Friday Report: Issue 59

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COVID-19 Actuaries Response Group – Learn. Share. Educate. Influence.

COVID-19 is still one of the hottest topics for scientific papers and articles. The COVID-19 Actuaries Response Group provides a bi-weekly Friday update with a summary of key papers and articles.

Vaccines

COVID-19 Cases and Hospitalizations by vaccination status and previous diagnosis

A [study](#) released by the United States' CDC examined age-adjusted incidence and hospitalisation rates among adults in the states of New York and California between May and November 2021. Their study population was divided into four groups to account for the possible combinations of previous laboratory confirmed COVID-19 diagnosis as at March 2021, and COVID-19 vaccination status as at May 2021.

The authors found that people who were both unvaccinated and had no prior COVID-19 diagnosis had the highest case and hospitalisation rates throughout the study. Prior to July, the lowest case and hospitalisation rates were among those who were vaccinated. In the later weeks of the study, those with prior infections, whether vaccinated or unvaccinated, had lower case and hospitalisation rates than those with vaccination only.

The table below shows the hazard ratios (with associated 95% CIs) for the unvaccinated with no infection prior versus each of the other groups in the week beginning 3 October 2021.

|	Unvaccinated without prior infection vs		
	Vaccinated, no prior infection	Vaccinated, prior infection	Unvaccinated, prior infection
Cases – New York	5.5 (5.3 -5.7)	20.8 (17.2 - 24.5)	15.7(13.6 - 17.9)
Cases – California	7.2 (7.0 - 7.4)	33.5 (28.5 - 38.6)	30.0 (26.0 - 34.1)
Hospitalisations – California	20.8 (19.2 – 22.4)	58.5 (30.2 – 86.8)	56.3 (28.3 - 84.3)

The authors suggest that this may reflect greater waning of immunity among the vaccinated than among the previously-infected.

Given the high numbers of hospitalisations and deaths from primary COVID infection, the authors conclude that vaccination remains the safest and primary strategy to prevent SARS-CoV-2 infections and associated complications.

Booster Progress

Since the New Year progress with booster jabs has continued to slow, with fewer than half a million done in England in the last week. Whilst some will be unable to come forward having recently had an Omicron infection, it's clear from the chart below that engaging with the young has been more difficult, even though these will have previously come forward for their full primary course.

On the positive side though, 91% of those over 50 who have completed the primary course have now had a booster, so those at most risk have largely had all the protection available to them.

England Boosted Proportion as of 19th Jan
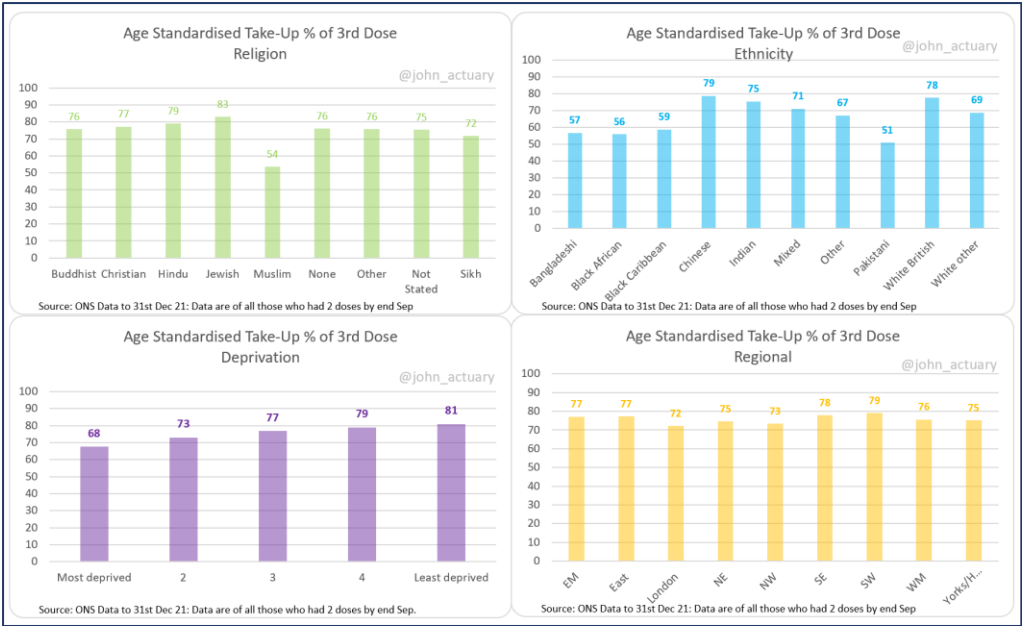(of all those with second doses)
@COVID19Actuary
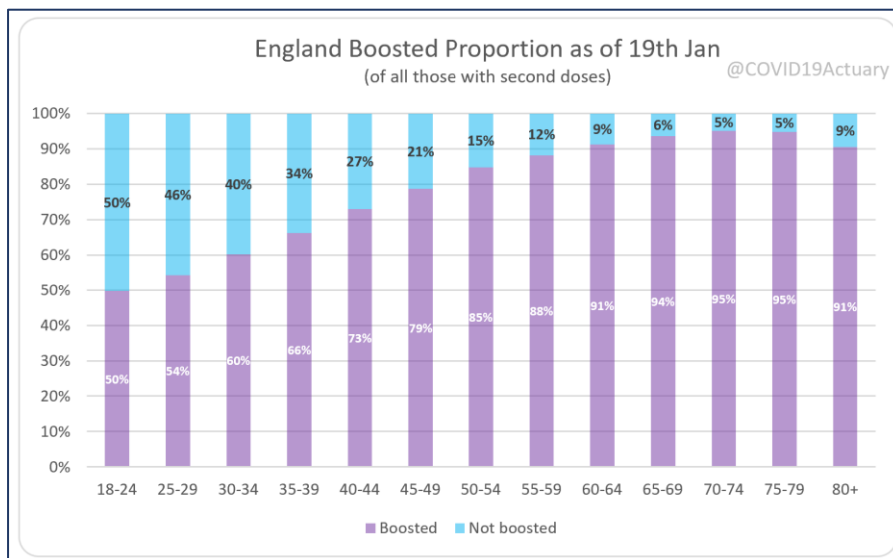
Booster doses are now available for those aged 16 and 17 who have the requisite three months' elapsed duration since their second dose. In due course around 600,000 will be eligible at these ages.

Socio-Economic Variations in Booster Take-Up (link)

It's been a feature of the vaccination programme that minority groups and those at the lower end of the socio-economic spectrum have seen lower take-up rates. New data from ONS show that this differential has continued into the booster programme, with lower take-up of the booster (when measured against all those who have had two doses) in the socio-economic groups that were associated with low vaccination uptake previously.

The data are age-standardised, thus allowing for the fact that many minority ethnic groups have a younger population. We can also see that take-up in London has been lower than in other regions, even after allowing for its younger population.

When this is added (or more accurately, multiplied) to the disparity seen in the original programme, some very wide variances are seen. As an example, whereas White British take-up of all three doses is 68%, it is exactly half that for Black Caribbean at 34%. Regionally the range widens to 70% in the South West to just 57% in London.

Age Standardised Take-Up % of 3rd Dose — Religion
@john_actuary
Source: ONS Data to 31st Dec 21: Data are of all those who had 2 doses by end Sep

Age Standardised Take-Up % of 3rd Dose — Ethnicity
@john_actuary
Source: ONS Data to 31st Dec 21: Data are of all those who had 2 doses by end Sep

Age Standardised Take-Up % of 3rd Dose — Deprivation
@john_actuary
Source: ONS Data to 31st Dec 21: Data are of all those who had 2 doses by end Sep.

Age Standardised Take-Up % of 3rd Dose — Regional
@john_actuary
Source: ONS Data to 31st Dec 21: Data are of all those who had 2 doses by end Sep

Vaccinating the Unvaccinated (link)

The above analysis moves us neatly onto the next review, where research on behalf of the Tony Blair Institute for Global Change investigates the reasons for hesitancy. Polling 1,500 people, of which half are unvaccinated, it finds that access to the vaccine is reported to be an issue for around 20% of those yet to be jabbed. Of the others, the main reasons given are concerns over the safety and efficacy of the vaccine.
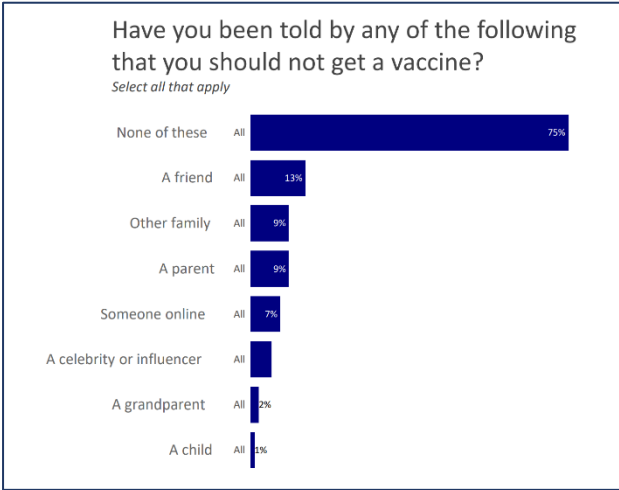
Maybe surprisingly, when asked who they have listened to in deciding whether or not to come forward, 75% say that nobody has told them not to have it.
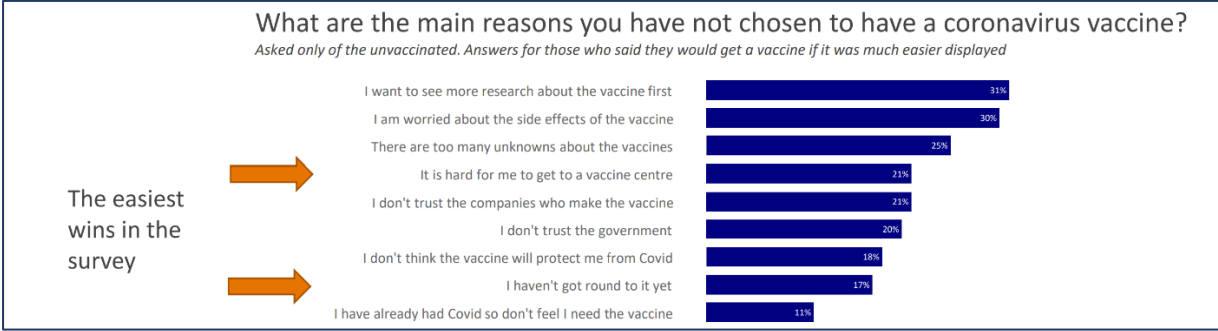
This analysis should be a useful tool for anyone involved in trying to increase uptake in the remaining vaccine hesitant population.

This research was conducted as part of a much more wide-ranging report published by the Institute, titled, "Living with COVID" (link). Recommendations in the report include offering a fourth dose to the Over 70s and immunosuppressed, implementing an antivirals strategy, and revamping the testing infrastructure.

Variants

Outcomes of laboratory-confirmed SARS-CoV-2 infection in the Omicron-driven fourth wave compared with previous waves in the Western Cape Province, South Africa

A pre-print cohort study included 5,144 public sector patients in the Western Cape with a laboratory confirmed COVID-19 diagnosis between 14 November-11 December 2021 (wave four). The study also included 11,609 patients from equivalent prior wave periods. The authors compared the risks of death (as well as hospitalisation) between the waves, adjusting for age, sex, comorbidities, geography, vaccination and prior infection.

Risk of death was lower in wave four compared to the Delta-driven wave three. The adjusted hazard ratios for death, with 95% confidence intervals, were as follows:

- Without adjustment for vaccination or prior infection: 0.27 [0.19, 0.38].
- With adjustment for vaccination or prior recorded infection: 0.41 [0.29, 0.59]
- With adjustment for vaccination or prior recorded infection, as well as undiagnosed prior infections: 0.72

In arriving at the 0.72 estimate, the authors assumed that prior infection reduces risk of death by 80% and that 15% of prior diagnosed infections were ascertained, based on the comparison of case and seroprevalence data.

The low rate of case ascertainment in South Africa makes it difficult to determine how much of the lower rates of severe outcomes during the Omicron wave is attributable to lower virulence as opposed to previously acquired immunity. This information is important for translating the observed South African experience to countries with different immunity profiles.

The study also reported on the relative risks of death in wave 1 (wild type) and 2 (Beta) relative to the Delta wave. After small adjustments for vaccination and prior infection, the death hazard ratios were

- Wave 1 vs wave 3: 0.55 [0.40; 0.77]
- Wave 2 vs Wave 3: 0.60 [0.48; 0.74]

Sensitivity of SARS-CoV-2 antigen-detecting rapid tests for Omicron variant

The emergence of each novel SARS-CoV-2 variant of concern (VOCs) requires investigation of its potential impact on the performance of diagnostic tests in use, including Antigen-detecting rapid diagnostic tests. A pre-print study by the University of Geneva compared performance for Delta and Omicron using clinical samples from vaccinated individuals with either Omicron or Delta breakthrough infection. Tests were also carried out using cultured virus (to compare to the results for the clinical samples). Four out of seven rapid test types showed significantly lower sensitivity to detect Omicron when compared to Delta. The remaining three had comparable sensitivity to Delta.

	Sensitivity (%)		
	Delta (n=34)	Omicron (n=36)	p[1]
Panbio	67.7	36.1	<.001
Standard Q	52.9	22.2	<.001
Sure Status	52.9	27.8	<.001
Onsite	64.7	47.2	<.001
Wondfo	76.5	75.0	.984
Tigsun	52.9	47.2	.634
Flowflex	91.2	88.9	.918

Table 2. Detailed sensitivity for the seven Ag-RDTs tested with clinical samples. [1] p-values for logistic mixed-effect models (with tests nested into patients) are reported.

The Flowflex test which is in common use in the UK was one of the three test brands that showed similar sensitivity of detection for Delta and Omicron samples.

Omicron sub-lineage BA.2

On 6 December 2021, BA.2 was designated as a sub-lineage of Omicron. In their Technical Briefing 34 which summarises the latest information on SARS-CoV-2 variants, UKHSA recorded that an increase in the number of sequences of this sub-lineage has been noted in the UK and Denmark. As of 10 January, 53 sequences of BA.2 have been identified in the UK and 2,093 sequences from 22 countries were reported on GISAID. This represents around 2% of the worldwide 'clades' (ie tracing back to a common ancestor) captured by GISAID.

Unlike BA.1, BA.2 does not have the spike gene deletion at 69-70 that causes S-gene target failure in TaqPath PCR tests. This means that caution is now required when interpreting comparative analyses which use S-gene target results as the only determinant of Omicron and Delta.

It is also not clear how the mutations will affect transmissibility and severity, although growth in sequence numbers (albeit from a small base) suggests it may have some transmission advantage over existing variants.

Other variants, such as Delta, have also shown development of sub-lineages, as illustrated by this schema from Nextstrain. 21I was Delta variant AY.2 whilst 21L is the BA.2 sub-lineage of Omicron.

Late today, the UKHSA declared BA.2 as a variant under investigation (link) with 426 cases identified so far in the UK, of which 243 are in London and the South East.
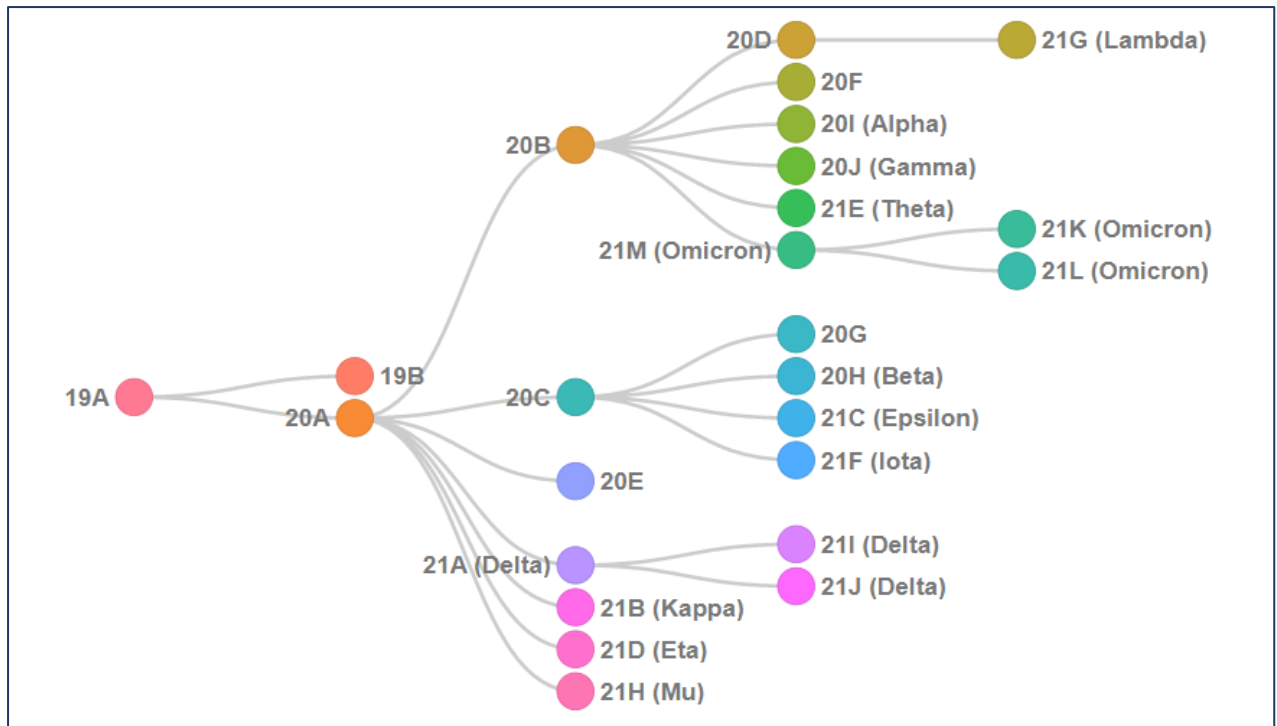
Clinical and medical news

Vaccination, Infection & Fertility (link)

A study by the US National Institutes for Health of over 2,000 couples reports that vaccination had no impact on the fertility rate. By contrast, a prior infection of the male partner within 60 days was observed to reduce the likelihood of a conception by 18%, although there was no longer term effect observed.

The study contains analysis by number of vaccinations for each partner, the type of vaccine given, and demographic factors such as nationality, but similar results were observed for all groups. It therefore concludes that the best way to avoid any short-term reduction in fertility is to be vaccinated, rather than risk a short-term reduction through infection.

Association between Vaccination Status and Long COVID (link)

A study from Israel has investigated whether being vaccinated makes any difference to subsequent Long COVID symptoms following infection. 951 infected people and 2,437 uninfected were studied, and the results show that those who had been vaccinated were between 50% and 70% less likely to report typical Long COVID symptoms than those who were unvaccinated.

It is noticeable from the chart below that for many conditions there was a lower reporting of symptoms by those double vaccinated and infected than for those who were uninfected. This appears counter-intuitive, so it is possible that the degree of benefit of vaccination in reducing ongoing symptoms is overstated. Nevertheless, on the evidence of this study, whilst vaccination may not prevent all infections, if one is infected it is likely to reduce the likelihood of long COVID symptoms by some degree.

Figure 1. Frequency of most reported symptoms among the uninfected, the vaccinated and the unvaccinated
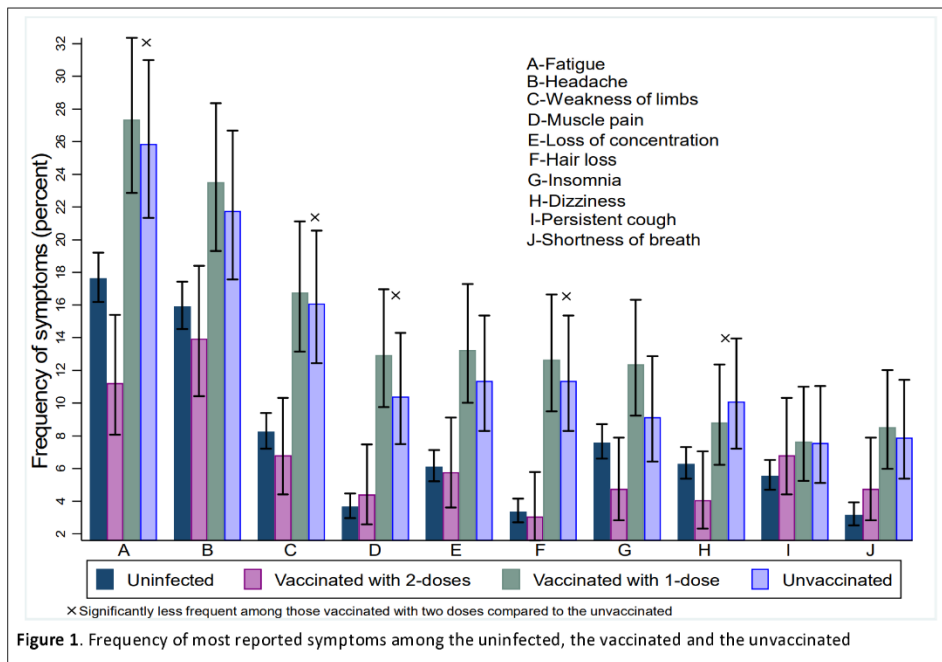
EAVE II

The COVID pandemic has been a potent catalyst to data collaborations and research, particularly in respect of electronic health records. At the end of last year, the EAVE II cohort was established in Scotland bringing together electronic data from 1.2 million patients and 250 general practices, looking at vaccine and anti-viral effectiveness (link). This cohort built on the earlier EAVE cohort focused on pandemic influenza, and will enable COVID progress to be tracked in near real-time. It was the EAVE II cohort that provided early UK evidence that the impact of the Omicron variant could be milder than the Delta variant (link).

A more recent study examining the whole population of Scotland through the EAVE II dataset investigated COVID complications for those with asthma (link). This found that 12.3% of infected adults with asthma had been admitted to hospital, 4.1% had required intensive care and 3.1% had died.

The study further identified that those who had recent prescriptions of oral corticosteroids for asthmas were more likely to have been admitted to hospital during the Delta wave of the pandemic than in the first wave in 2020. In addition, the data provided further evidence that vaccination provided protection against COVID-19 hospitalisation for those with and without asthma, and hence the importance of prioritising boosters for those with asthma.

The benefits of these large population datasets for evaluating and guiding interventions are significant, and this is a great boost for public health in Scotland.

Distribution of anti-virals gathers pace

Back in October 2020, Sajid Javid announced that options on 480,000 courses of molnupiravir and 250,000 courses of paxlovid (link) had been purchased, subject to approval by the MHRA. Anti-virals interfere with the replication of the virus and reduce the severity and duration of symptoms. Oral anti-virals offer the opportunity to treat patients at home, outside of hospitals. Approval was granted by the MHRA for molnupiravir in November, and for paxlovid at the end of December.

As noted in a previous Friday Report, molnupiravir was initially made available to very vulnerable groups, such as cancer patients and transplant recipeints (link). The distribution of molnupiravir is controlled rather than on the basis of self-reporting, with distribution to the patient's home via 70 NHS Covid medicine delivery units (directory attached).

The figure below provides an overview of the layered treatment pathway, involving COVID Medicines Delivery Units, GP practices and NHS 111 Referral (link)
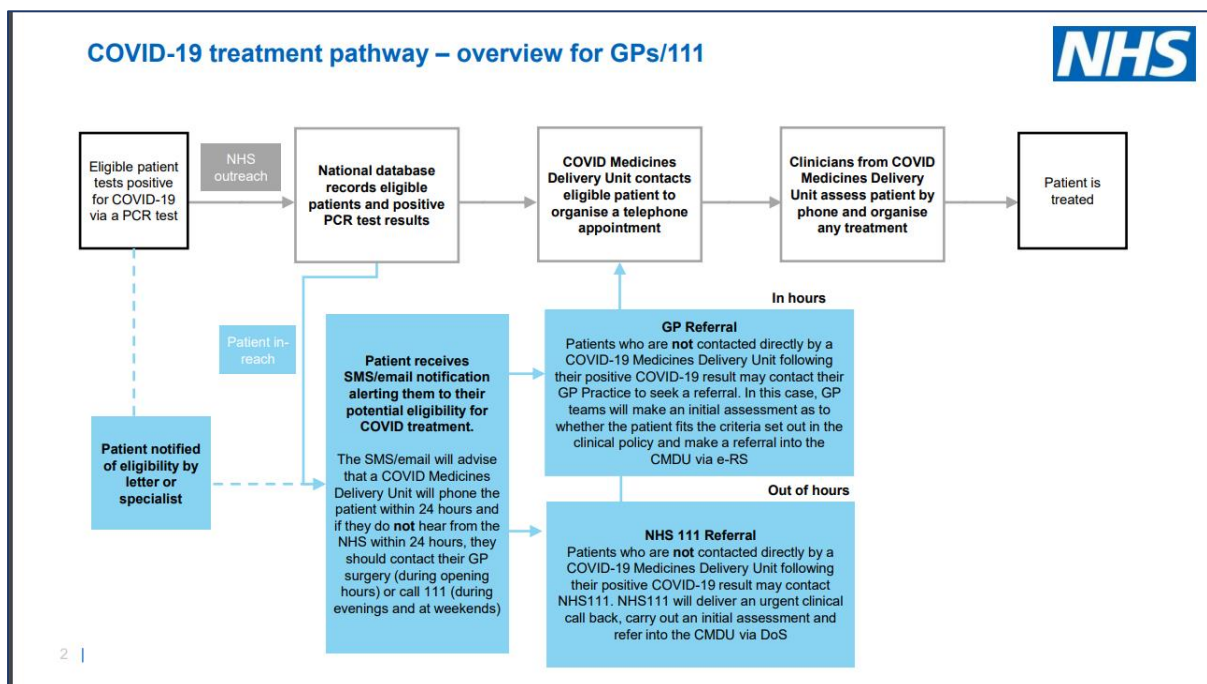
The broader multi-centre PANORAMIC study of molnupiravir is focusing on those who are over age 50 or between ages 18-49 with an underlying health condition. 3,000 of the 10,000 participants have been recruited by Public Health Wales since 8 December, requiring individuals to have a positive COVID test and symptoms for less than 5 days (link).

The UK increased its order to 2.75 million courses of paxlovid (link) in December following clinical trials that indicated that paxlovid reduced the risk of hospitalisation or death following mild to moderate Covid infection from 7% to 0.8% in high-risk groups (a relative risk reduction of 89%). The PANORAMIC study has deliberately used a "platform" design so that further antivirals or antibody treatments, such as paxlovid, can be included if indicated. The significant procurement reflected the expectation of a tsunami of Omicron cases when there was significant uncertainty over the relative severity of Omicron as compared to Delta, but would also enable the possibility for use with household contacts.
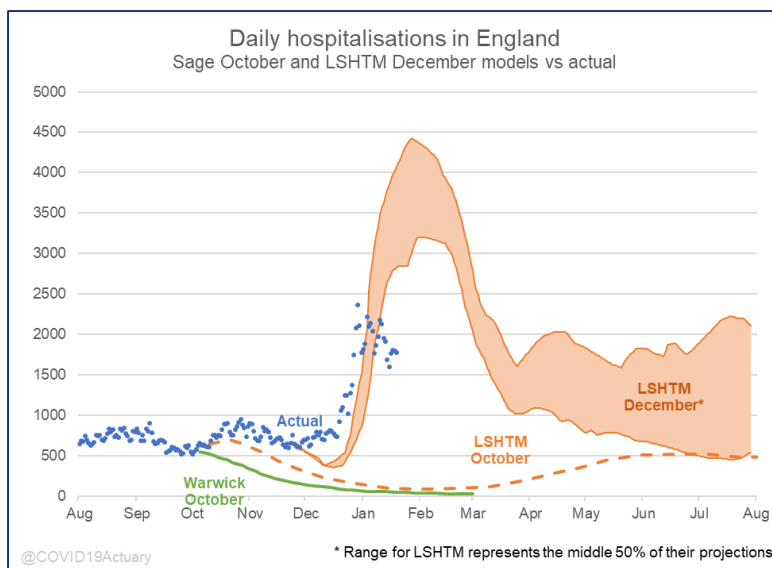
Modelling

We first monitored actual hospitalisations in England against projections in Friday Report 48 (link). This updated our bulletin (link) summarising papers from London School of Hygiene and Tropical Medicine (LSHTM), Warwick University and Imperial College London which modelled the move to step 4.

We noted in Friday Report 54 that the group of universities had published updated papers, setting out projections from October through the winter, and focussing on the impact of boosters and the mixing behaviour of individuals. The papers set out a large range of possible outcomes – the trajectories in the chart below show two example projections from these papers.

Following the discovery of the Omicron variant, on 11 December, LSHTM issued an updated report (link), modelling the potential consequences of the variant on transmission and health outcomes in England. It's worth noting that this is currently a preprint, and has not yet been peer reviewed. On 22 December, an update was published with additional scenarios.

As with previous papers, there are a large number of projections, which vary by the assumed extent of immune escape, various aspects of the booster rollout, and the reintroduction of control measures. In the chart, we have illustrated the numbers of hospitalisations projected, based on their "High immune escape, High booster efficacy" scenario.

In their new papers, LSHTM did not publish a single projection for each scenario, instead they have produced a range based on their simulations. In the chart, we have illustrated the middle 50% of their projections (that is, based on their modelling, there is a 25% chance of an outcome better than the simulation, and 25% worse).

It is clear that, based on the modelling, the Omicron variant has significantly increased the projected number of hospitalisations expected, and that until recently the numbers were broadly in line with projections.

The most recent data suggests that hospital admissions from the Omicron wave have peaked – assuming no further uptick, the peak will be significantly lower than the modelled scenarios.

We will continue to monitor how actual experience lines up with this projection.

Data

Global Excess Mortality

A recent article in Nature describes models that compare global excess deaths to the 5.5 million COVID-19 deaths recorded to date. The IHME estimates between 13 million deaths with a confidence interval of 9 - 19 million deaths.

The Economist magazine estimates a range of 12 - 22 million excess deaths worldwide. Their model used machine learning to identify more than 100 national indicators that seem to correlate with excess deaths in more than 80 countries where data are available. These features include official deaths, the scale of COVID-19 testing and the results of antibody surveys, but also geographical latitude, the degree of Internet censorship and the number of years a country has been a democracy. The Economist's models suggest a greater extent of under-reporting in lower income countries.

The article describes the difficulty of setting an appropriate baseline for the current year's mortality. In particular, using a 5-year average without adjustment will understate the baseline for growing and ageing populations - we describe these issues in our recent blog, noting that the ONS has decided to use the five years 2016-19 and 2021 as a comparator for 2022 experience.

The World Mortality Dataset, which is described in more detail in our guest blog by Ariel Karlinsky, estimates that there are around 6.5 million excess deaths compared with the 4.1 million COVID-19 deaths recorded for the countries represented in their dataset. Their approach fits a trend through deaths counts in recent years which implicitly allows for population ageing and growth.

The Nature article also described the creative methods employed by various researchers to estimate deaths in countries where reliable data is difficult to come by, including telephone surveys asking households about deaths and counting graves using satellite images.

ONS Infection Study (link)

With ONS now providing a welcome flash summary two days early, only four days after the end of the week being studied, the latest data are more encouraging, with substantive falls in three of the four nations. Only Northern Ireland is showing a small increase, although not statistically significant given the small sample size. England has fallen from a peak of 6.9% to 5.5%.
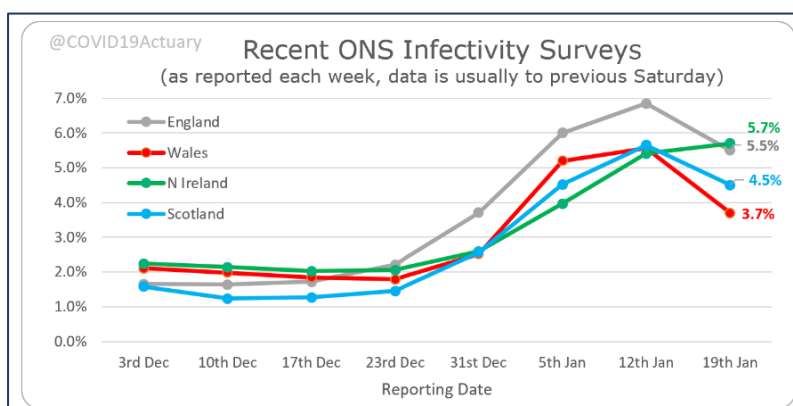

Only the North East showed an increase, with others falling, notably London and the North West. By age, the youngest age group (age 2 to school year 6) bucks the trend, while the 70+ group appears a little later to peak, which is slightly worrying given the greater potential for serious illness.

Note that the ONS study is a randomly sampled exercise, and recent changes in the PCR testing regime for community testing will not affect it.

ONS Antibody Report (link)

We've seen over the last few months how antibody levels have waned and then increased again as the booster roll-out has progressed. The ONS has now enhanced its graphs to show the booster roll-out, and has also introduced a new, higher, threshold of antibody level.

Source: Office for National Statistics – Coronavirus (COVID-19) Infection Survey
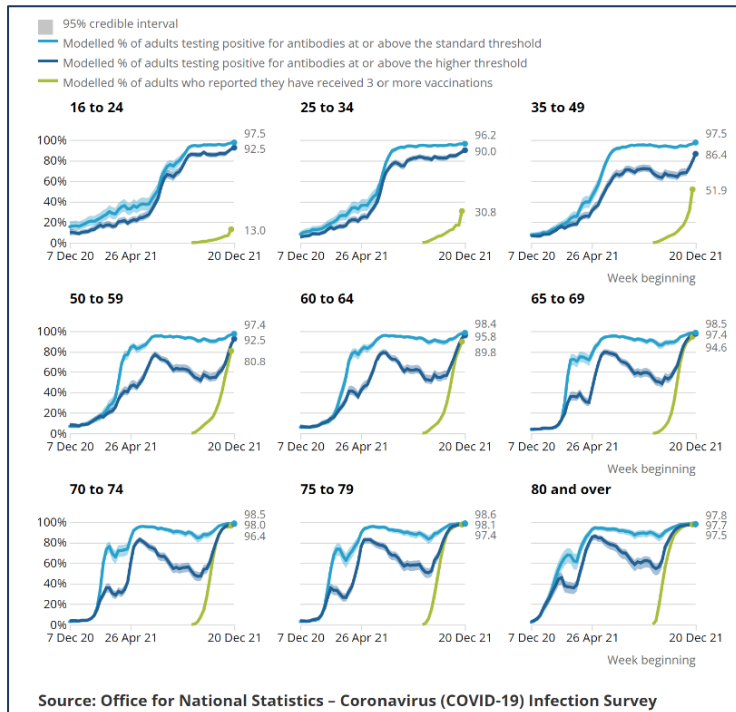
The impact of the waning and subsequent booster effect is much clearer in terms of this new higher threshold, showing the restorative effect it has in terms of higher levels of antibodies.

Overall levels of antibodies is now put at 97% - note that this will include those who have not been vaccinated but have naturally acquired immunity from having been infected at some stage.

**Hospital "Primary Diagnosis" Data**

One of the first things the current Secretary of State for Health & Care did on his appointment was to ask the NHS to provide data in respect of those in hospital with COVID, to identify what proportion of them were in for some other condition but had also tested positive. Accordingly we now have a weekly update of beds occupied in acute hospitals, split between those for whom COVID is the main reason for the treatment (colloquially "for COVID") and those for whom it is not ("with COVID").
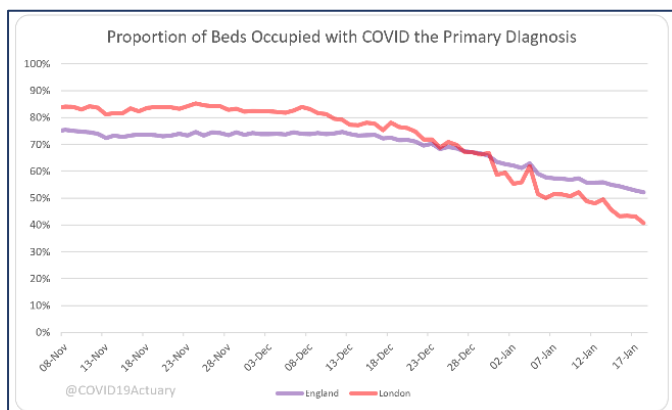
Recently we have seen the proportion where COVID is the primary diagnosis fall, to around 50%, with London falling first. With a rapid rise in community infections, we'd expect unrelated admissions who test positive on admission to increase first; COVID-related admissions will have the usual lag (7 - 10 days).
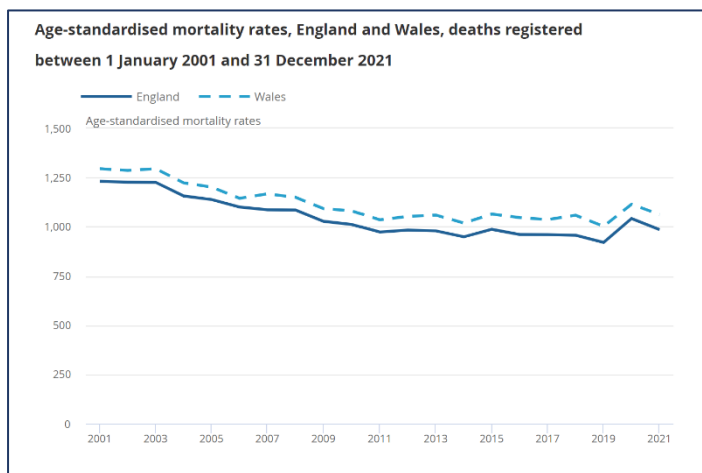
In addition, the notes accompanying the report are clear to caveat the data by explaining that many "incidental" admissions will have COVID as an underlying cause (eg a COVID-induced stroke).

We can see from the graph to the right that there has still been an increase in the number of beds occupied by those with a primary diagnosis of COVID, although it's encouraging to see that there has been a levelling off, and in recent days early signs of a reduction in beds occupied by "for COVID" patients.

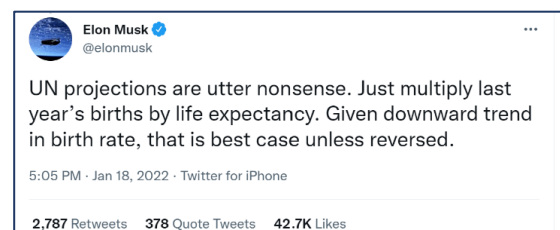England Acute Hospitals: "Primarily COVID" Beds
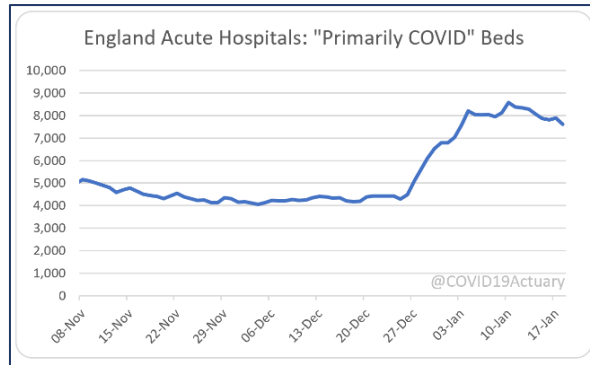
2021 Age-Standardised Mortality

The ONS (link) has today published its provisional figure for age-standardised mortality for 2021, which at 984.7 per 100,000 is 5.4% lower than 2020, but still 7.1% higher than 2019. (This latter figure is very close to the Continuous Mortality Investigation's figure of 6.9%.)

Age-standardised mortality rates, England and Wales, deaths registered between 1 January 2001 and 31 December 2021

In relation to previous years, 2021 is broadly comparable with 2015, (which was seen at the time to be an outlier due to a particularly bad flu season), but prior to that one needs to go back to 2010 before mortality rates climb higher.

And Finally … (link)

Meanwhile, not content with launching space rockets and building electric cars, Elon Musk, followed by a staggering 71m on Twitter, has suggested population projections can be simplified to a multiplication of just two numbers.

Elon Musk
@elonmusk

UN projections are utter nonsense. Just multiply last year's births by life expectancy. Given downward trend in birth rate, that is best case unless reversed.

5:05 PM · Jan 18, 2022 · Twitter for iPhone

2,787 Retweets   378 Quote Tweets   42.7K Likes

We want revolutionary actuaries.
ELON MUSK

We recall that two years ago he expressed an interest in recruiting revolutionary actuaries, and wonder whether this is the result of his new expertise. We are hoping, for his next trick, he can advise insurance actuaries on how to streamline Solvency II calculations down to one simple spreadsheet!

21 January 2022