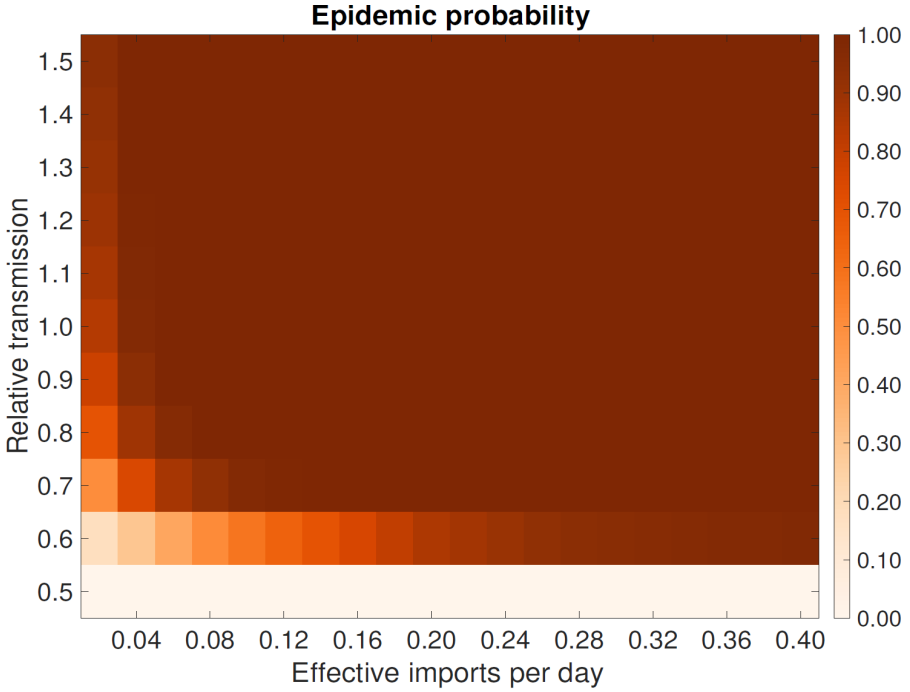
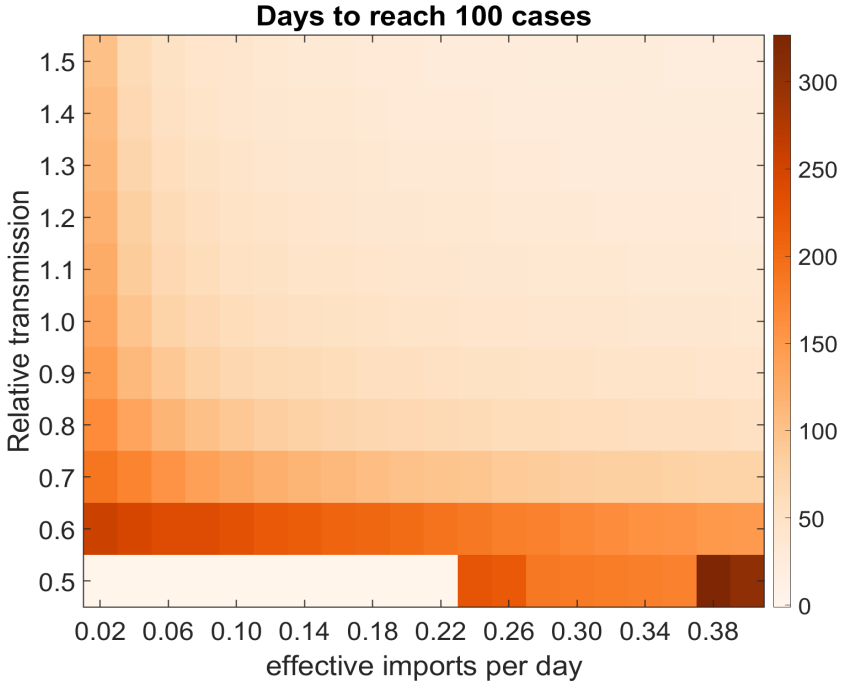
MANCHESTER 1824
The University of Manchester

Stochastic importations

Figure: Sensitivity of relative transmissibility (compared to resident variants) versus a given count of VOC effective imports per day (corresponding to the second generation cases that result from a single index case) of **(left)** epidemic probability; **(right)** days to reach 100 cases.





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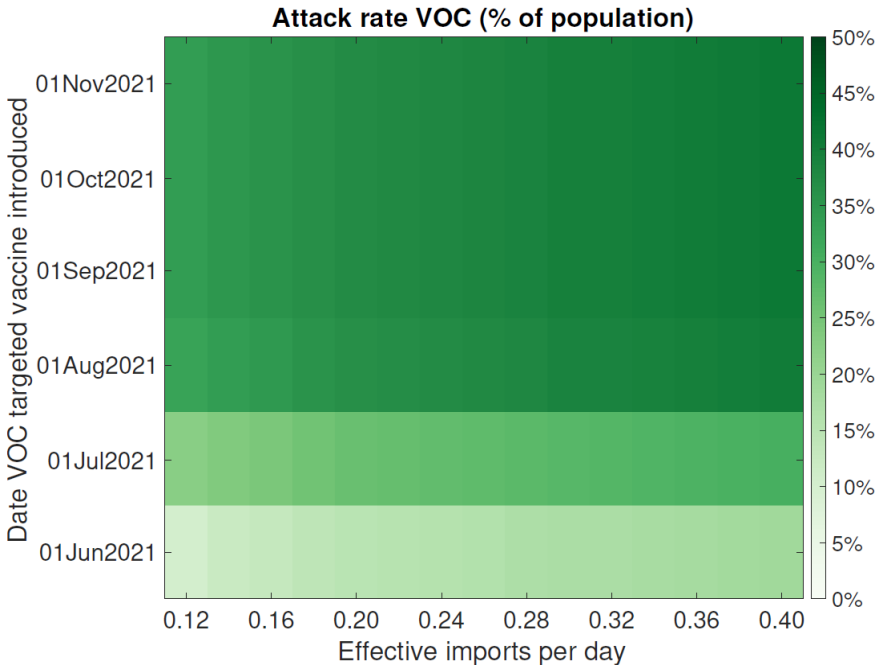
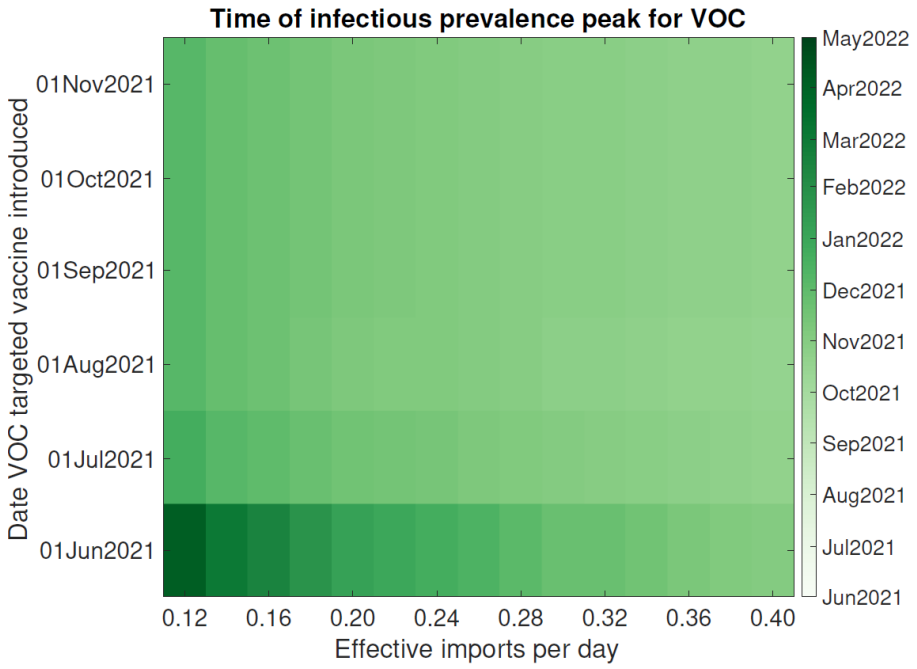
VOC targeted vaccine

Figure: Sensitivity of epidemic outcomes to the introduction time of a VOC targeted vaccine for VOC E.





- Timing of VOC targeted vaccines has a variable impact, dependent upon lag until it is available, VOC transmissibility and the improvement in vaccine efficacy.

Summary

(1) Exploring parameter space and discerning general principles

- Novel variants can lead to waves of infection beyond what we would expect from the wildtype.
- Even if the novel variant is not more transmissible than the wildtype, large waves of infection possible if the variant has immune escape.

(2) Potential effects of variants on burden of severe cases

- Even though the vaccines protect against severe infection, the number of infections can be high, and so the number of hospitalisations can be high.

(3) Timing of VOC targeted vaccines

- Variable impact, dependent upon lag until it is available, how much more transmissible the VOC is and the improvement in efficacy.

Acknowledgements

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School of Mathematics, University of Manchester, UK.

Katrina Lythgoe.
Big Data Institute, University of Oxford, UK.

UK Research and Innovation

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Possible future waves of SARS-CoV-2 infection generated by variants of concern with a range of characteristics
L Dyson, EM Hill, S Moore, J Curran-Sebastian, MJ Tildesley, KA Lythgoe, T House, L Pellis, MJ Keeling (2021)
Nature Communications **12,** 5730
doi:10.1038/s41467-021-25915-7

Webpages:
https://tinyurl.com/warwickCOVID; https://edmhill.github.io;

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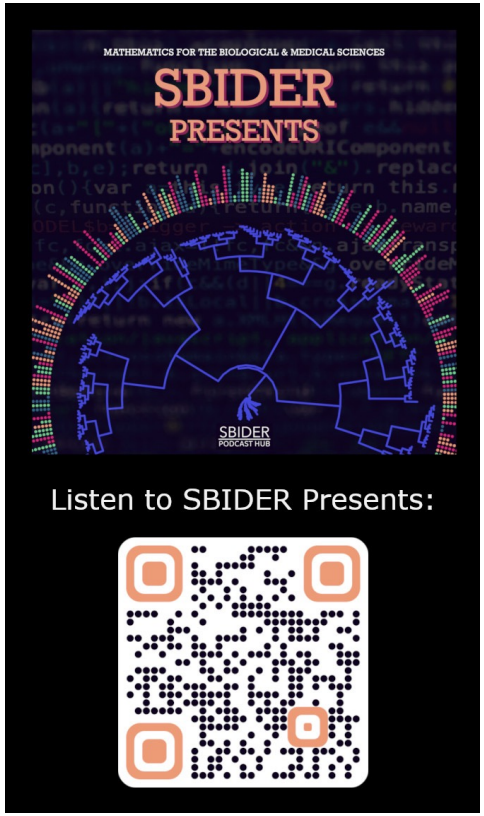

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