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Friday Report: Issue 47

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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 regular Friday update with a summary of key papers and articles.

Vaccination

AZD2816 Booster Trials (link)

We reported in Issue 45 early preliminary results (link) that suggest a modified version of the AZ vaccine (AZD2816) may be more effective against the Beta and Delta variants than the existing AZD1222 vaccine currently in use. The intention is to use it as a booster jab, regardless of whether the individual has had the AZ or mRNA vaccines.

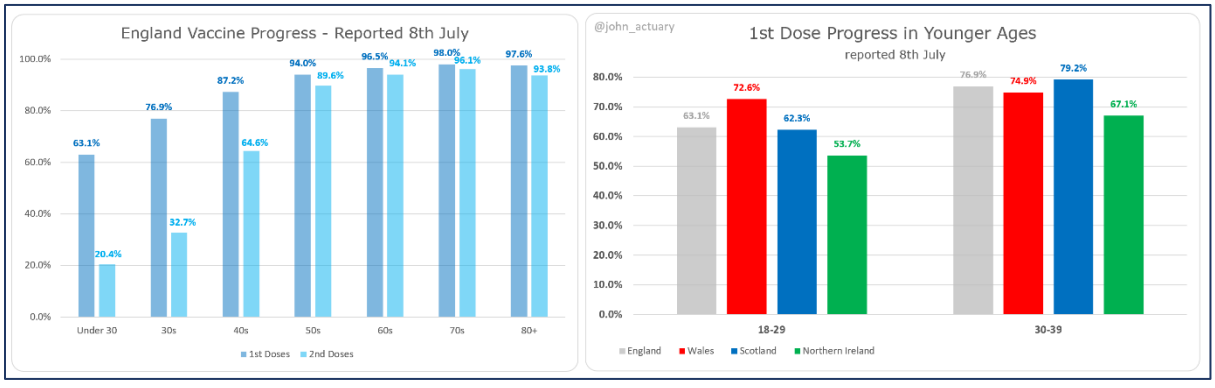
Clinical trials are now beginning, with 2,250 volunteers being recruited in the UK, Brazil, Poland and South Africa. The study period is six months long, so it is unlikely that the jab will be available in time for this autumn's booster programme. Our (Pfizer vaccinated) volunteer in the programme reports that AZD1222 will be used as the control, so no participant will be disadvantaged by possibly missing out on the autumn booster jab.

UK Progress and Take-up Rates

Vaccination rates in the UK have slowed in the last couple of weeks, with the weekly rate now under 2m. There are several reasons, most notably that we are drawing to the end of the first dose programme, with under 1m needed to jab all those coming forward promptly for their vaccination. Second doses are now following the eight week timeline, and looking back two months there were relatively few first doses being administered, so this is limiting the number of second doses currently.

Finally, whilst the government is cagey about vaccine supply, with second doses now down to the age groups which were given mRNA first doses, it's clear that both programmes are competing for the same supply, and this is likely to limit the scope to push either programme any faster.

Looking at the current position, with Wales now "mopping up" any late bookings, it appears to have landed at around 72.5% take up below 30, and 75% in the thirties. With all four countries broadly finished above 30, Northern Ireland appears to be the outlier, and looking at recent progress is likely to repeat that shortfall below 30 too.



Pfizer-BioNTech vaccine efficacy in Israel

The Israeli Ministry of Health (link) monitors vaccine effectiveness by using surveillance data to ascertain cases of laboratory-confirmed SARS-CoV-2 infections and other outcomes, as well as vaccine take-up among Israeli residents aged 16 years and older.

Their latest round of data from 6 June to 3 July 2021, which coincides with the spread of the Delta variant in Israel, showed a marked reduction in effectiveness of the mRNA BNT162b2 vaccine against infections. There was only a small reduction observed for severe outcomes including hospitalisations and deaths, as shown in the table below.

SARS-COV-2 events among fully vaccinated (>7 days post 2nd dose) vs unvaccinated (no doses) residents in Israel aged 16 plus in the period 6 June to 3 July 2021

	% population vaccinated	Infections	Symptomatic infections	Hospitalisations	Severe or critical hospitalisations
Fully vaccinated observations	78% as at 11 May 2021*	1,271 (65%)	514 (62%)	23 (83%)	11 (83%)
Unvaccinated observations	22%	257 (35%)	108 (38%)	14 (17%)	6 (17%)
Vaccine efficacy (6 June to 3 July)		**64.0%**	**64.2%**	**93.0%**	**93.4%**
Vaccine efficacy range in 4-wk rounds wef 31 Jan		94.3% to 96.9%	95.6% to 97.9%	97.1% to 99.0%	98.2% to 99.0%

** Sources: Our World in Data vaccine count as at 11 May 2021, less 900 children included in trials (link). Population denominator age 16+ as per (link).*

Vaccine effectiveness is calculated as *{1 – incidence in vaccinated / incidence in unvaccinated}*, where incidence rates have been adjusted for age, sex and calendar week.

The 64% figure for vaccine effectiveness against infections is lower than the 88% (CI 78 to 93%) result from a study of Delta variant cases for 2 doses of Pfizer in England (link). The 93% figure for effectiveness against hospitalisation is in line with another study also on data in England to determine that 2 doses of Pfizer-BioNTech is 96% (CI 86 to 99%) effective against hospitalisation (link).

Quoting this Israeli study, data Pfizer has issued a statement that a third booster dose of the vaccine could counter waning immunity levels. The company is also developing a new formulation the targets the full spike protein of the Delta variant (link).

Coronavac efficacy in Chile

Chile began vaccinating from age 16 in February 2021 using Coronavac (aka Sinovac), an inactivated virus vaccine. In this study (link), data from the public national healthcare system that covers 80% of the population was used to ascertain effectiveness of the vaccine in preventing infection and other outcomes, allowing for differences in individual and clinical characteristics. 10.2 million participants were included, of which 54% were unvaccinated and 41% were vaccinated with two doses. 2.4% of participants developed laboratory-confimed COVID-19 during the study.

Among persons who were fully vaccinated with 2 doses, the adjusted vaccine effectiveness was:

- 66% (CI 65 to 67%) for the prevention of COVID-19 infection
- 88% (CI 87 to 89%) for the prevention of hospitalisation
- 90% (CI 89 to 91%) for the prevention of ICU admission
- 86% (CI 84 to 88%) for the prevention of death

Vaccine efficacy in Canada (link)

A pre-print study in Ontario, Canada assessed vaccine effectiveness against symptomatic infection, hospitalisation and death in the presence of Variants of Concern (VOCs) for mRNA-1273 (Moderna), BNT162b2 (Pfizer-BioNTech) and ChAdOx1 (AstraZeneca). 421,073 symptomatic individuals were included, of whom 6.8% tested positive for non-VOC SARS-CoV-2 and 9.7% tested positive for a VOC. There were 14,168 COVID-19 hospitalisations or deaths.

Vaccine effectiveness was calculated as *1 – (odds of vaccination among cases / odds of vaccination among controls) x 100%*, after adjusting for co-variates.

The key result of the study for the Delta variant is an efficacy of one Pfizer dose for hospitalisation or death being in line with the 83% single dose efficacy reported in a UK study (link).

Full Delta variants result are shown below, based on 991 cases and 165 hospitalisations or deaths, including unvaccinated individuals. Data volumes are relatively low for Moderna and AstraZeneca resulting either in wide confidence intervals or inability to report results. The lower bound of result for 2 doses of Pfizer-BioNTech efficacy against infection is the same as the equivalent central estimate in the Israeli study noted earlier.

Outcome	Doses	Pfizer-BioNTech	Moderna	AstraZeneca
Positive case count	1 dose	277	56	22
	2 doses	6	Up to 5	0
Hospitalisation count	1 dose	50	Up to 5	Up to 5
	2 doses	Up to 5	Up to 5	0
Symptomatic infection	1 dose	56% (45 to 64)	72% (57 to 82)	67% (44 to 80)
	2 doses	87% (64 to 95)	Insufficient follow-up	Insufficient follow-up
Hospitalisation or death	1 dose	78% (65 to 86)	96% (72 to 99)	88% (60 to 96)
	2 doses	Insufficient data		

United States investigation into myocarditis associated with COVID-19 mRNA vaccination

After reports of myocarditis and pericarditis in mRNA vaccine recipients, which predominantly occurred in young males after the second dose, the Advisory Committee on Immunization Practices (ACIP) has reviewed the cases of myocarditis with regard to the benefit vs risk balance of mRNA COVID-19 vaccination (link).

Myocarditis is an inflammation of the heart muscle. Symptoms typically include chest pain, shortness of breath or palpitations. Pericarditis is an inflammation of the thin tissue surrounding the heart (the pericardium).

Under the Vaccine Adverse Event Reporting System (VAERS), 687 cases of myocarditis in people aged under 30 after mRNA vaccination were reported during the period 29 December 2020 to 11 June 2021. During this time, 30 million first doses and 22 million second doses of mRNA vaccines were administered to that age group.

The ACIP concluded that the benefits of mRNA COVID-19 outweighs the risks, including in adolescents and young adults.

The following results below show the COVID-19 related ICU admissions exceeding the myocarditis cases for all age/gender combinations.

TABLE 2. Individual-level estimated number of COVID-19 cases and COVID-19–associated hospitalizations, intensive care unit admissions, and deaths prevented after use of 2-dose mRNA COVID-19 vaccine for 120 days and number of myocarditis cases expected per million second mRNA vaccine doses administered, by sex and age group* — United States, 2021

	No. per million vaccine doses administered in each age group (yrs)†				
Sex/Benefits and harms from mRNA vaccination	**12–29**	**12–17**	**18–24**	**25–29**	**≥30**
Male					
Benefit					
COVID-19 cases prevented§	11,000	5,700	12,100	15,200	15,300
Hospitalizations prevented	560	215	530	936	4,598
ICU admissions prevented	138	71	127	215	1,242
Deaths prevented	6	2	3	13	700
Harms					
Myocarditis cases expected¶	39–47	56–69	45–56	15–18	3–4
Female					
Benefit					
COVID-19 cases prevented§	12,500	8,500	14,300	14,700	14,900
Hospitalizations prevented	922	183	1,127	1,459	3,484
ICU admissions prevented	73	38	93	87	707
Deaths prevented	6	1	13	4	347
Harm					
Myocarditis cases expected¶	4–5	8–10	4–5	2	1

Abbreviations: ICU = intensive care unit; VAERS = Vaccine Adverse Event Reporting System.
* This analysis evaluated direct benefits and harms, per million second doses of mRNA COVID-19 vaccine given in each age group, over 120 days. The numbers of events per million persons aged 12–29 years are the averages of numbers per million persons aged 12–17 years, 18–24 years, and 25–29 years.
† Receipt of 2 doses of mRNA COVID-19 vaccine, compared with no vaccination.
§ Case numbers have been rounded to the nearest hundred.
¶ Ranges calculated as ±10% of crude VAERS reporting rates. Estimates include cases of myocarditis, pericarditis, and myopericarditis.

Clinical and medical news

Long COVID and 'Freedom Day'

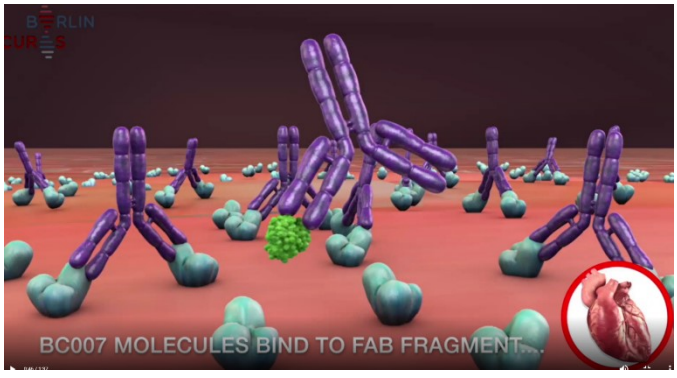
The letter by 100 scientists in the Lancet on Thursday (link) highlighted a variety of health risks associated with the removal of all mandatory restrictions on social distancing and masks.

The main concern expressed is that, despite the weakening of the link between cases and both hospitalisation and deaths, increasing numbers of infections could drive a rapid increase in the numbers likely to suffer from Long COVID. In addition to many studies in this country, such as PHOSP-COVID (link) led by Leicester University, the US Long COVID Alliance (link) supporting sufferers and sponsoring research, has estimated that 25-35% of those infected with COVID-19 will go on to experience continuing symptoms for up to 12 weeks or longer.

By way of reference, modelling presented by Imperial College to SAGE indicated of the order of 20 million new infections under their central scenarios (link) if mandatory restrictions were to be removed on 26 July. This compares with the estimate from the Nowcasting & Forecasting group at University of Cambridge that so far there have been of the order of 13 million infections (link). Given the high proportion of the older population now double vaccinated, the new infections would be more concentrated amongst the younger .

Treatment for auto-antibodies

The evidence for the role of auto-antibodies in Long COVID continues to build. The drug BC007 was originally developed by Berlin Cures in 2016 to treat heart failure. As illustrated in this truly wonderful video (link), the BC007 molecule attacks the Fab segment of auto-antibodies and neutralises the ability of the auto-antibodies to interfere with cell surface receptors.



This experimental drug was recently used at the Erlangen Eye Clinic in Germany to treat glaucoma, on the pre-supposition that auto-antibodies were limiting blood circulation in the eye. The drug BC 007 was originally developed to treat heart failure. As well as rapid improvements in blood flow in the eyes and reductions in the levels of auto-antibodies, classic symptoms of Long COVID such as loss of taste and difficulty with concentration also disappeared. A wider trial is now being initiated.

SARS-CoV-2 and alteration of blood cells

A further study (link) has investigated whether the classic COVID signs/symptoms of shortness of breath, hypoxia and hypercoagulation may result from changes to the structure of red and white blood cells. Abnormal coagulation and thrombotic events are major contributors to COVID-19 mortality.

Researchers at the Max Planck Centre for Physics and Medicine found that the shape and deformability of cells infected with SARS-CoV-2 were different compared with the controls. Erythrocytes (responsible for gas exchange) were found to be smaller and less deformable. This would reduce their oxygen-carrying capability and would reduce gas exchange in capillaries. The white cells were found to be more deformable and this would accentuate immune responses.

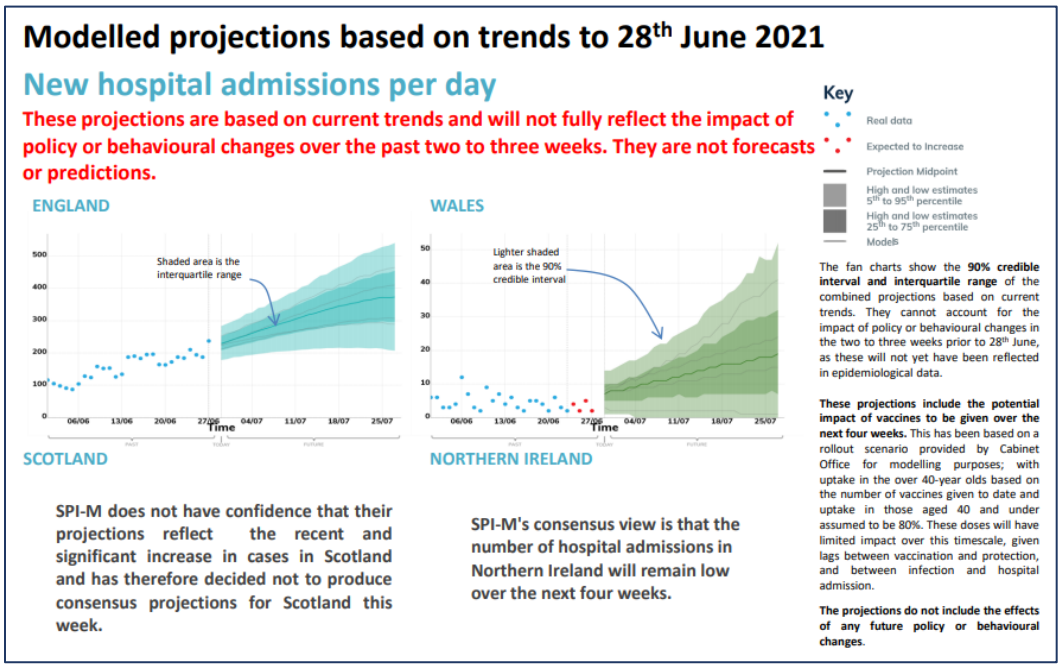
Erythrocytes have a life span of 120 days, principally because they lack a cell nuclei and are unable to synthesize new proteins. Hence any damage or alteration caused by the virus could not be repaired and would lead to functional impacts for at least 120 days. Even longer durations could be explained by the increased demands placed on the spleen in having to filter out these abnormal and damaged cells, and the resulting impairments to normal function that might lead to further damage to newer cells.

The outstanding question that needs to be urgently addressed is whether these changes in the red and white blood cells were caused by the SARS-CoV-2 virus or if there were prior differences that made the individuals more susceptible to the virus.

Modelling

UK medium-term hospitalisation projections

The Scientific Pandemic Influenza Group on Modelling, Operational sub-group (SPI-M-O) presented hospitalisation and death projections to SAGE on 30 June with the documents published 9 July (link). These projections were based on trends in observed data to 28 June and do not allow for the effects of future policy or behavioural changes.



In England, 461 admissions were reported for 7 July and the average number of daily admissions was 379 per day from 1 to 7 July. These figures exceed the 95th percentile of the SPI-M-O projection.

Data

REACT infection study (link)

Round 13 of the Imperial College REACT infection study was published yesterday, and impressively covers the period up to Sunday 5th July, a two day turn-around. Since the last round (a month earlier), infection levels have quadrupled, from 0.15% to 0.59%, and within the study period, R is estimated at 1.87, with a 6 day doubling period.

Two points are particularly noteworthy. The first is that there is a clear disparity between the sexes, with males (0.71%) being 50% more likely to be infected than females (0.47%). Increased social mixing related to Euro 2020, whether at home or in pubs, is likely to be driving much of this relative change, and with England having made it through to Sunday night's final, that effect is likely to continue for some days.

The second point of interest is that there is a clear link between vaccination status and infection levels. Those yet to be vaccinated are over three times (1.16%) more likely to be infected than those with two doses (0.33%). However, there is also a clear pattern of increased infections at younger ages, shown below, and we don't have an analysis that adjusts for this effect. So how much of that increase is due to age related and other factors is not clear.

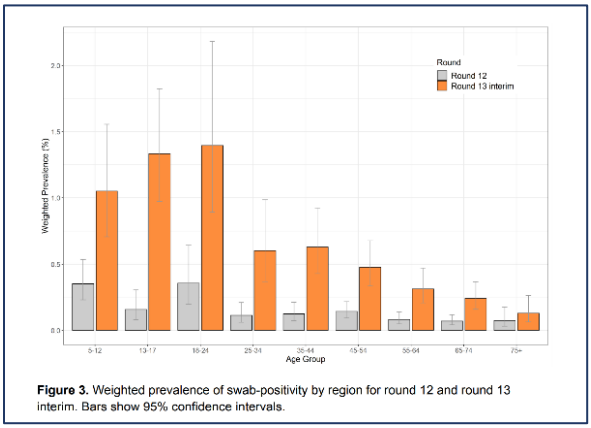


Figure 3. Weighted prevalence of swab-positivity by region for round 12 and round 13 interim. Bars show 95% confidence intervals.

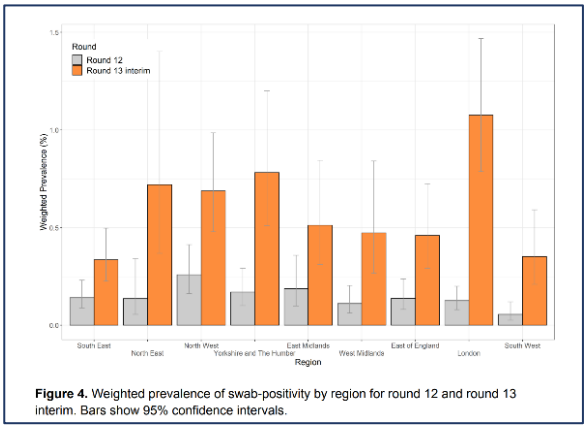
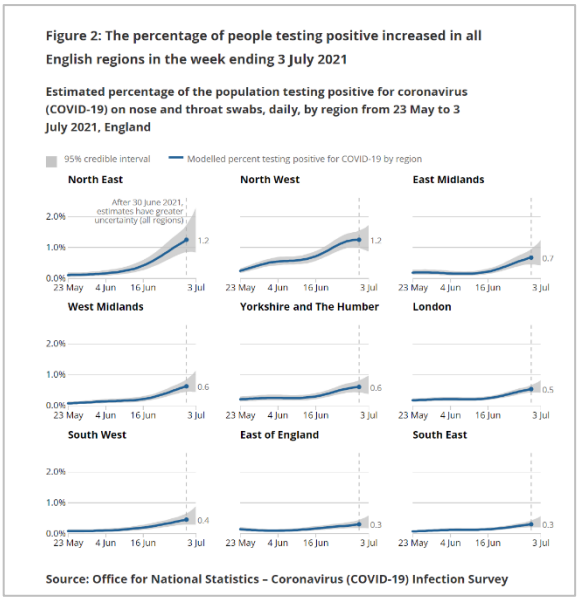


Figure 4. Weighted prevalence of swab-positivity by region for round 12 and round 13 interim. Bars show 95% confidence intervals.

The regional analysis shows that London has had the biggest increase, being an eight-fold increase in the last month, from 0.13% to 1.08%.

Finally, it should be noted that the headline figure of 0.59% is the average over the two-week period, and doesn't reflect the position at the end of the study period. A visual check of the graphs provided suggests that this is much closer to 1.0%.

Also this week we have the usual ONS infection survey (link) which shows typical increases in levels of 50% across the UK. One contrast with REACT is in relation to the regional split, with ONS showing the North East and North West as the highest regions.

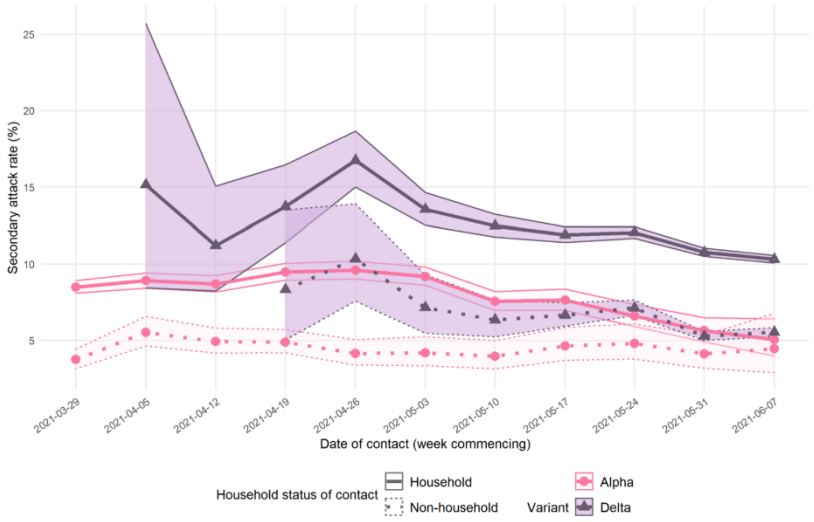


PHE Variant Surveillance (link)

The now regular technical briefing on Delta has moved to fortnightly, but in today's release not much of the data had been updated.

One point to note though is that the Secondary Attack Rate of Delta is gradually falling, and is now not dissimilar to the levels we saw for Alpha a couple of months ago. Whilst this might instinctively be interpreted as "Delta isn't more transmissible after all", the differential with Alpha remains, and both are falling as increased vaccination, particularly amongst younger age groups, is helping to dampen transmission.

Figure 12. Secondary attack rates amongst household and non-household contacts of non-travel cases of Alpha and Delta, with 95% confidence intervals (29 March 2021 to 13 June 2021, variant data as of 5 July 2021, contact tracing data as of 7 July 2021)
(Find accessible data used in this graph in underlying data)



No new data has been released for outcomes as NHS trusts submit emergency care attendances by the 21st of each month, but given the interest in proportions of people hospitalised with the Delta variant by vaccination status, we reiterate the figures provided up to 21 June 2021.

	Total	Unvaccinated	Vaccination status unknown	<21 days post dose 1	>= 21 days post dose 1	Received 2 doses
All cases						
Ages <50	111,008	70,664	12,900	8,453	13,391	5,600
Ages >= 50	12,404	1267	1,252	109	4,542	5,234
Cases that resulted in overnight inpatient admission						
Ages <50	1,283	987	24	106	118	48
Ages >= 50	615	195	4	11	140	265
Implied hospitalisation rate						
Ages <50	1.2%	1.4%	0.2%	1.3%	0.9%	0.9%
Ages >= 50	5.0%	15.4%	0.3%	10.1%	3.1%	5.1%

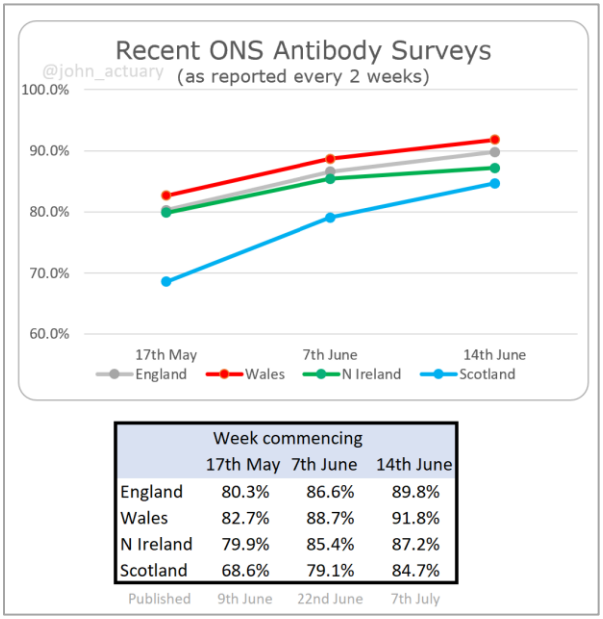
The table shows that, as expected, risk of hospitalisation is higher for people ages 50 and older even when comparing like for like vaccination status.

Encouragingly risk of hospitalisation is lowest for those who received a first dose more than 21 days prior and those who received two doses compared to unvaccinated and recently vaccinated groups.

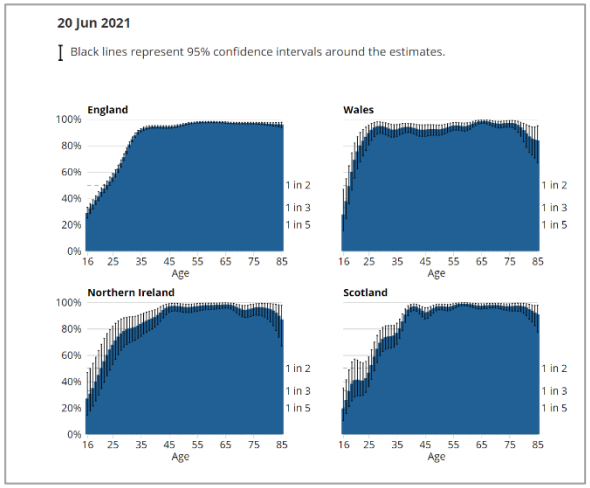
ONS Antibody data (link)

The latest fortnightly analysis by ONS on antibody levels in adults (whether from infection or vaccination) shows a continued increase, with Wales becoming the first nation to top 90%. At first sight the increase looks lower than in the previous report, but that added three weeks to the data, whereas this report only adds one more week.

One slightly odd feature is that the point we noted in the last Report, whereby there were initial signs of a lowering of levels in the oldest lives, isn't replicated in this latest update for England. However, the other three countries do show the effect. It's possible that earlier second vaccinations in the devolved nations accounts for the difference, but until we have more data, that won't become clear.



	Week commencing		
	17th May	7th June	14th June
England	80.3%	86.6%	89.8%
Wales	82.7%	88.7%	91.8%
N Ireland	79.9%	85.4%	87.2%
Scotland	68.6%	79.1%	84.7%
Published	9th June	22nd June	7th July



"R" Estimate (link)

The latest estimate by SAGE is that R is between 1.2 and 1.5 in England, an increase on last week's range of 1.1 to 1.3.

The regional estimates are shown in the table.

Region	R	Growth rate % per day
England	1.2 to 1.5	3 to 7
East of England	1.1 to 1.5	2 to 7
London	1.1 to 1.4	2 to 6
Midlands	1.2 to 1.5	4 to 8
North East and Yorkshire	1.3 to 1.6	5 to 8
North West	1.1 to 1.2	1 to 4
South East	1.3 to 1.6	4 to 9
South West	1.3 to 1.6	5 to 8

And finally …

Probably the least concerning aspect of the pandemic has been its impact on language. The lexicographers at the Oxford English Dictionary latest quarterly update on linguistic trends and etymological breakthroughs covers a lot of ground, and – hopefully a good sign, Delta variant permitting – very little relates to the pandemic, unlike the many new entries of 2020.

We have news on the essential word '*Unmute*': "We've revisited our entries for both *mute* and *unmute*, adding two new senses to *mute* (referring to muting a person and muting social network notifications), and three new senses to *unmute*".

News also on *staycation*, *social distance* ("first recorded in 2004, but familiar to many of us only since 2020") and the history of the phrase *to throw caution to the wind*. If this has been used in commentary about the roadmap, note that in 1868 it was an Irish proverb advising circumspection!

In the lexicographers' own words, "*keep on keeping on*" …

9 July 2021