Space Matters in COVID-19 Modelling

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w/ A. Kleczkowski, J. Enright, K. Atkins, G. Rossi, A.-S. Ruget

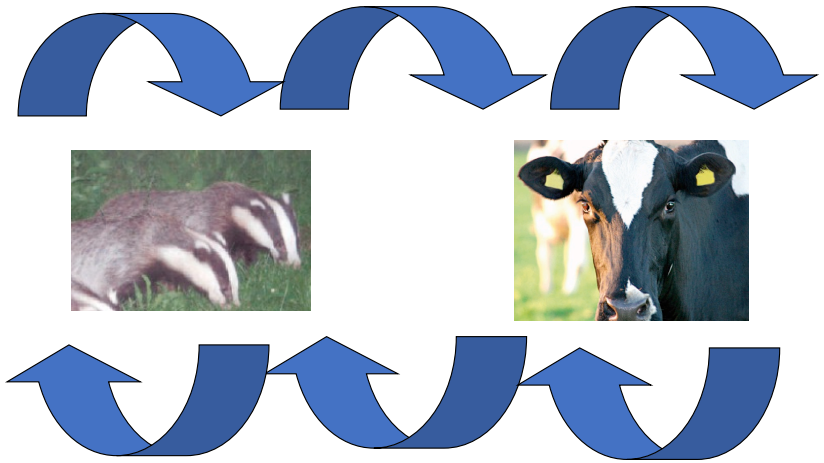
A whistle stop tour of work done by many

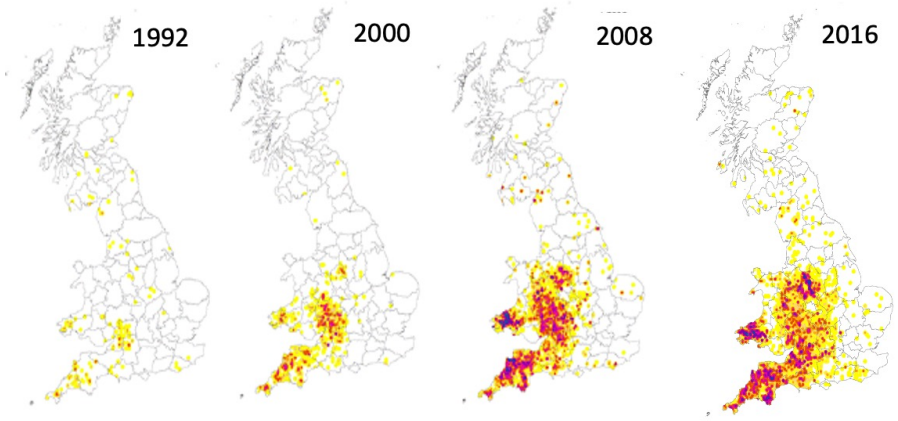
- Why are people like cows?
  - Building on previous work
- Regional differences in case ascertainment
  - Useful insights arise from practical questions
- Random Forest models of vaccination and omicron spread
  - Working in the new world of complex datasets
- Working with the Scottish Govt and SPI-M.
  - Simplest is often the best.

Why are people like cows?

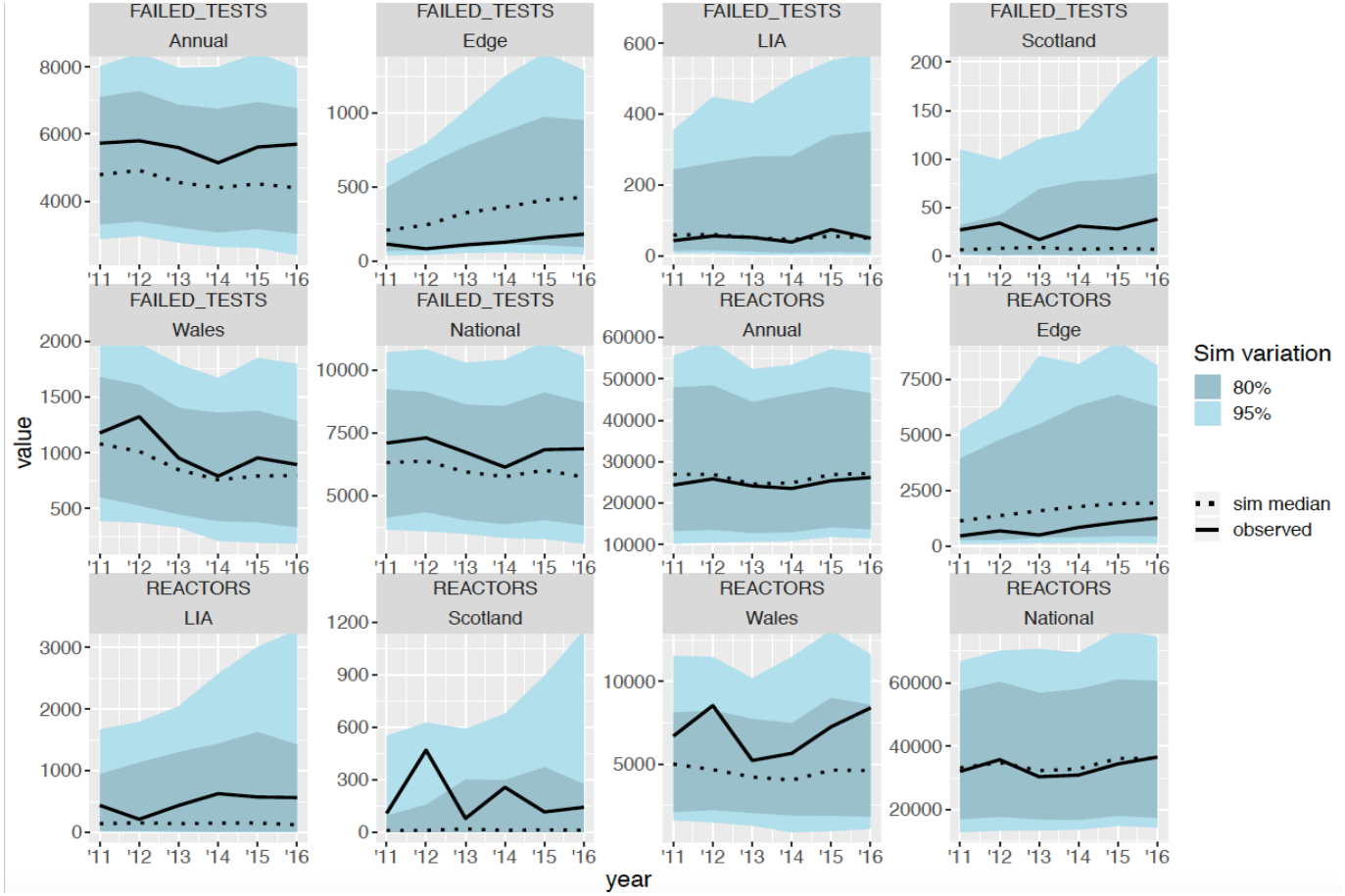
Building on previous work: a model of bovine Tuberculosis in cattle and badgers

Modelling bovine Tuberculosis in Badgers & Cattle





12 million agent simulation model of all recorded cattle movements in Great Britain, fitted to observed regular testing data



Model fit using Approximate Bayesian approach (ABC-SMC)

23rd March 2020

In six weeks …

“Tuberculosis modelling initiative”	“Scotland Coronavirus Model”
Herds	Output areas ~ 150 persons
Livestock movements	Commuter movements
Regular herd testing	Community PCR test results

Conditions of lockdown make human infections behave more like livestock ones – spatial factors matter

(though the models do not depend on this)

'A national emergency': what the papers say about the UK's coronavirus lockdown

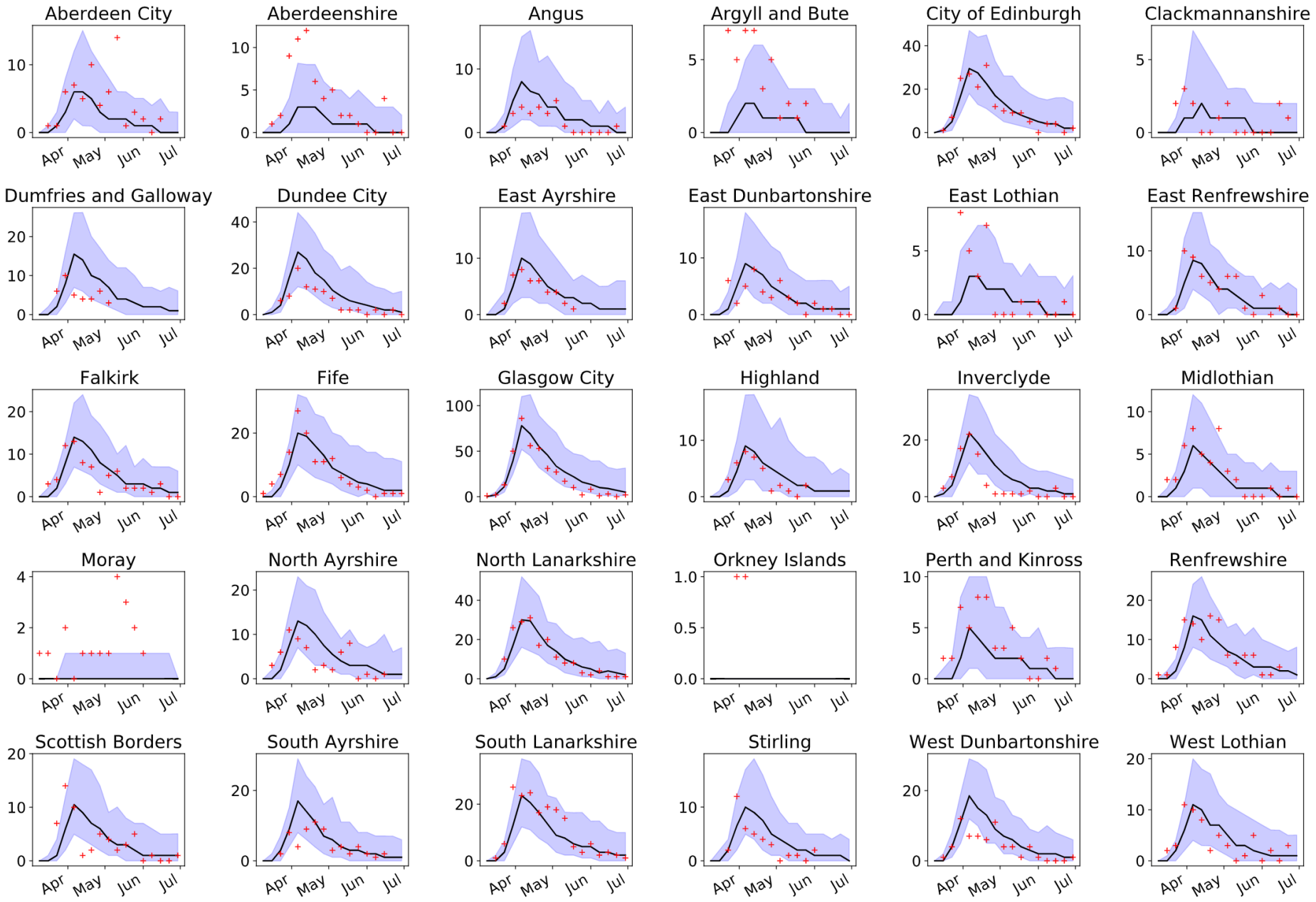
National newspapers all scrambled to give extensive coverage of Boris Johnson's historic announcement

- Johnson puts UK into lockdown
- Coronavirus – latest updates
- See all our coronavirus coverage

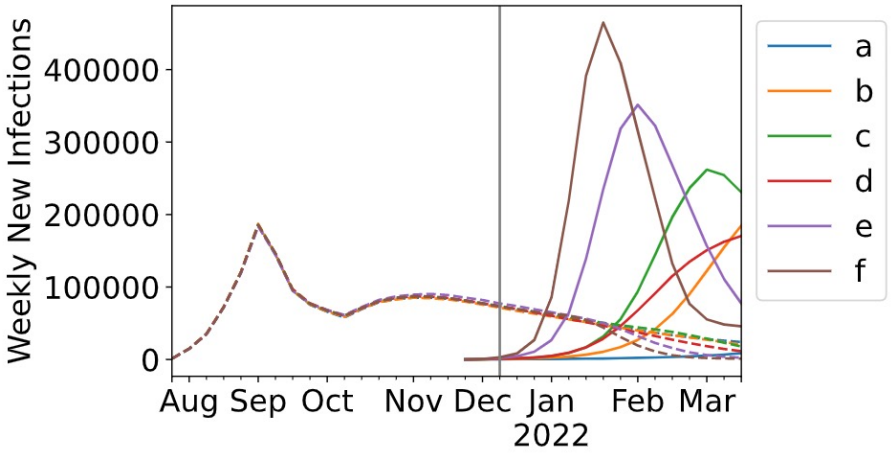
The UK papers all focused on Boris Johnson's latest measures to tackle the coronavirus pandemic. Composite: Various

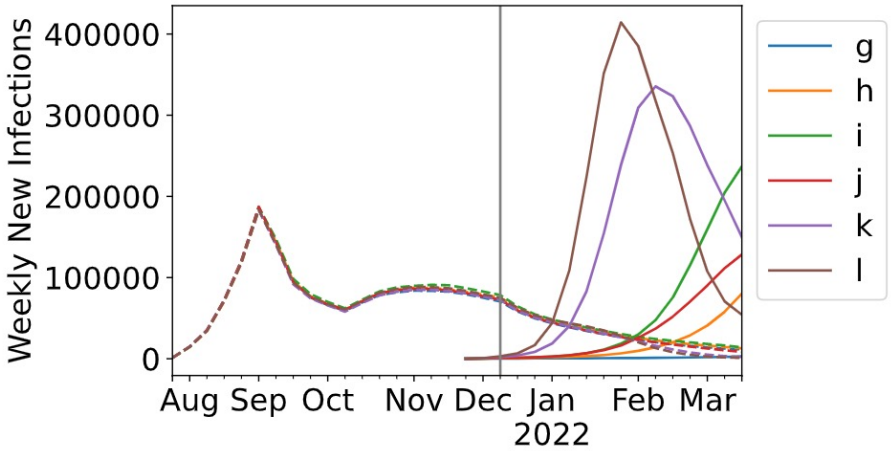
SCoVMod fit to initial epidemic

- Initial model fitted to
- Number of deaths per Local Authourity per week
- Number of datazones (6K in Scotland) with deaths per Local Authourity per week
- Used to provide weekly "**Medium Term Projections**" to the Scottish Government



Early evaluation of the potential for Omicron variant spread





Use SCoVMod to evaluate what combination of

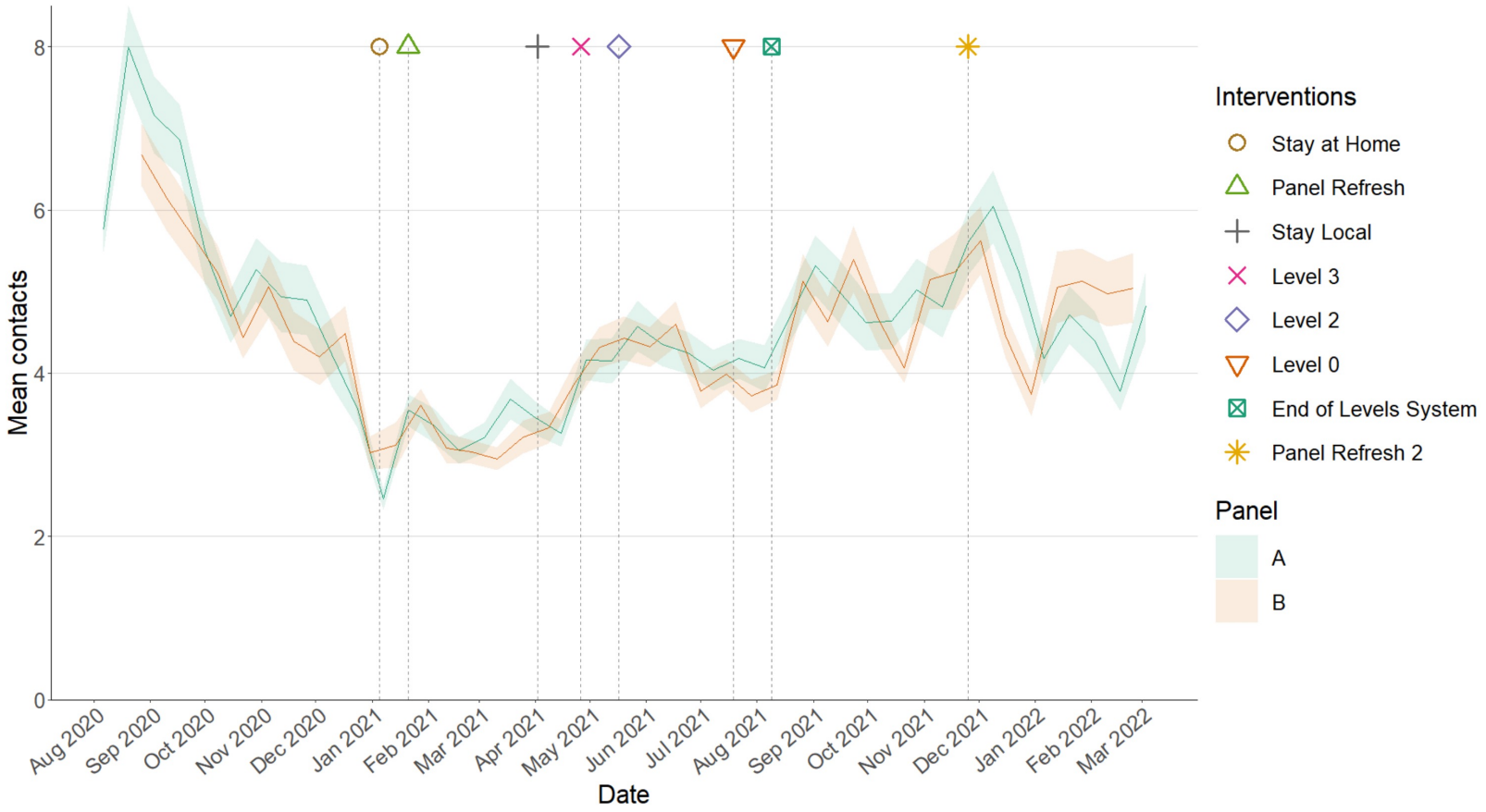
- **escape from prior immunity** (natural plus vaccination) plus
- **higher transmission rate**

Could result in observed patterns of transmission in early December 2021

Model results showed a substantial increase in cases even if measures were immediately put place

		Vaccine Escape Level		
		1	2	3
Transmission Level	1	a	b	c
	2	d	e	f
	1+NPI	g	h	i
	2+NPI	j	k	l

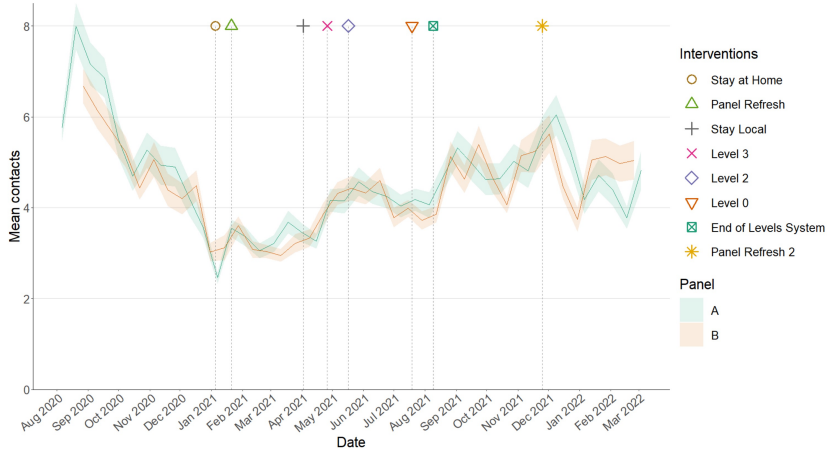
But the omicron emergency ‘fizzled out’



Some evidence of a decline in contact rates (Scottish Contact Survey)

From https://www.gov.scot/publications/coronavirus-covid-19-modelling-epidemic-issue-no-94/documents/

But the omicron emergency ‘fizzled out’



Some evidence of a decline in contact rates (Scottish Contact Survey)

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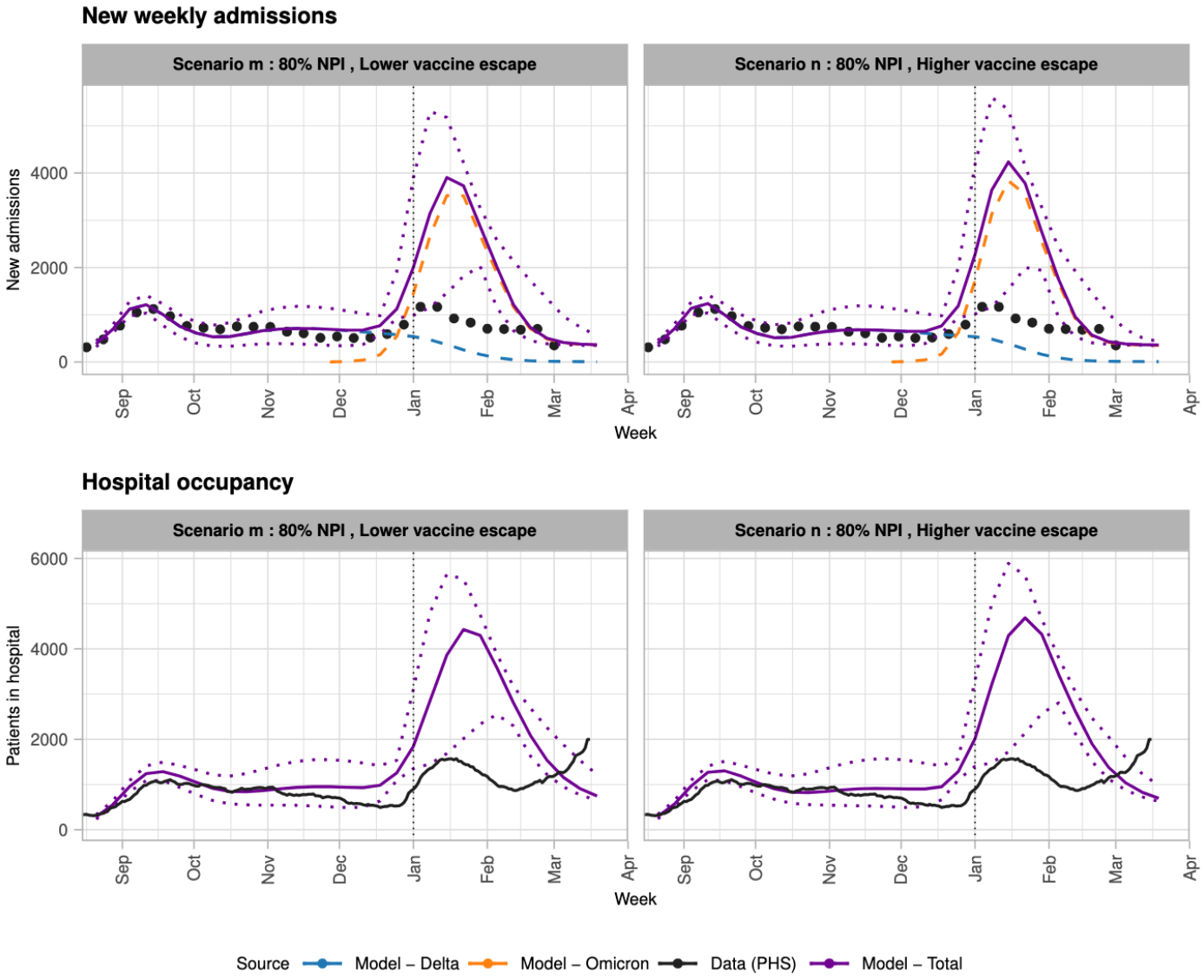
Severe illness substantially less likely than for Delta variant

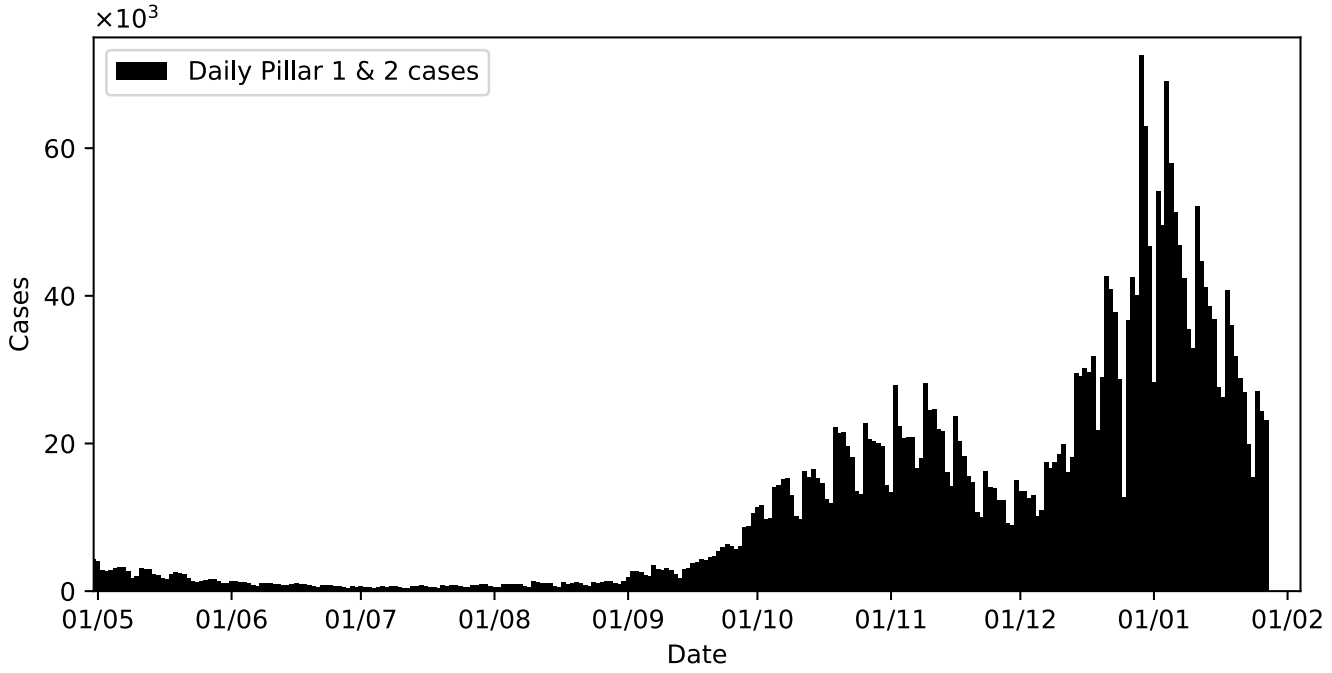


Regional differences in case ascertainment

Useful insights arise from practical questions: How do we estimate true incidence from case data?

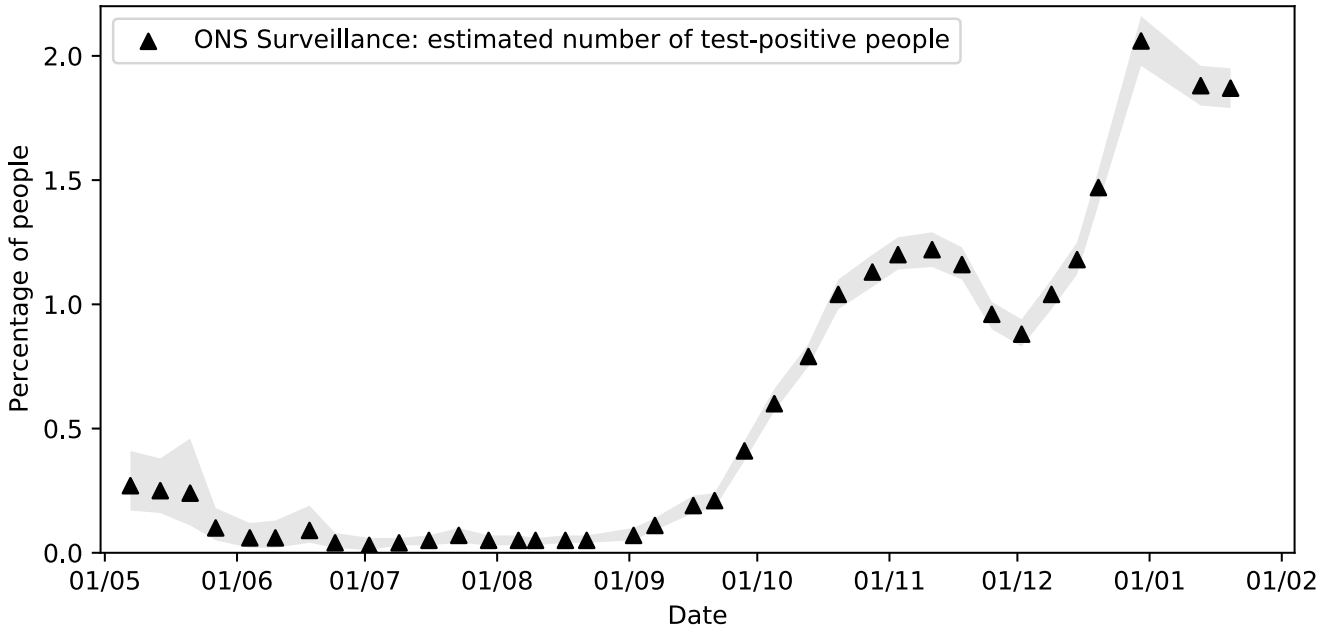
Evaluating case ascertainment

- Initial efforts focused on modelling deaths (sporadic testing results)
- How should we incorporate case data?
- Two key datastreams:
  - ONS surveillance (overall prevalence of disease)
  - Self-reporting via community testing (symptomatic



$C(t)$ = reported pillar 1 & 2 cases on day t

Claim that true incidence can be estimated by exploiting ONS surveillance data



$M(t)$ = number of test-positive people

What is the relationship between ONS positivity and Pillar 1 & 2 test cases?

Assumed unbiased estimator of true prevalence

With some careful book-keeping …

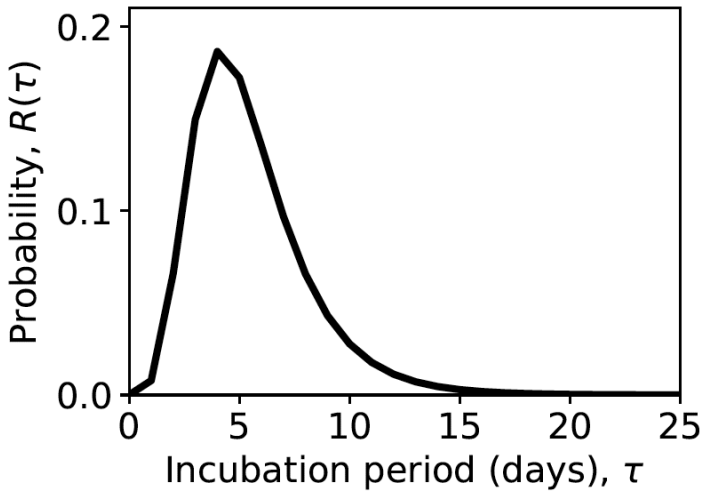
Probability of acquiring infection on day X

Probability a test is taken on day T (δ = 1 day after symptom onset)

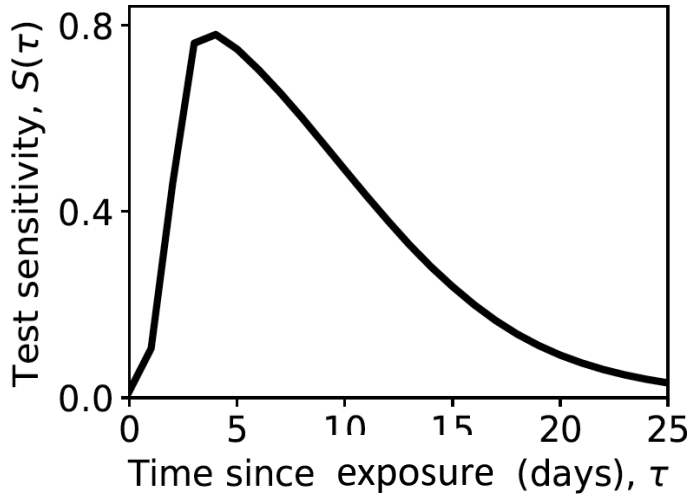
Probability a test taken on day τ will be positive

$$P(\ x = X\ \&\ t^{+} = T\ ) = B(X)R(T - X - \delta)S(T - X)$$

Probability of a positive test on day T given infection on day X

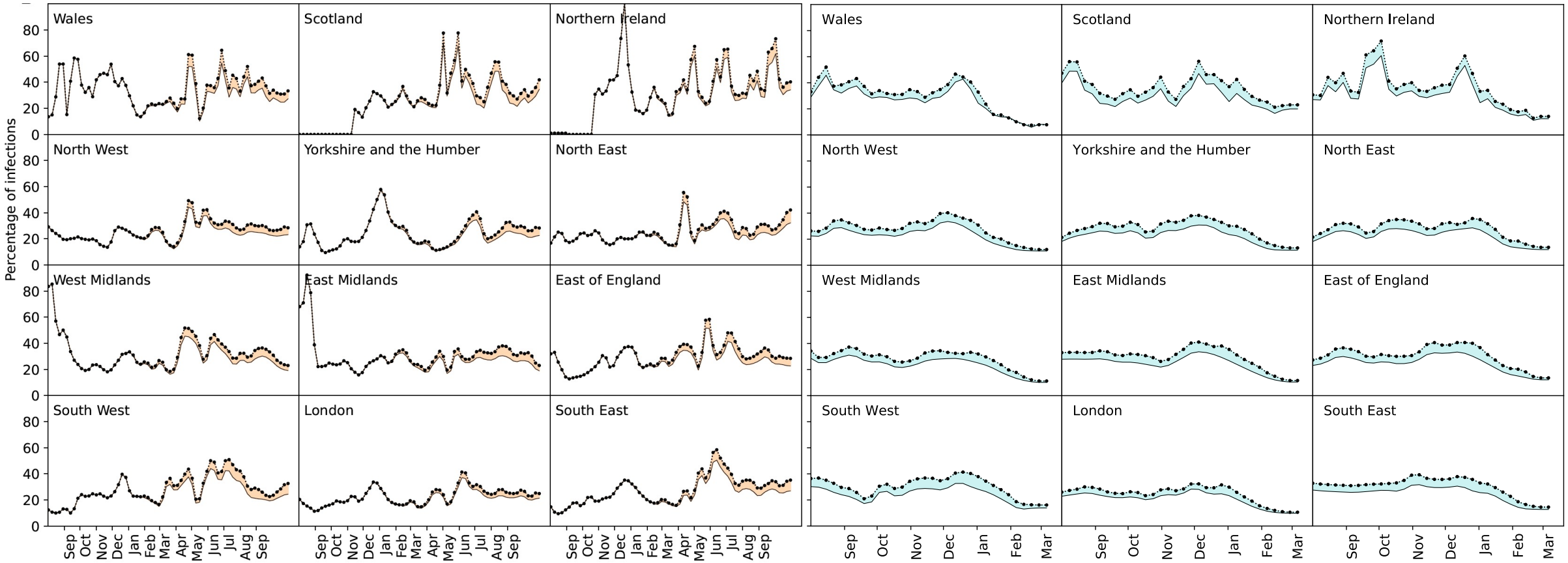


Lauer et al. *Annals of Internal Medicine* 2020

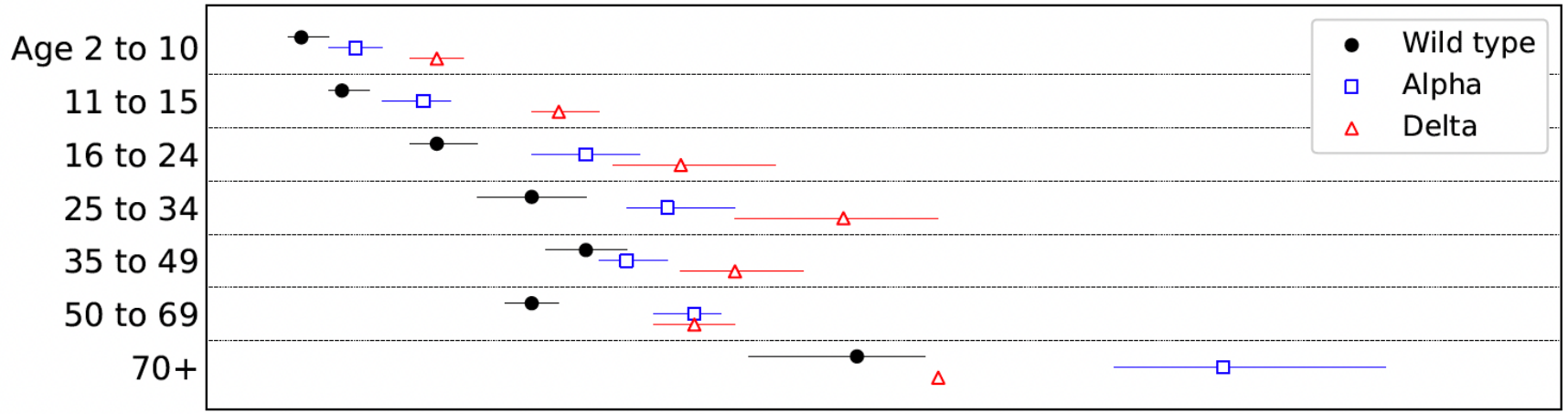


Hellewell et al. *MedRxiv*. 2020

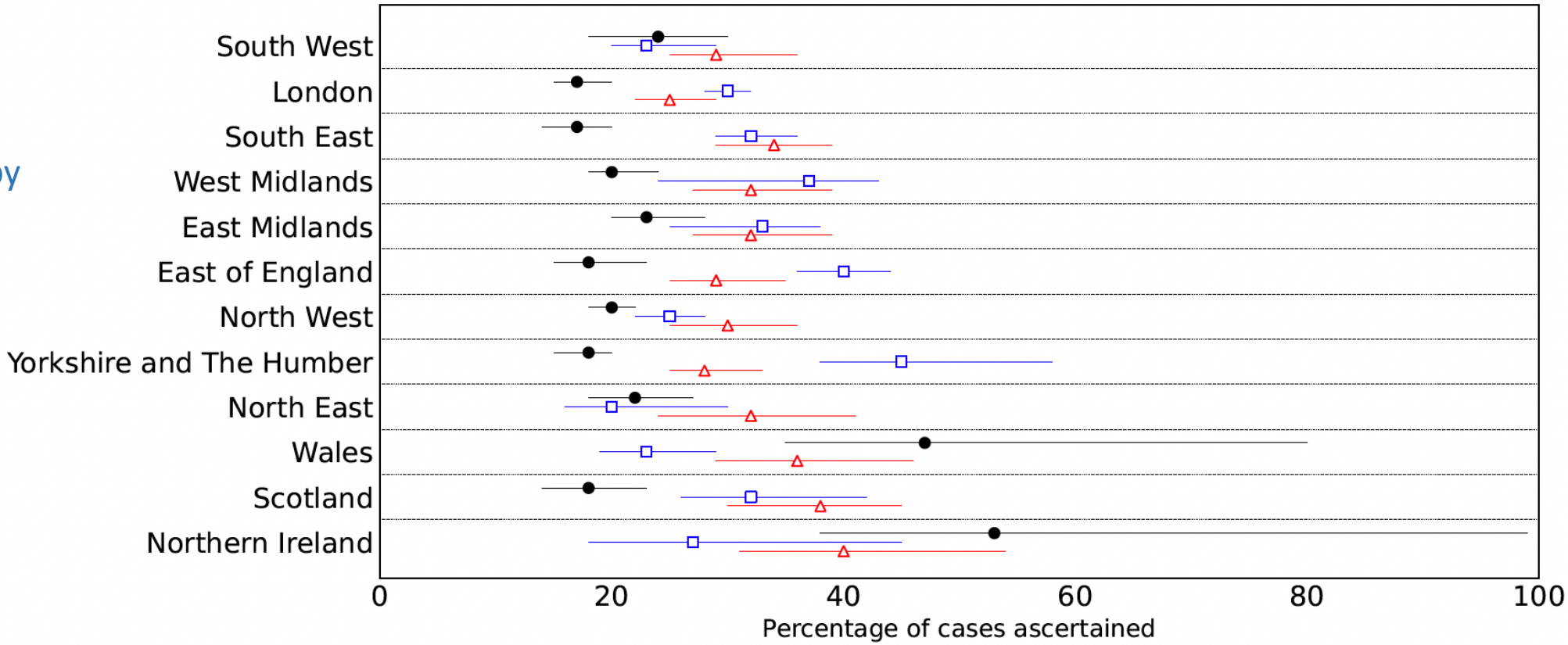
Estimates of case ascertainment by region



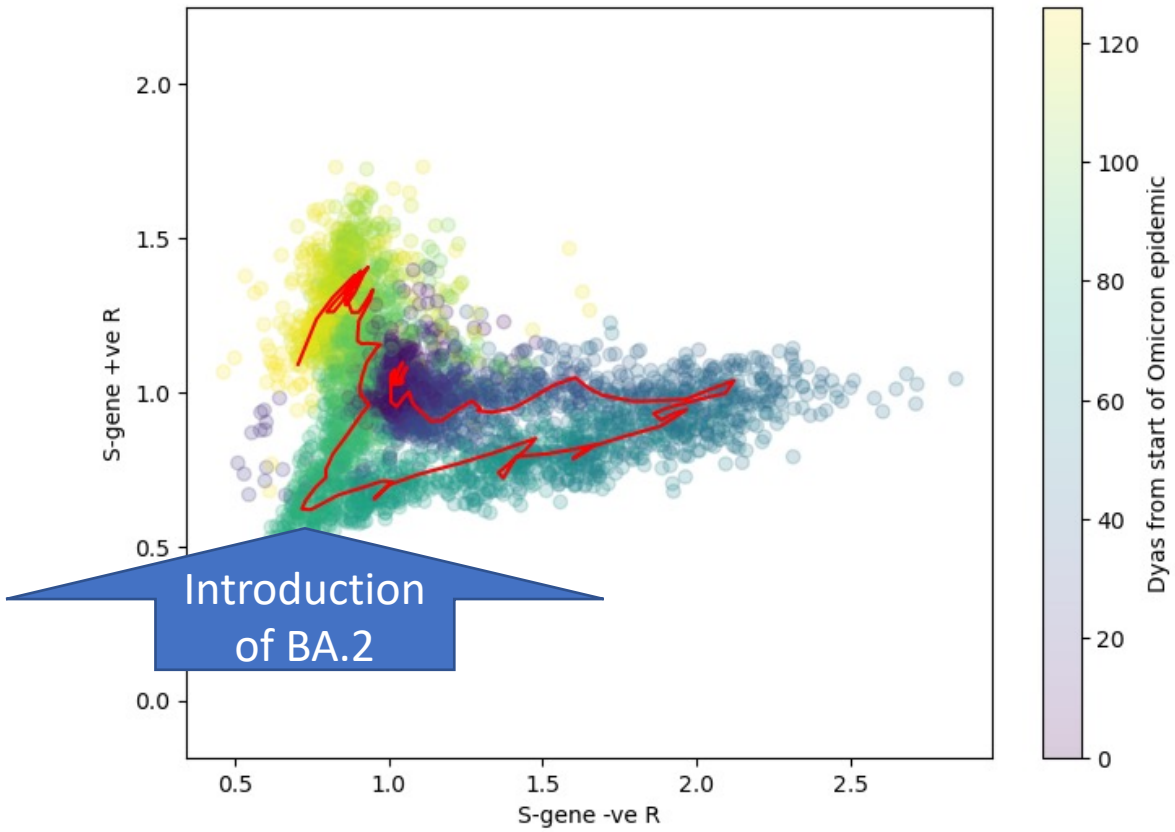
Consistent differences in ascertainment by age

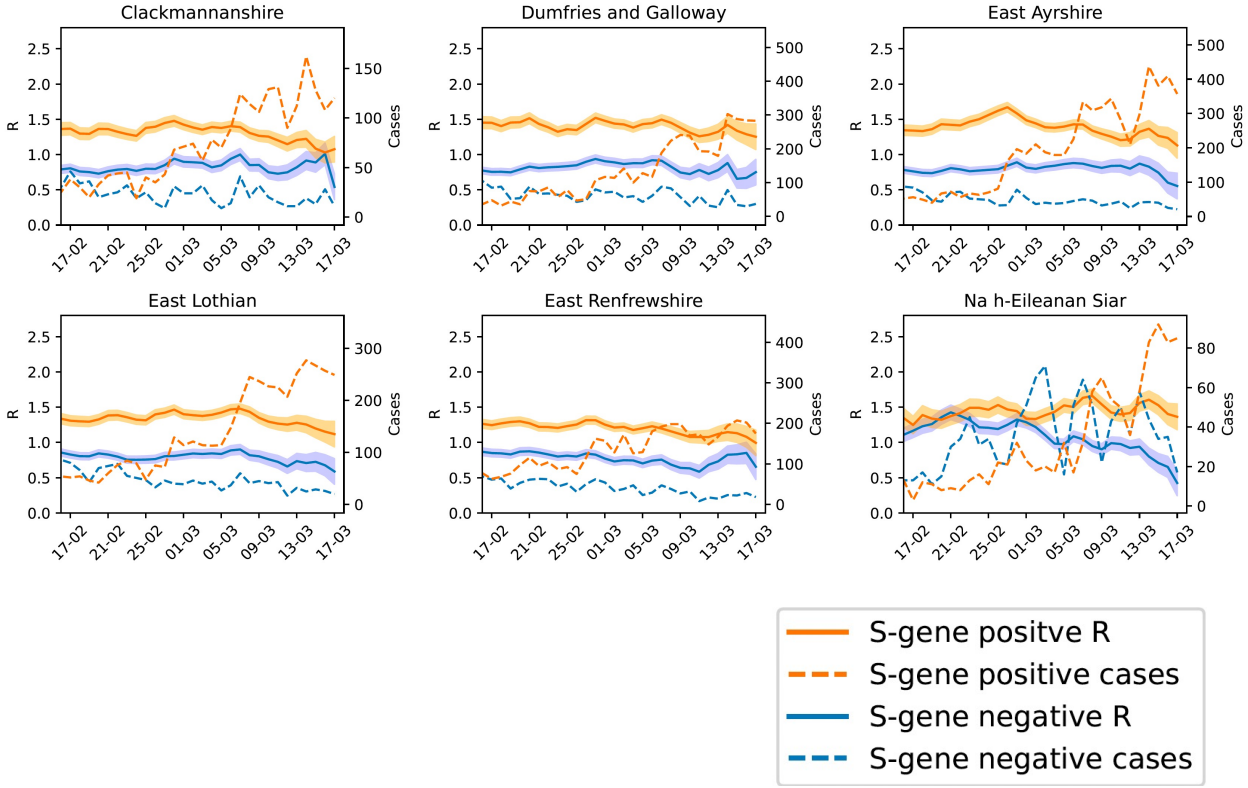


Variant dependent differences in ascertainment by region



Reproduction rates of COVID-19 also vary by Local Authourity



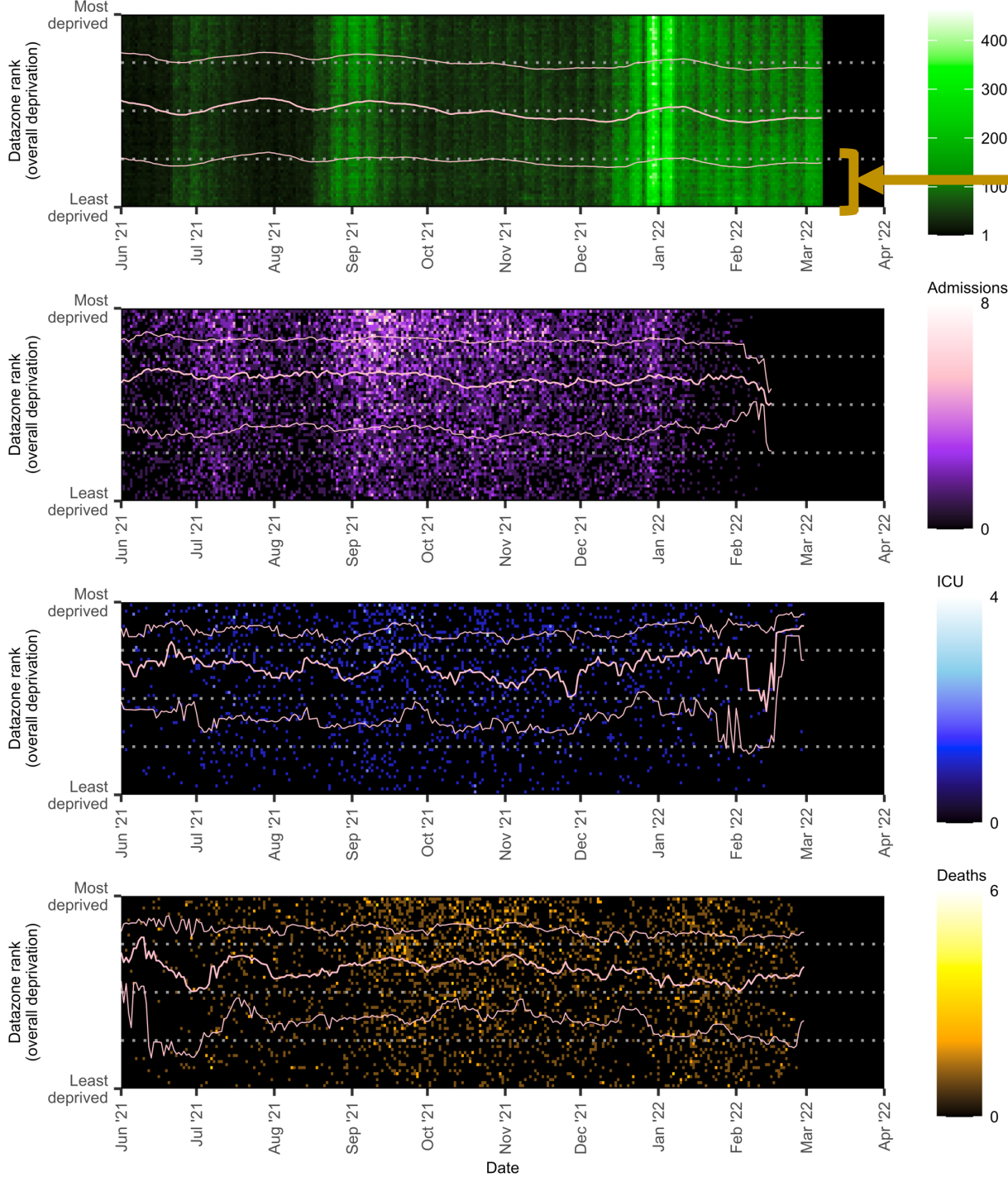


Random Forest models of vaccination and omicron spread

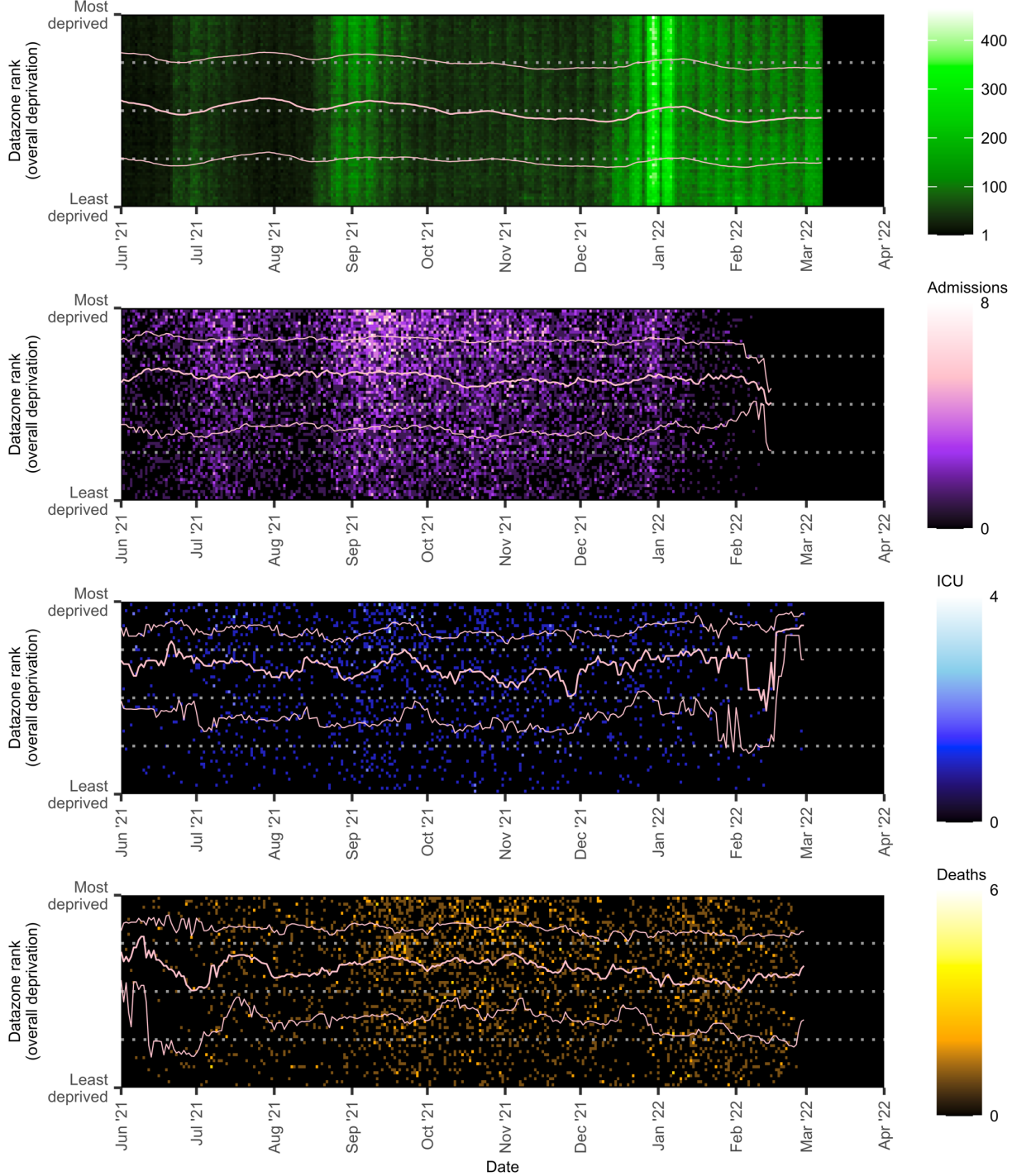
Working in the new world of complex datasets: Can we explain the variation observed at regional levels?

COVID-19 has generated an unprecendent volume of disease relevant data

- Community testing data to estimate incidence
  - PCR
  - Lateral flow tests
- ONS survey of prevalence
- REACT Survey
- COMIX
- Zoe App
- Viral sequence data
- Negative test results
- Commuter patterns
- Mobility patterns
- Contact tracing app (“pingdemic”)
- Demographic data
  - Deprivation
  - Ethnicity
  - Age
  - Gender
- Vaccine uptake



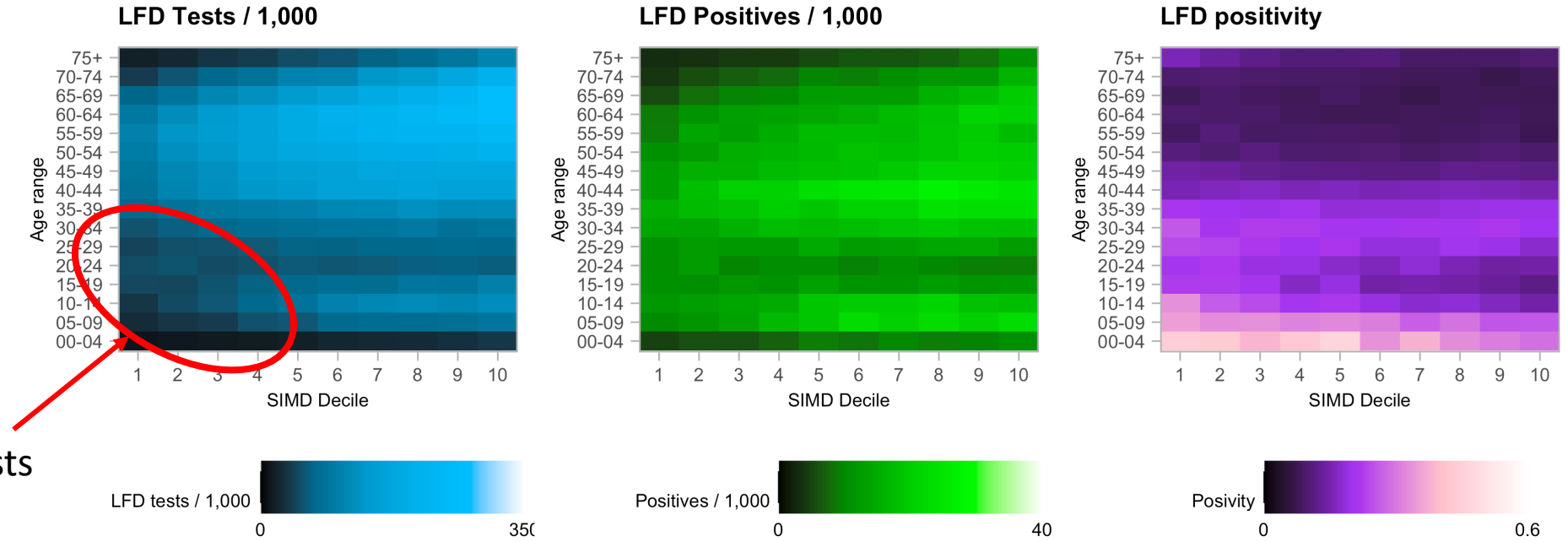
One quarter of cases (narrower gap indicates greater clustering of cases)

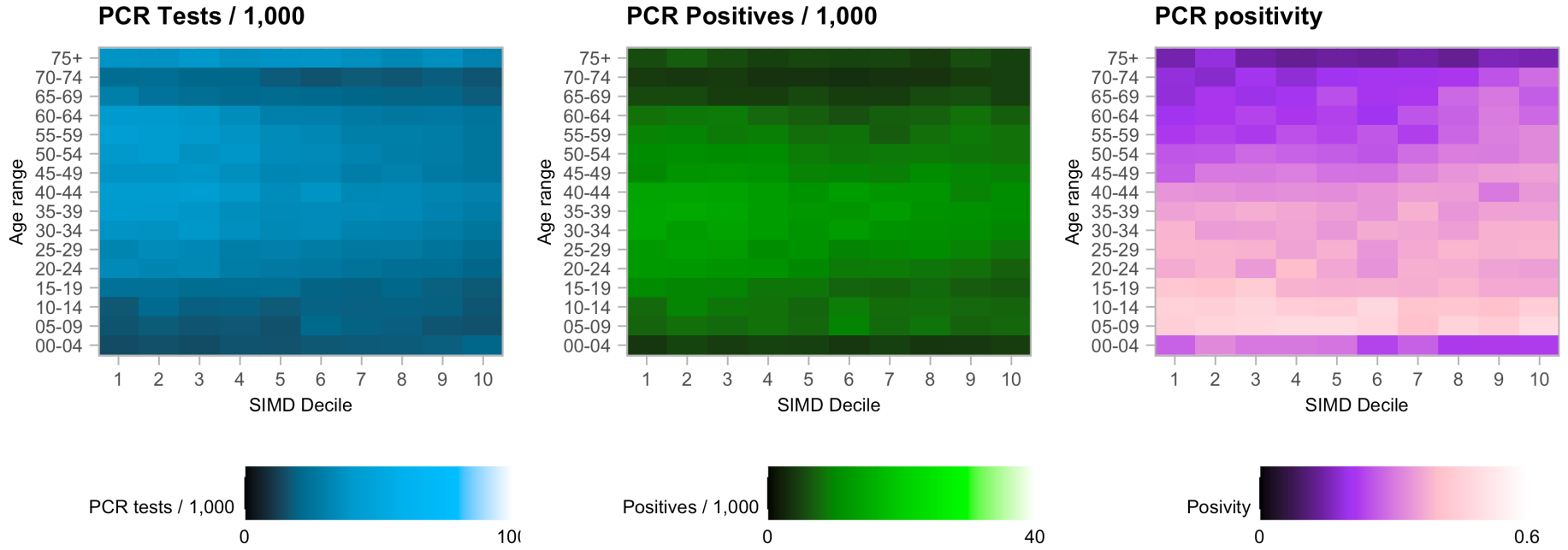


Cases tend to be evenly distributed across DZs

Testing and positivity - week ending 2022-03-19

The fewest tests recorded





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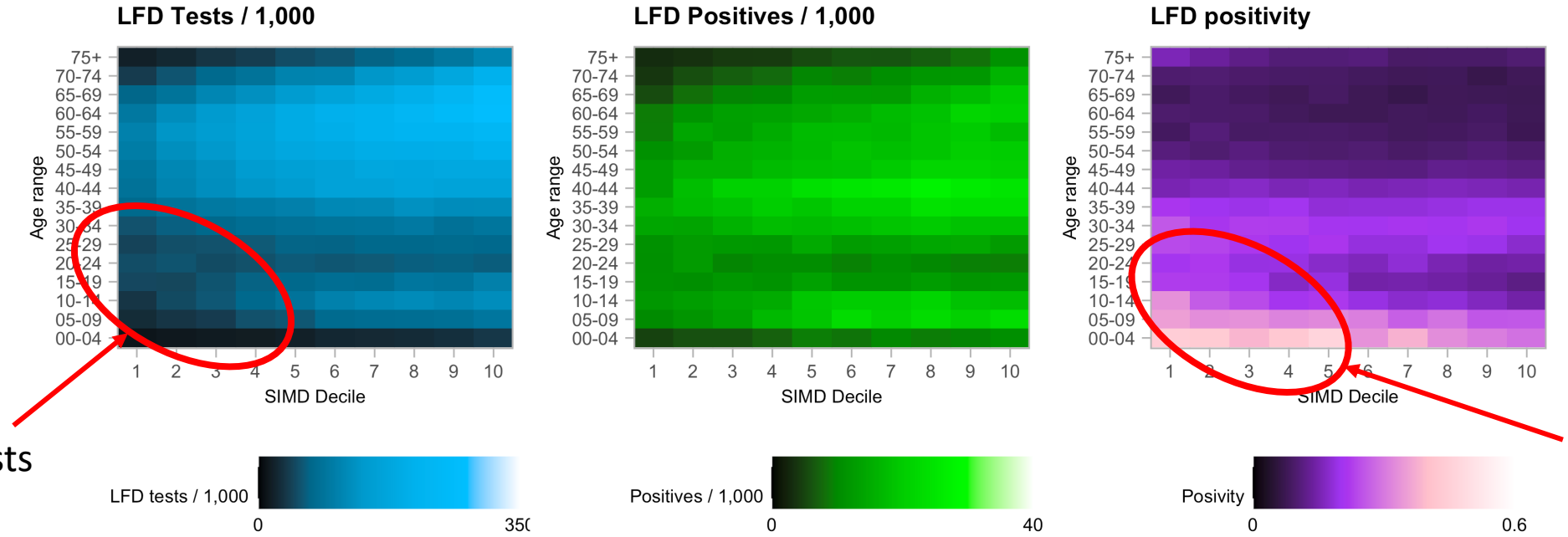
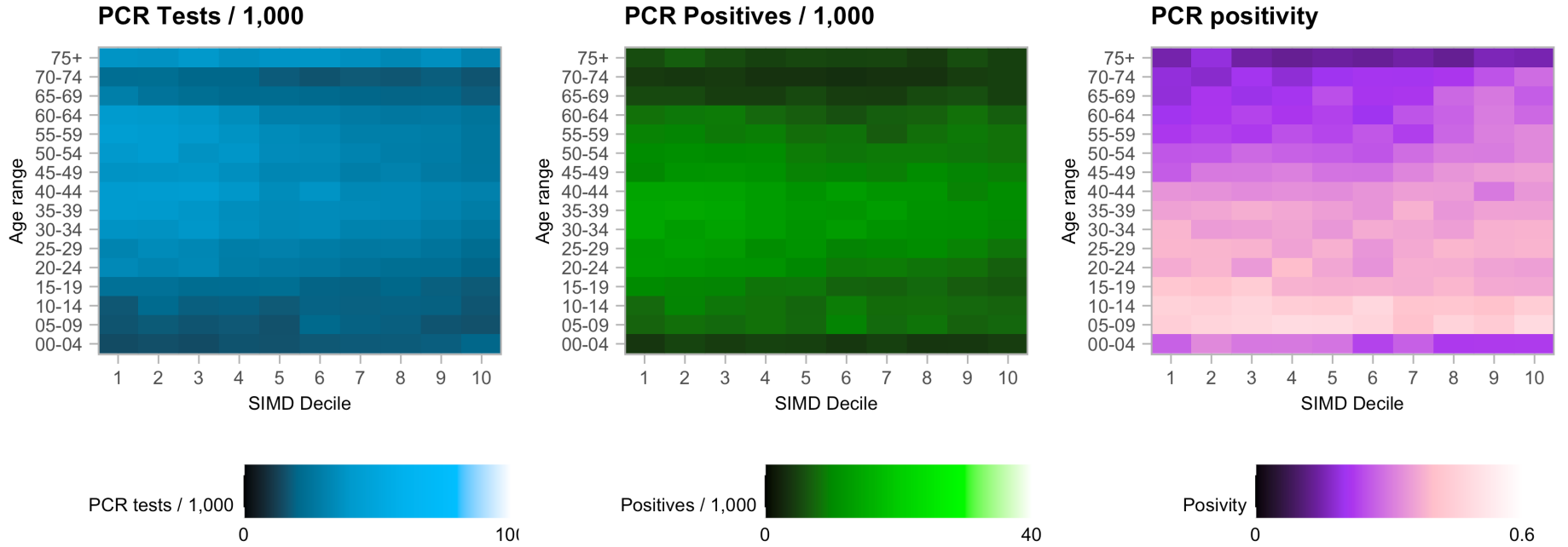
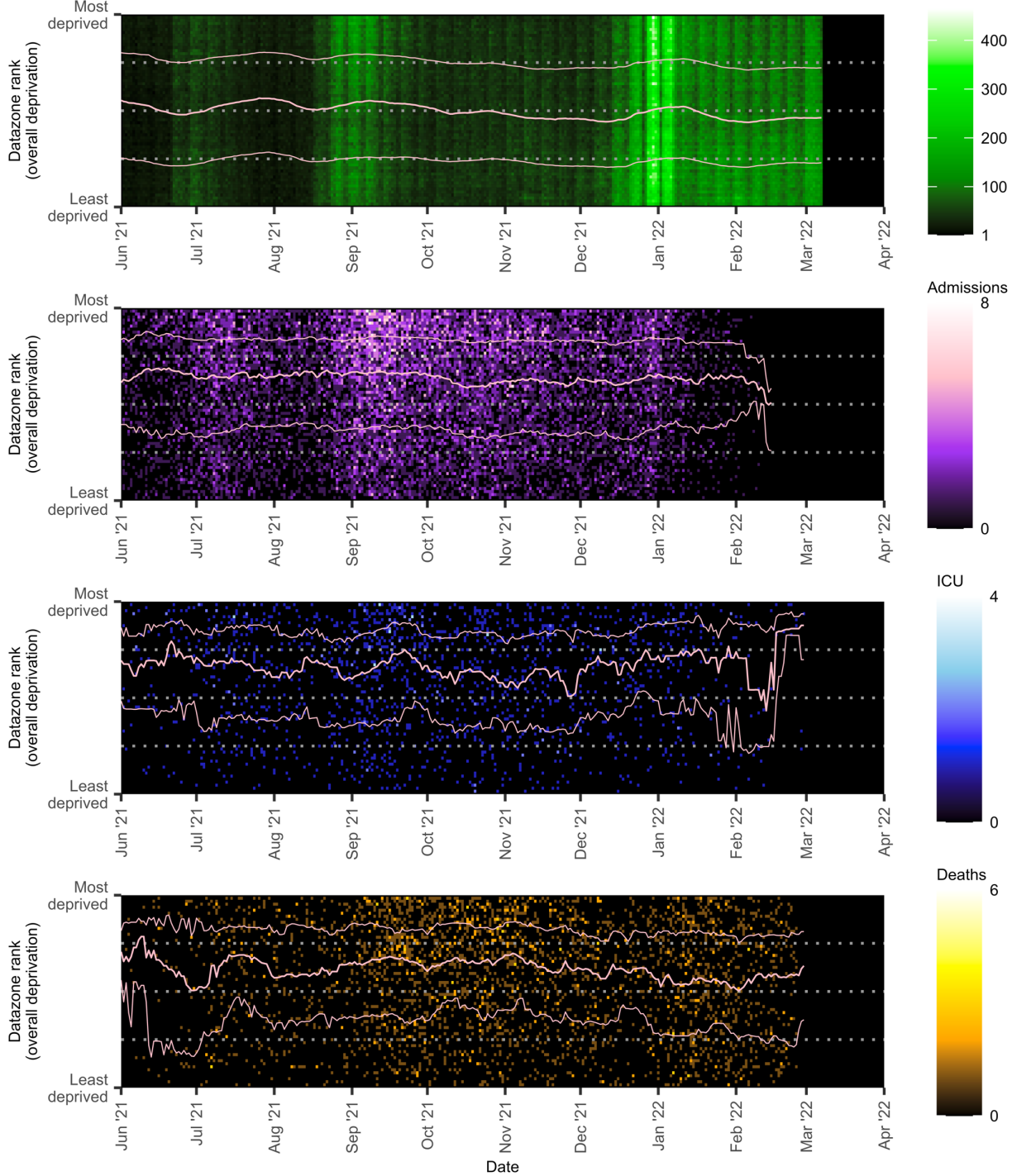


The fewest tests recorded

The highest positivity



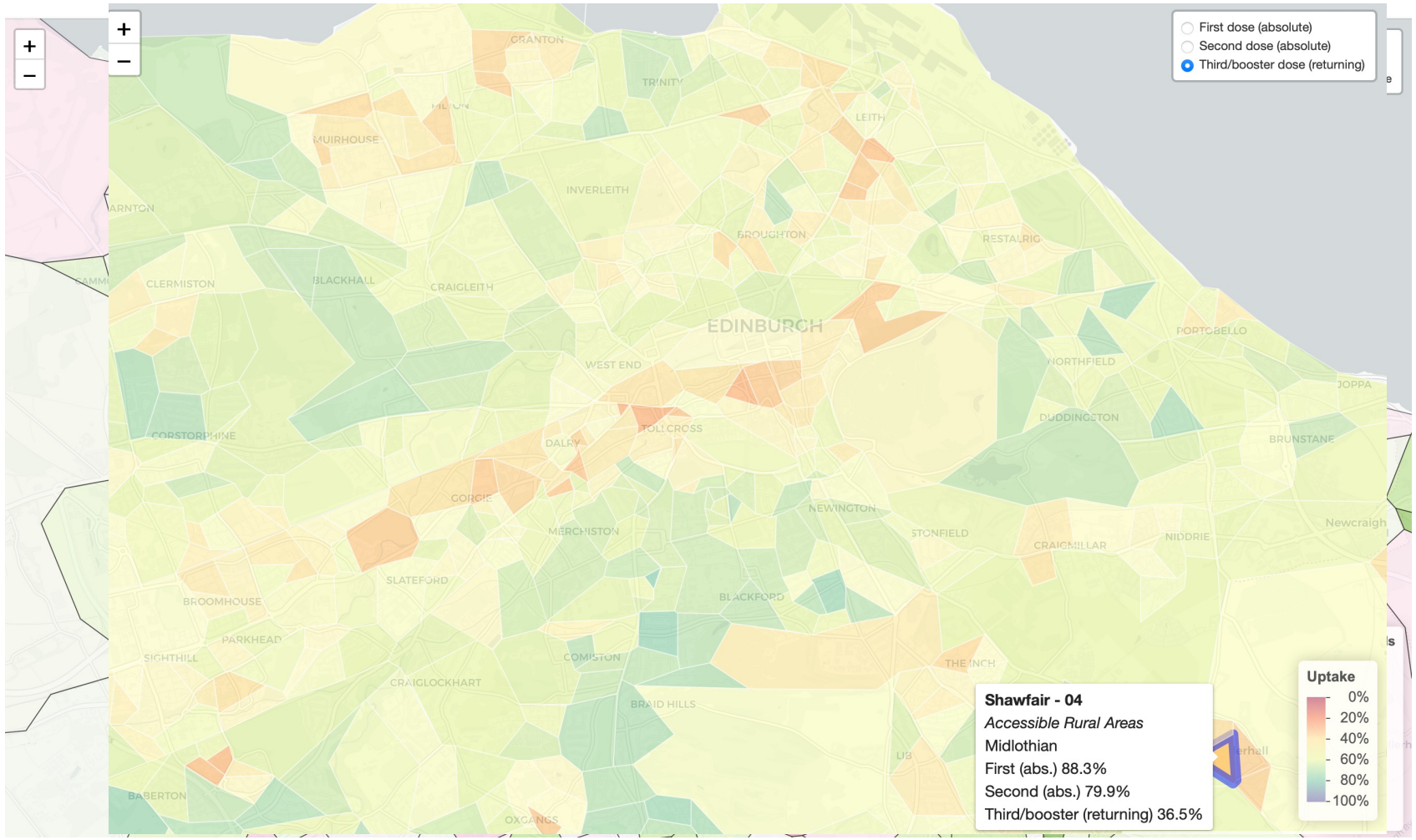
Are people taking tests but not recording negatives or not taking them at all?

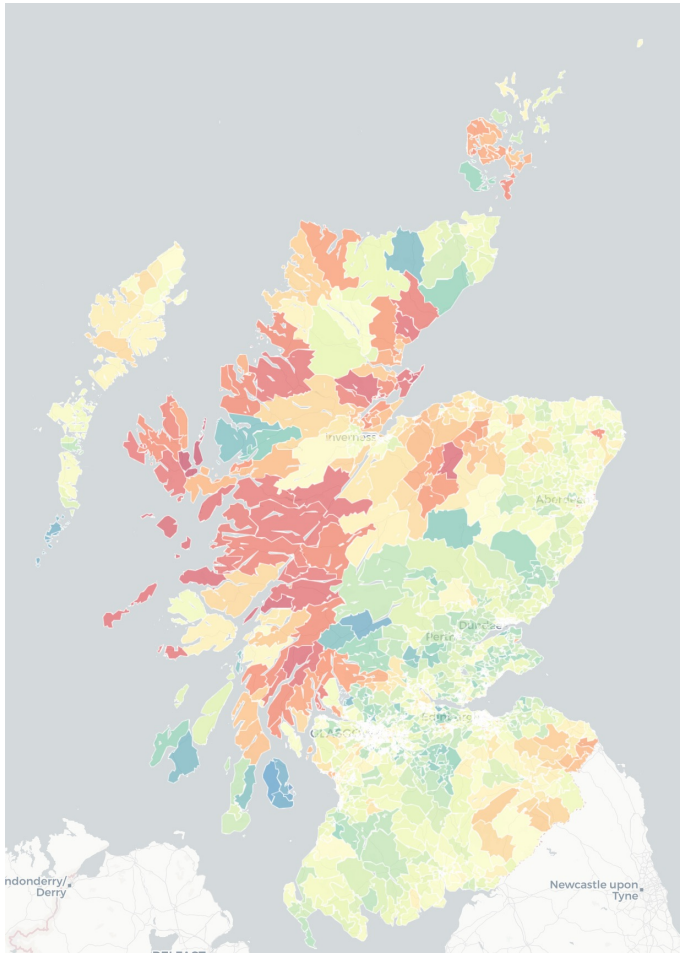


Cases tend to be evenly distributed across DZs

More severe outcomes tend to be concentrated in deprived areas

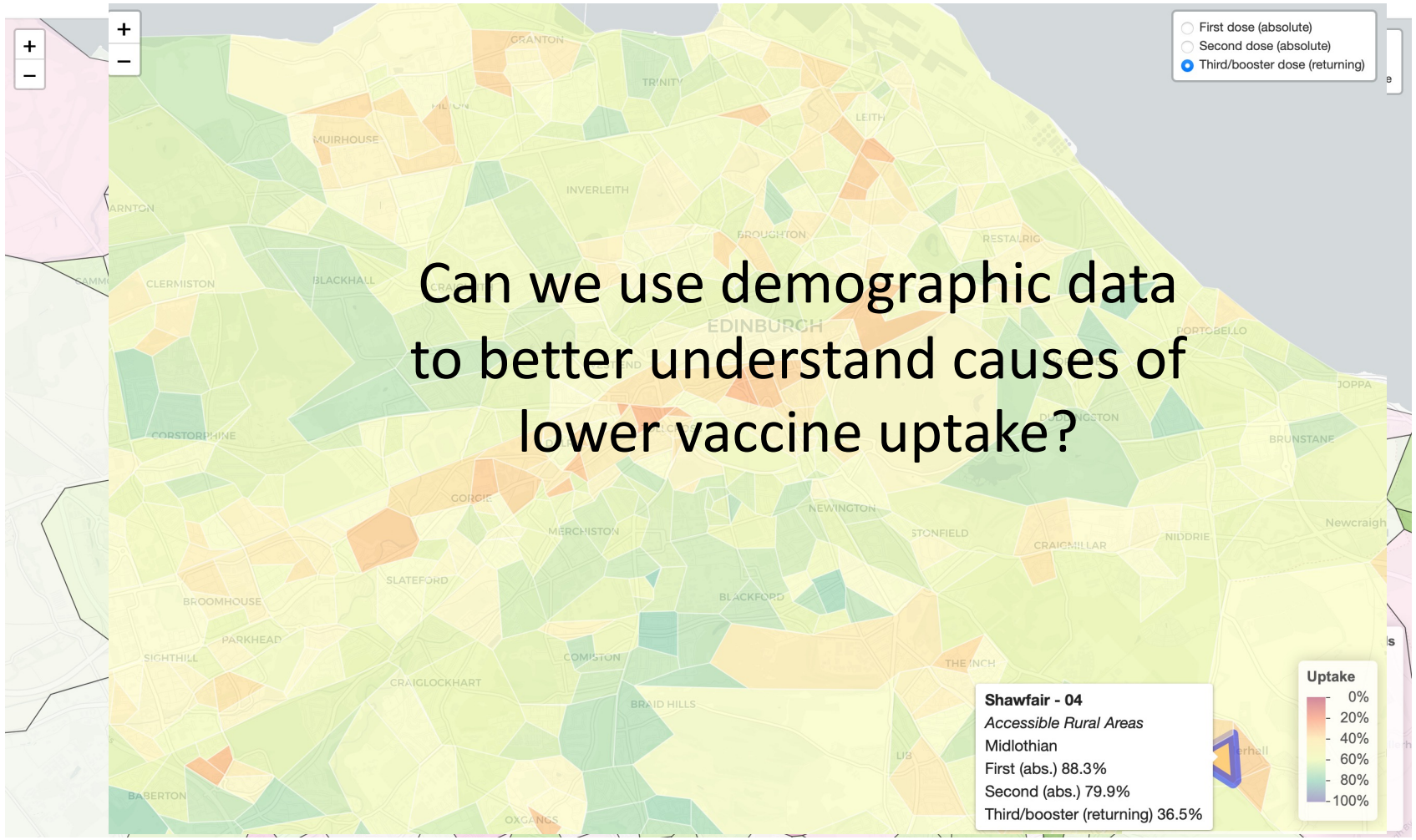
Vaccine uptake at the datazone level (< 1500 popn)

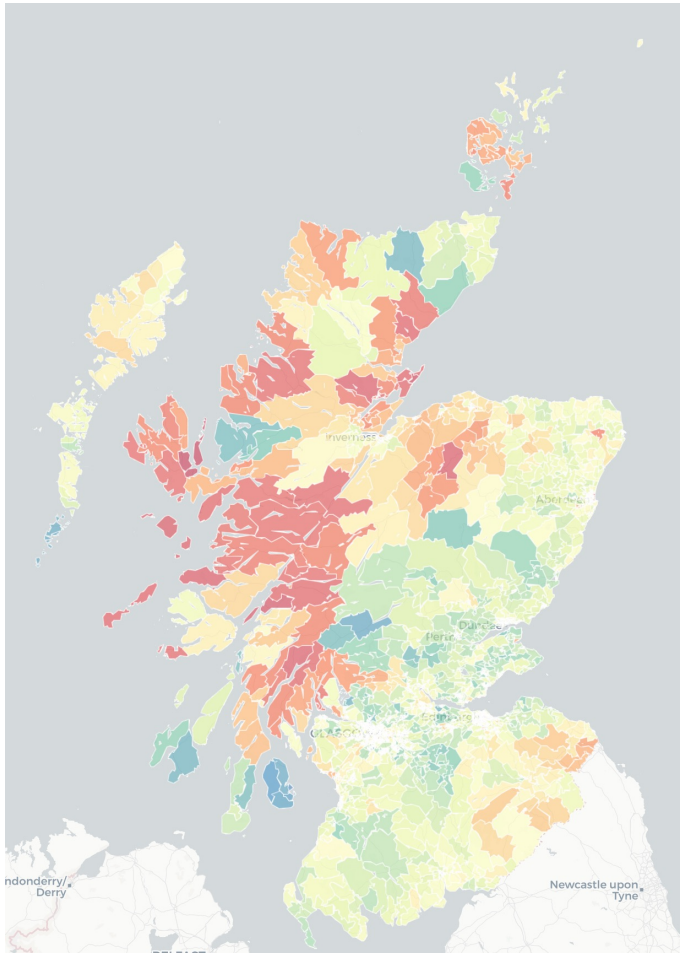




Substantial deficit in vaccine uptake associated with rural access (11th Nov 2021)

Vaccine uptake at the datazone level (< 1500 popn)





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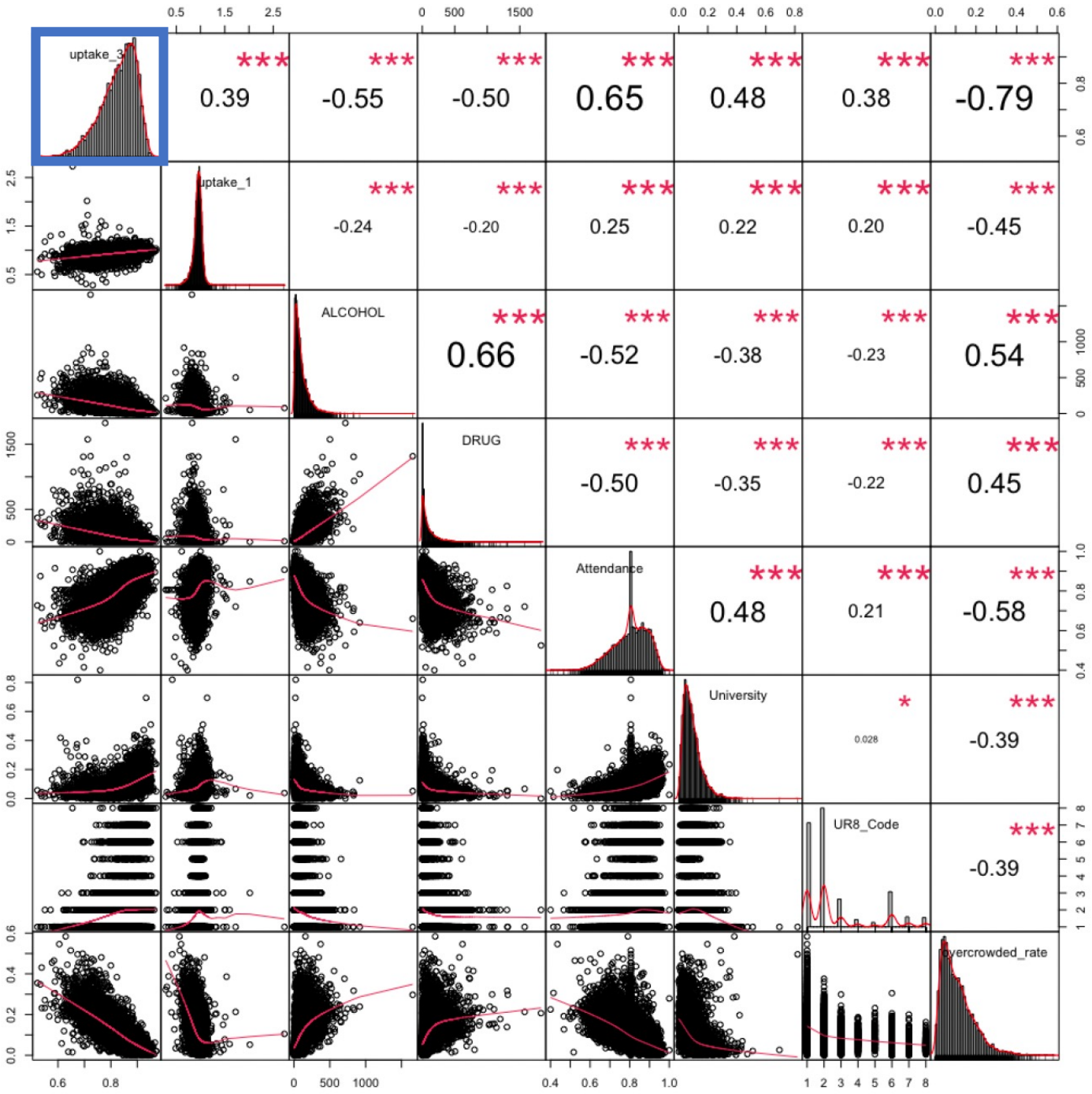
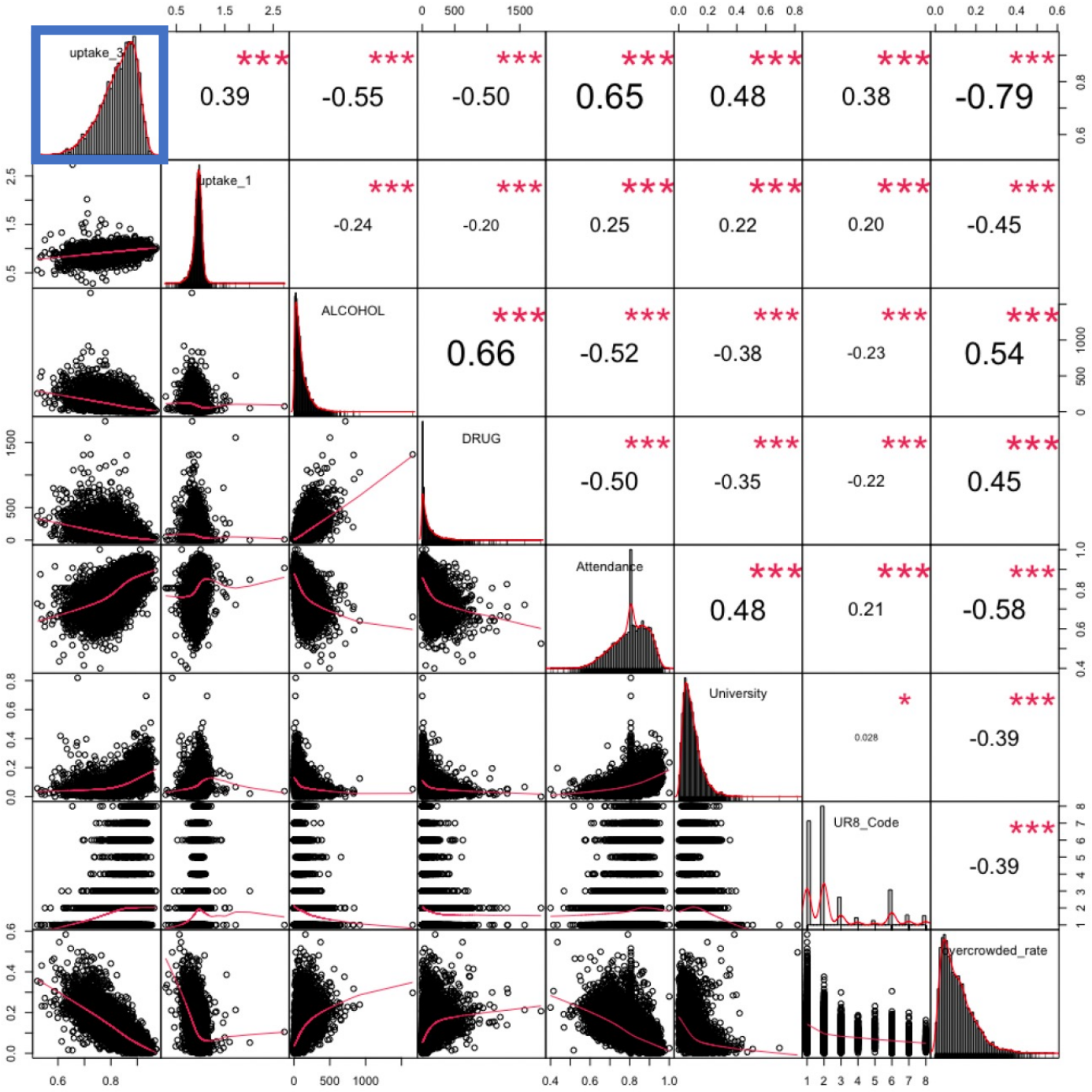


A large number of univariate correlations of deprivation factors with booster/3rd dose uptake

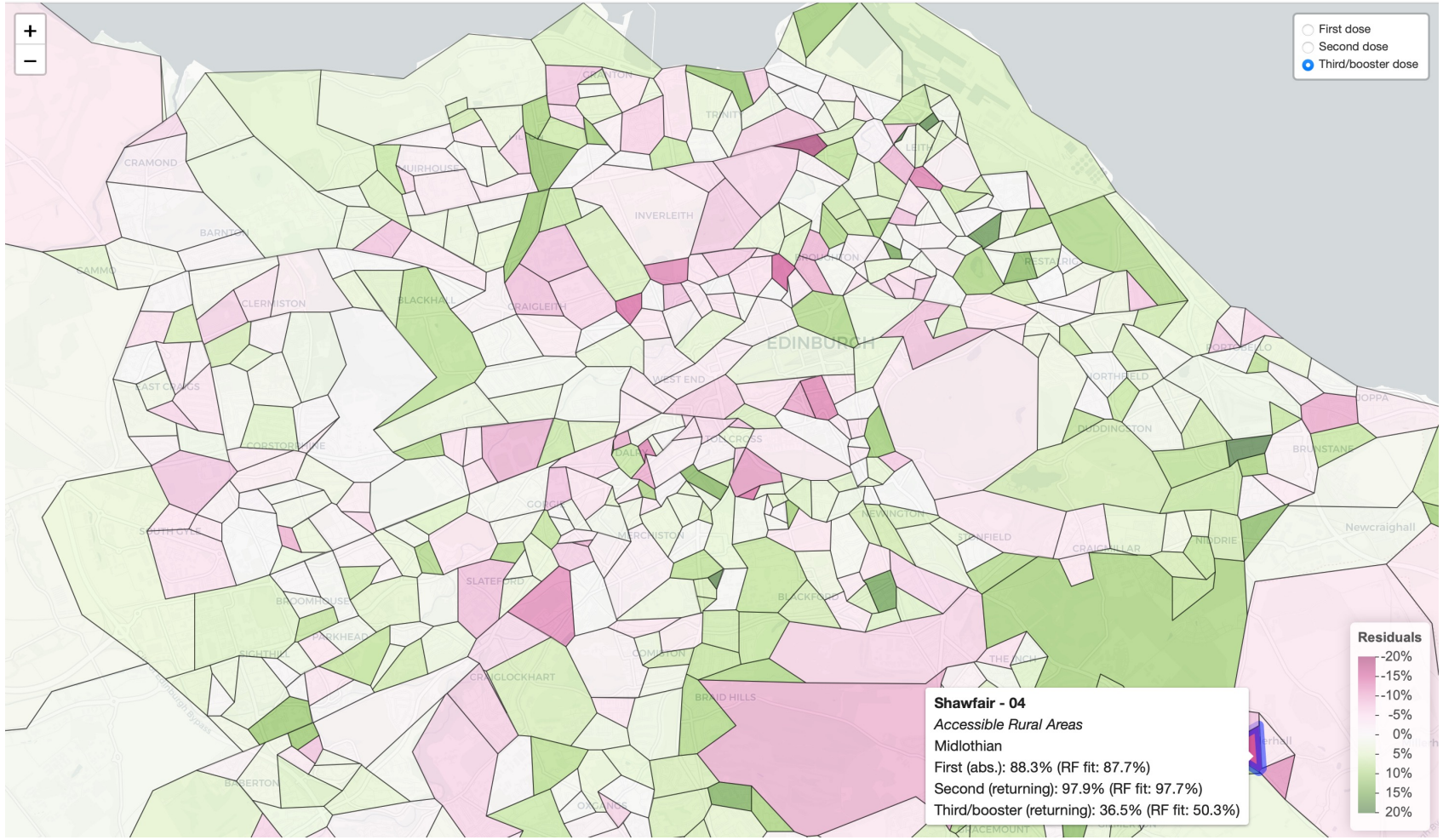
Data are dense and extensive – but highly correlated

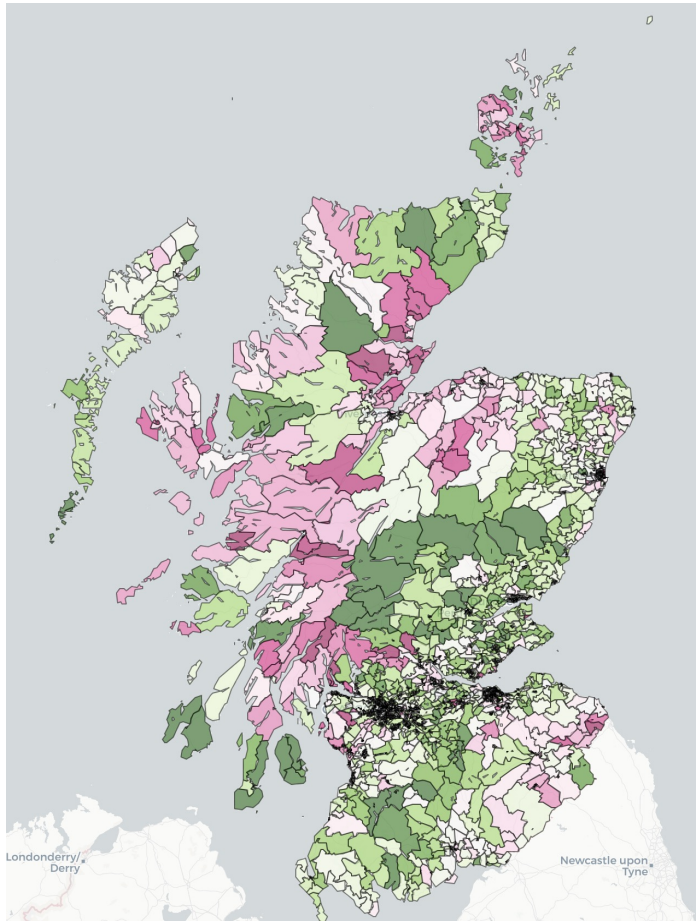


Random Forest Models

- Supervised learning (training datasets)
- Ensemble of sub-trees (limited number of features and sub-sample of data)
- Avoids overfitting even when data variance is high (i.e. doesn't fit noise)

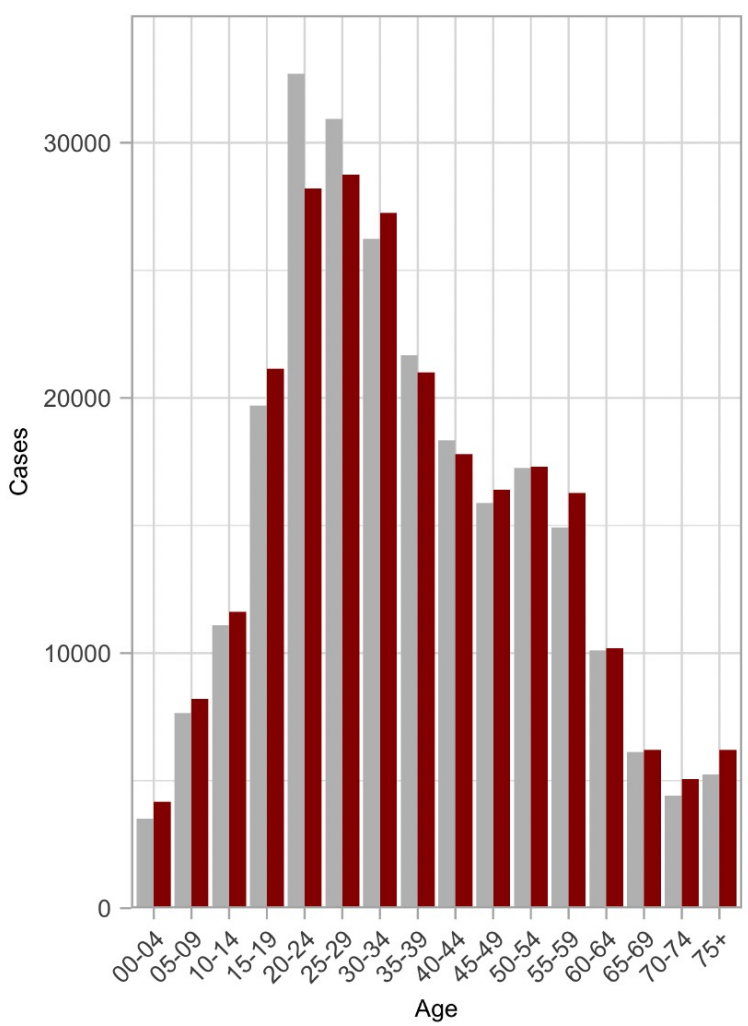
Evaluating vaccine uptake – residuals from Random Forest model

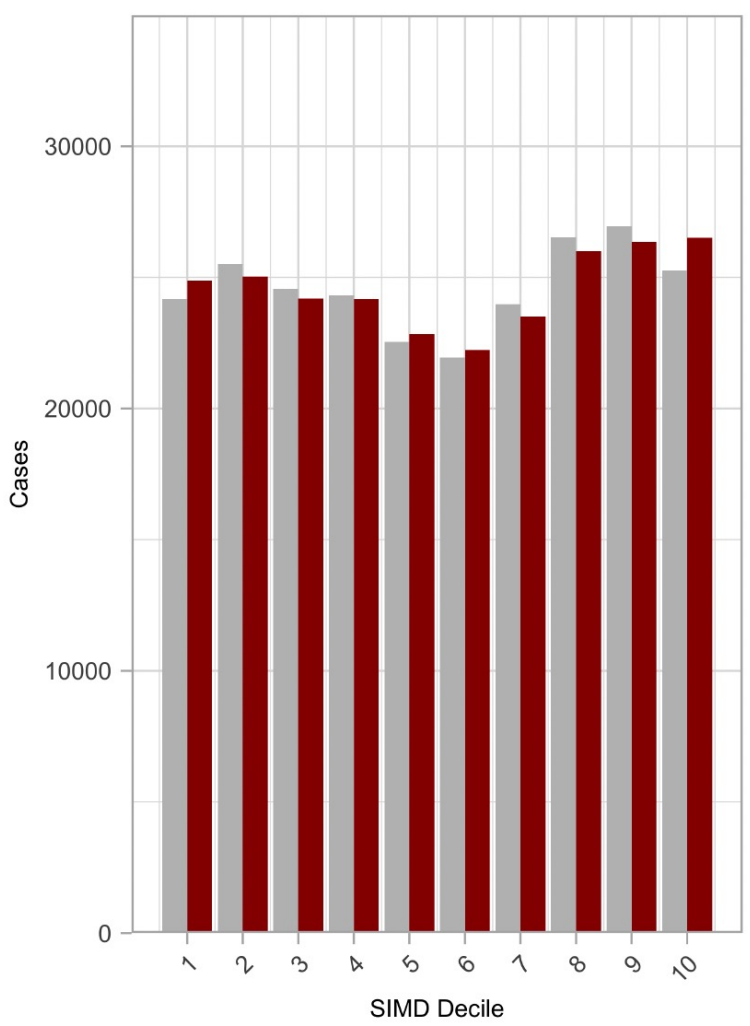


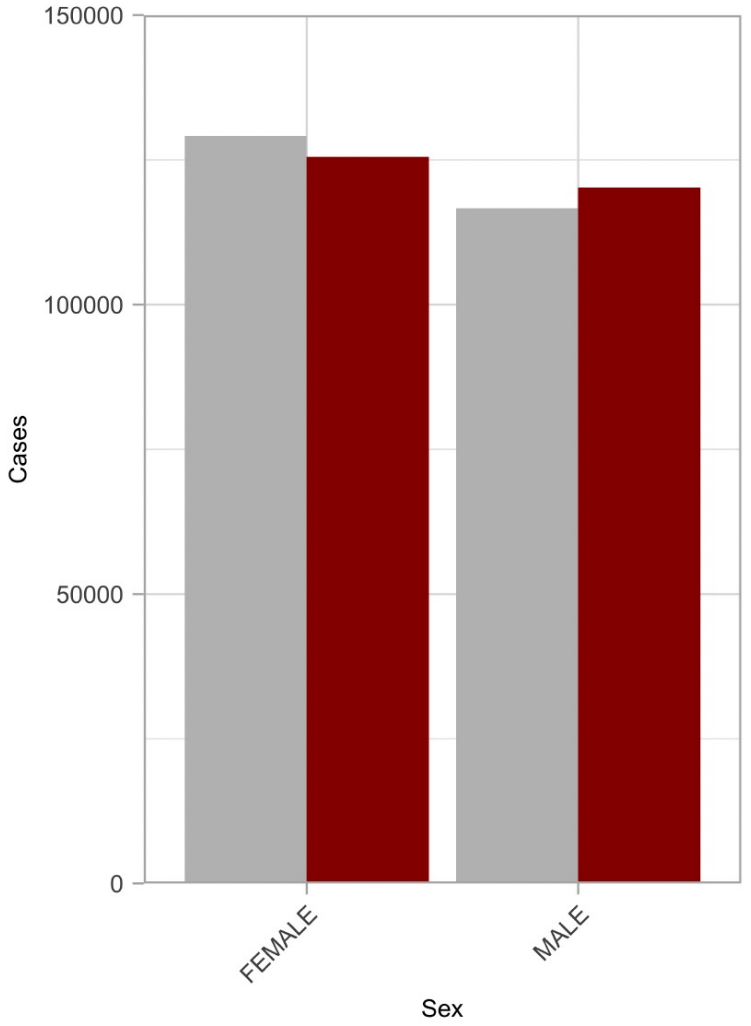


Lower uptake explained by deprivation and age.
Residuals from Random Forest models show areas with unexplained variation

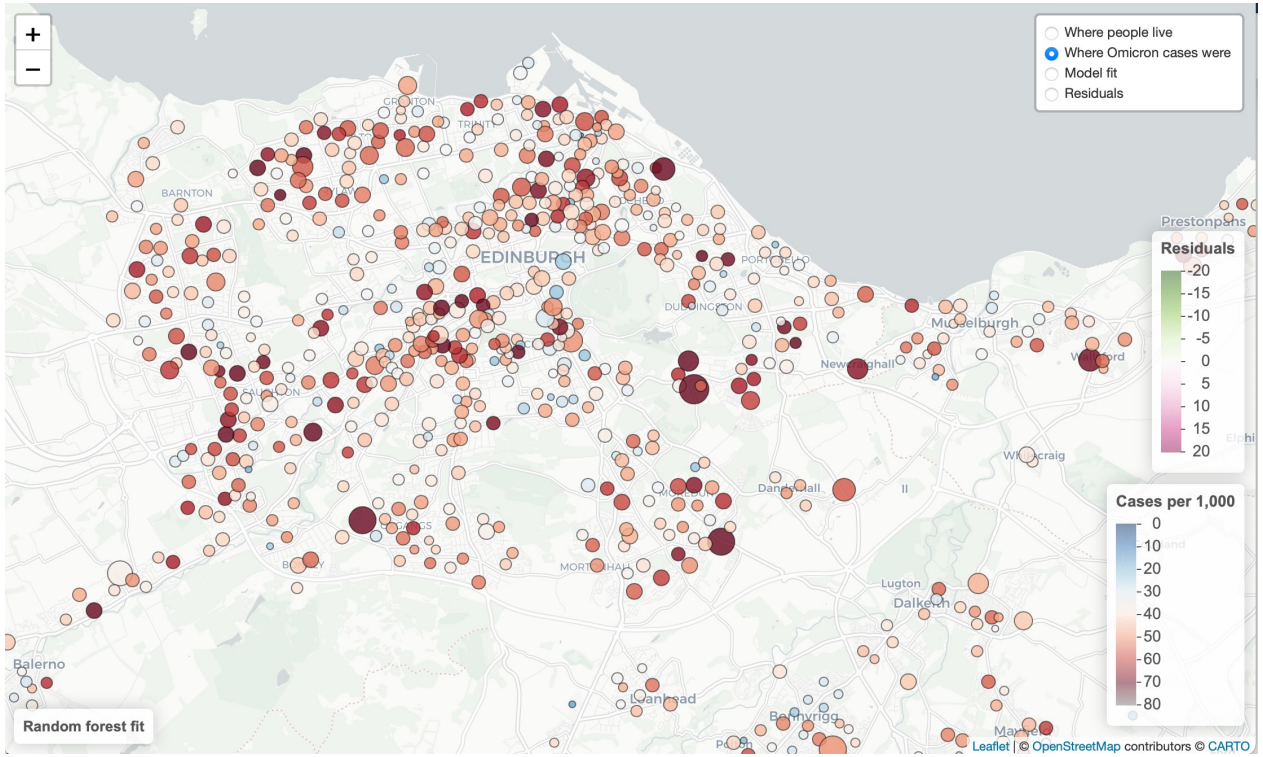
Early Omicron age/deprivation/gender patterns

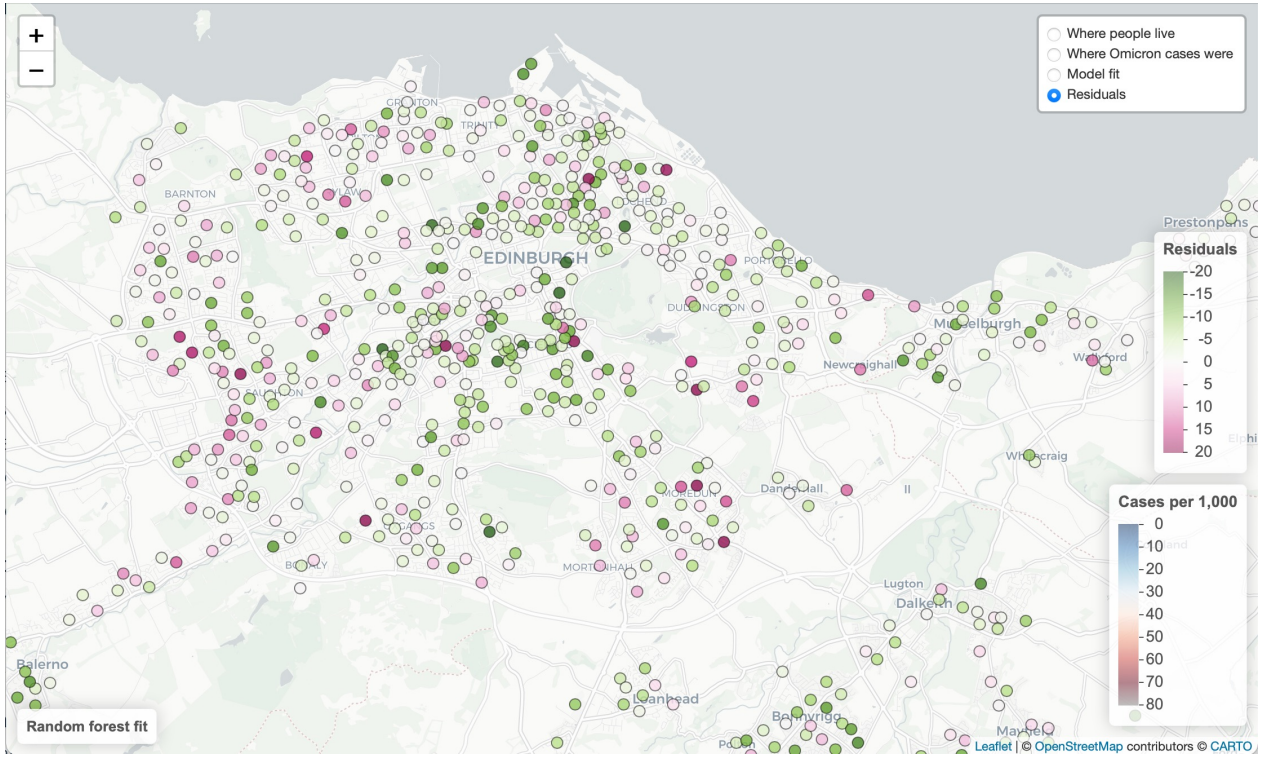




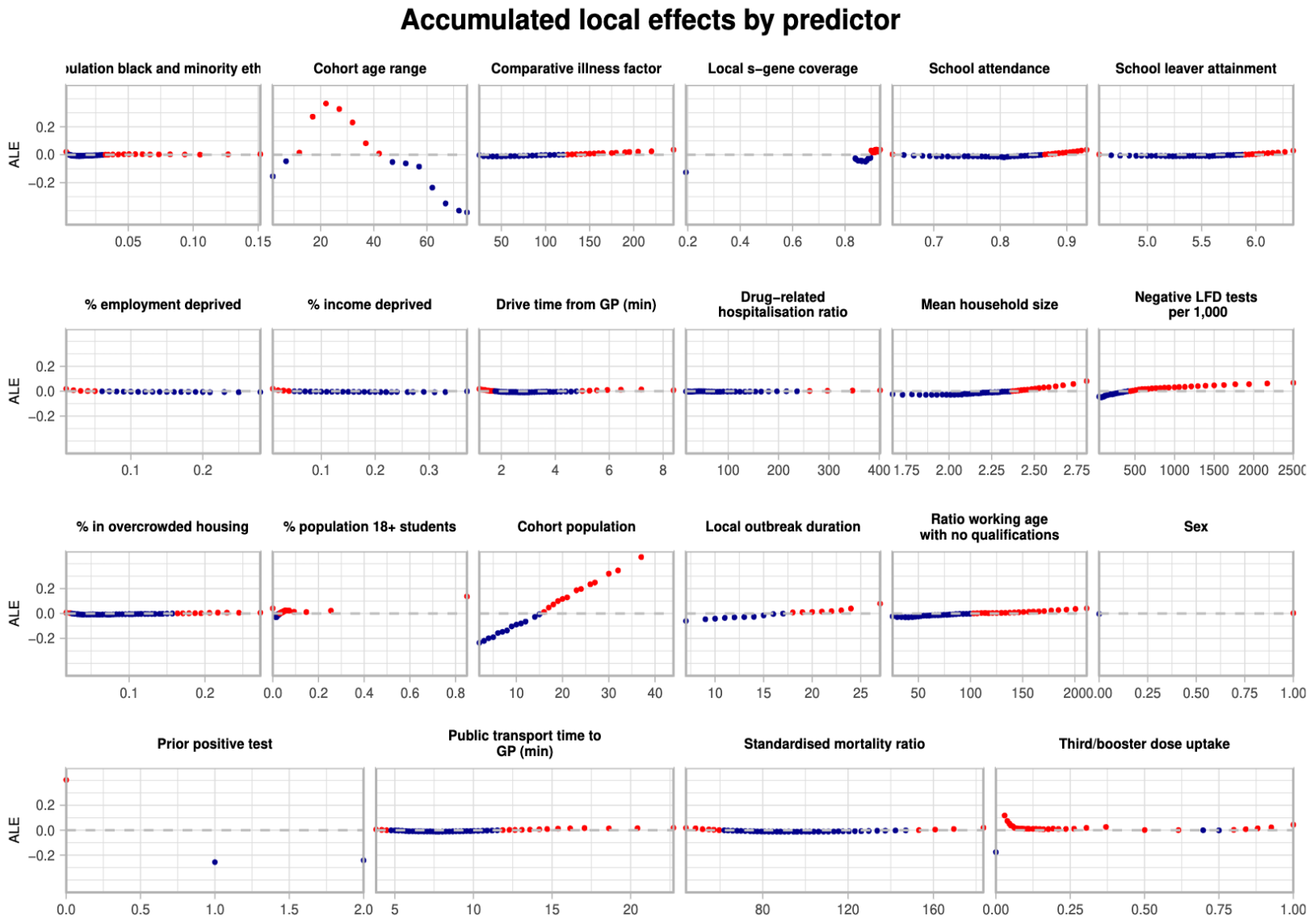


Some unaccounted for spatial clustering

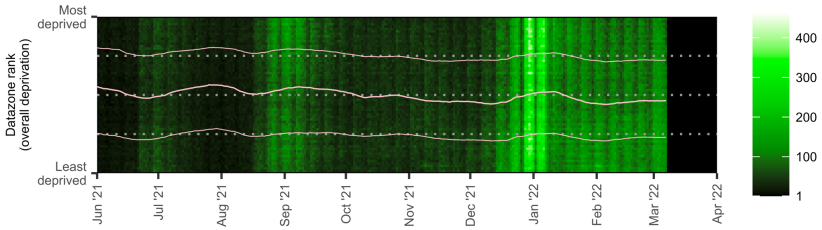




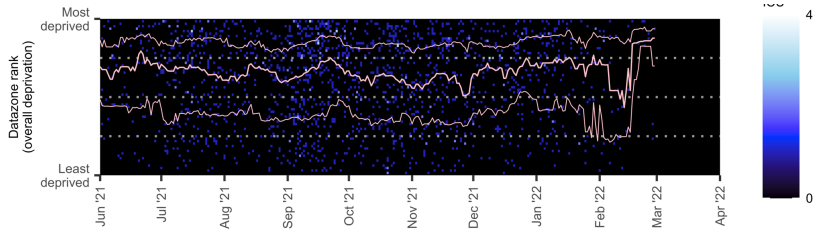
- Census issues (e.g. location of student populations & new neighbourhoods)
- Behavioural patterns
- Epidemiological risks vs. ascertainment deficits



Early phase spread of omicron almost entirely driven by **age** and **population size**



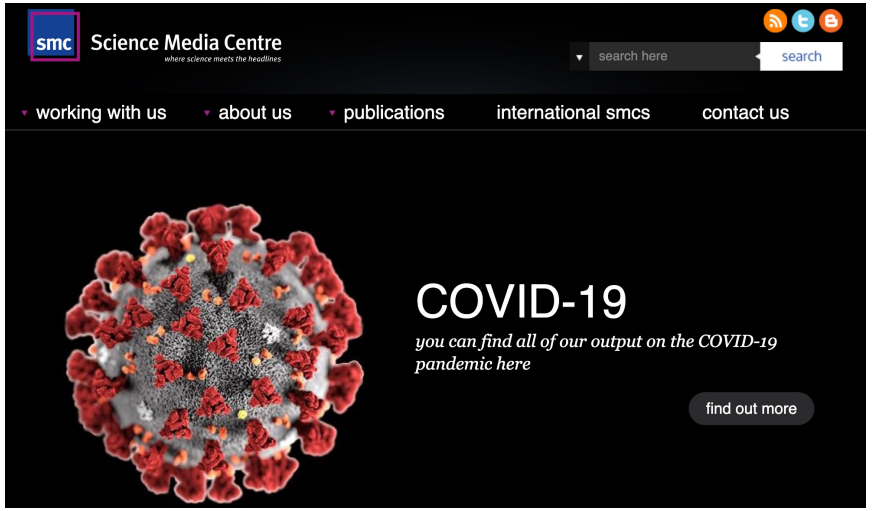
Further analysis of severe outcomes and late phase spread ongoing



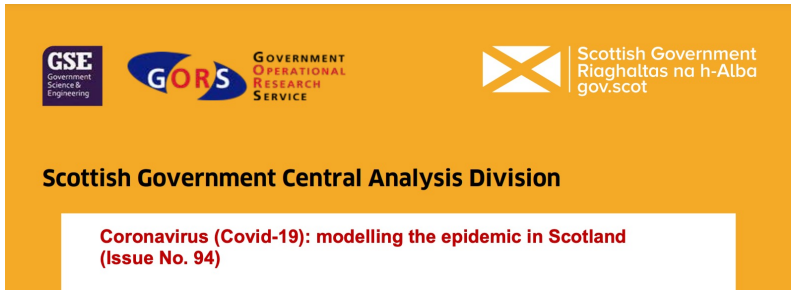
Some thoughts on working with the media and government

Working with the media (why its worth it)

- Many scientists spent considerable amounts of time informing the public via the media
- Important to help people understand the evidence
- Rewarding when you get a positive response
- Separate out personal opinions from roles advising government



Providing advice to government



- Working with the Scottish Government Modelling Team
  - Weekly ”medium term” projections of cases by Local Authourity/LA
  - LA level R estimates
- Analysis of vaccine uptake
  - Shared weekly with Health Boards to assess vaccination campaign progress
- Spatial analysis, influence of age and deprivation

Providing advice to government

- Up to weekly meetings with several subgroups
- Estimates of current and future trends in the UK
- Assessment of future control strategies
- Interpretation of datastreams

Transparency data

List of participants of SAGE and related sub-groups

Updated 4 March 2022

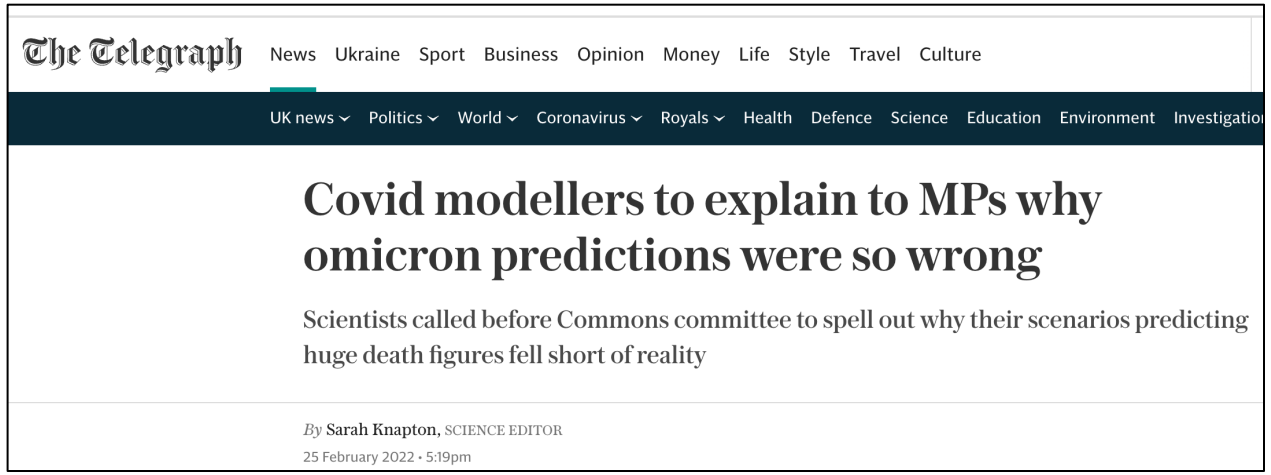
Scientific Pandemic Influenza Group on Modelling (SPI-M)

SPI-M gives expert advice to the Department of Health and Social Care and wider UK government on scientific matters relating to the UK's response to an influenza pandemic (or other emerging human infectious disease threats). The advice is based infectious disease modelling and epidemiology. Find out more about SPI-M.

Contents

Some thoughts on government advice

- Simpler is often better when situations change rapidly
- Consensus matters (“ensemble modelling”)
- Just because you were wrong, doesn’t mean you made the wrong decision (and vice versa)

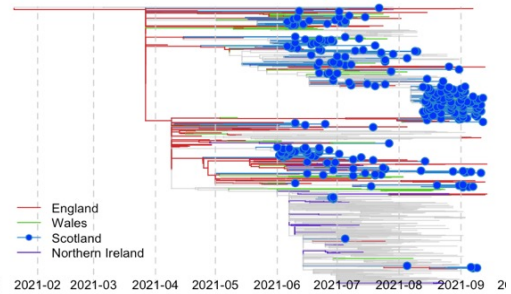


Some key questions for the future

- How does immunity decline over time influence the rate of re-infection?
  - Vaccination schedules & uptake
  - Waning immunity
  - Past infection history
  - Strain cross-protection
- How do different strains compete in space and time?
  - Did omicron act like a vaccine with severe side effects?
  - What drives variant emergence?
- What might happen in a winter of flu plus COVID?
  - Interactions between testing, isolation and human behaviour
  - Hospital burdens and deaths

Computational models plus viral phylogenetics

Contact me: rowland.kao@ed.ac.uk
Applications closing 4th April 2022

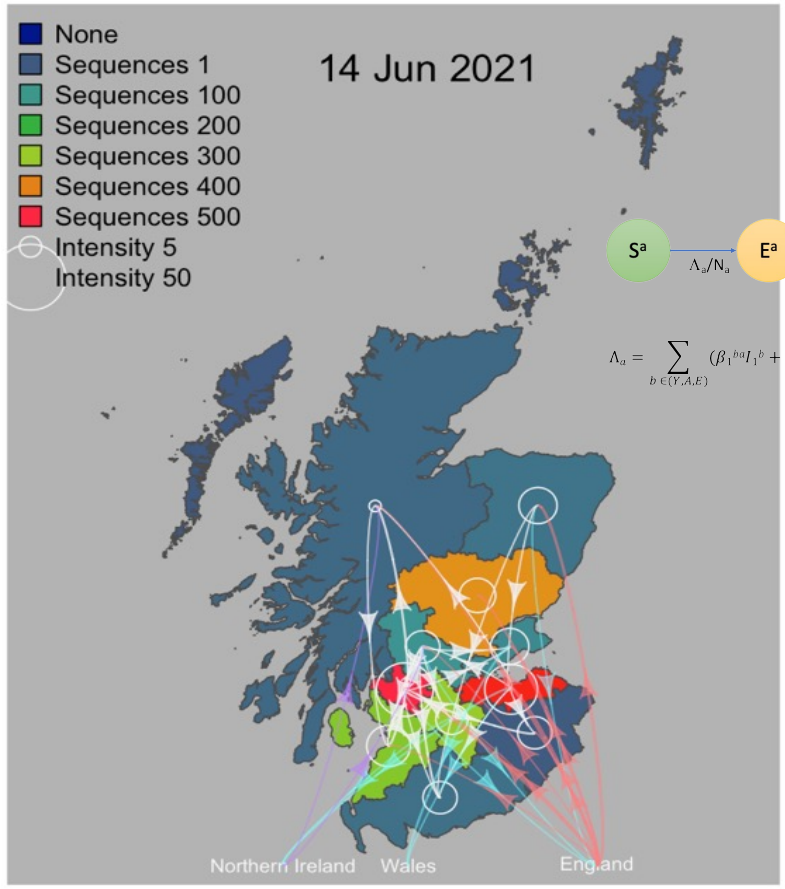


University Of Edinburgh
United Kingdom

Postdoctoral position - infectious disease dynamics incorporating SARS-CoV-2 viral sequence data

We are looking for a postdoctoral scientist with strong mathematical and data analytical skills, who is interested in applying their skills to working on infectious diseases. The successful candidate will work on the development of models of COVID-19 incorporating exceptionally well recorded demographic, testing and viral sequence data, in order to jointly estimate epidemiological and evolutionary parameters, and inform models of control.

In this position, you will be a member of a substantial team working on COVID-19 modelling, collaborating with Drs. Samantha Lycett (University of Edinburgh), Joseph Hughes (University of Glasgow), Sema Nickbakhsh and Alison Smith-Palmer (both PHS). Using a combination of machine learning, mathematical and simulation-based approaches, and subject to an extension of currently held data agreements, you will analyse COVID-19 data on vaccination rates, cases, severe cases and deaths recorded at fine geographical scale, and tied directly to SARS-CoV-2 viral sequences (https://doi.org/10.1101/2021.01.08.20248677). You will use this exceptional combination of data to estimate the importance of a wide range of risk factors (including distance, population density, vaccination proportion, deprivation, and commuting patterns for different job classes) in determining the rate of spatial spread across the course of the SARS-CoV-2 epidemic in Scotland. Working with a research software engineer, your work will inform the further development of an existing large scale agent-based simulation model (https://doi.org/10.1101/2020.11.25.20144139) currently being used by PHS to generate medium term projections of COVID-19 cases in order to inform future control policies.



Embed viral sequence data into spatial models

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- Anthony Wood*

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- Katie Atkins (Usher Institute, Edin)
- Jess Enright (Glasgow)
- Adam Kleczkowski (Strathclyde)
- Chris Robertson (Strath & PHS)
- Gael Beaunée (INRAE)
- Oliver Tearne (APHA)
- Mark Arnold (APHA)

- Mel Giarchi & Scottish Govt modelling team
- eDRIS Team (PHS)